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Food as medicine

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Food as medicine

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Editorial: Food As Medicine

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Editorial on the Research Topic
Food As Medicine

"Let food be thy medicine"—a mantra famously attributed to Hippocrates—captures the central role of nutrition and dietary patterns in human health. Not only is the food we consume linked to prevention of diseases of dietary deficiency such as scurvy, pellagra, and Kwashiorkor, so too is it related to diseases of caloric abundance, such as type 2 diabetes, obesity, and hypertension. Moreover, patterns of food consumption are increasingly linked to restoration of health and maintenance of disease-free states following diagnoses such as cardiovascular disease, stroke, and cancer. Our ever-expanding knowledge of the human microbiome's role in health and disease continues to implicate patterns of food consumption to microbial diversity and function, and their impact on mood, cognitive status, and metabolic health. Never has the scientific examination of Hippocrates' famous tenet been more timely and needed. Food As Medicine is complementary to the field of lifestyle medicine, which promotes health behavior change across six domains, including nutrition, exercise, sleep, stress, or substance use/exposure to prevent, treat, and potentially reverse lifestyle-related, chronic disease.

In this *Food As Medicine* Research Topic, we holistically examine the role of nutrition and dietary patterns on health and disease states at the individual, community, and population levels. We aimed to synthesize the current state of knowledge in the Food As Medicine arena, and highlight effective nutrition-based interventions while also elucidating gaps in our understanding and identifying scientific strategies to close them. The methods highlighted in this Research Topic are representative across evidentiary pathways and include illustrative cases, systematic reviews, cohort studies, intervention trials and protocols, and expert reviews and commentary.

One core goal for the *Food As Medicine* Research Topic was to showcase high-quality, original research demonstrating improvements in intermediate health metrics or hard endpoints based on nutrition interventions administered to individuals with current illness. The Research Topic has additionally proposed approaches to operationalize and validate effective tools and strategies at a population and health care systems level.

Of the 23 papers ultimately accepted and published, two report on Food As Medicine correlates in individual patients (Goldner and Staffier) or small cohorts (Rowley et al.); six are clinical trials reporting on Food As Medicine interventions for specific chronic diseases such as: overweight and obesity (Kelly et al.; Kirbach et al.; Baden et al.), hypertension (Sijangga et al.), metastatic breast cancer (Lee et al.), and type 2 diabetes (Koh et al.); six are feasibility studies or other programmatic evaluations of lifestyle-based nutrition interventions (Albert et al.; Friedman et al.; Nyong et al.; Folta et al.; Staffier et al.; Karlsen et al.); three are topical reviews (Rosenfeld et al.; Qu et al.; Merlo et al.); one is a methods paper (Klowak and Boggild); three are knowledge and nutrition assessment studies among populations targeted for dietary interventions (Bai et al.; Li et al.; Quach et al.); and two are perspectives (Ayoob; McDougall).

Forty-eight percent of articles featured in the *Food As Medicine* Research Topic reported findings in equity-deserving groups including: Individuals who are deaf and hard of hearing (Friedman et al.); pregnant women (Rowley et al.); members of a US Latina/o/x community (Koh et al.); members of a US African American Faith-based community (Nyong et al.); members of a US Filipino community (Sijangga et al.); children (Li et al.); individuals of low socioeconomic status (Folta et al.; Bai et al.; Klowak and Boggild); and women with highly gendered chronic diseases such as systemic lupus erythematosus (Goldner and Staffier) and metastatic breast cancer (Lee et al.).

The specific organ systems addressed by research featured in the *Food As Medicine* Research Topic include: brain and neuronal health (Merlo et al.; Klowak and Boggild); cardiovascular and cardiometabolic health (Albert et al.; Rowley et al.; Koh et al.); periodontal health (Qu et al.); and gastrointestinal health (Quach et al.).

In Goldner and Staffier, three patients with systemic lupus erythematosus and Sjogren's syndrome followed a dietary protocol comprised predominantly of raw foods and emphasizing leafy greens, cruciferous vegetables, omega-3 polyunsaturated fatty acids, and water, and over the course of 4 weeks noted dramatic improvement in clinical symptoms, with complete symptom resolution out to many years of follow-up. Such anecdotal evidence for dietary control of autoimmune diseases provides a tantalizing foundation on which to base further prospective studies aiming to disentangle the influence of lifestyle on inflammatory processes.

In Rowley et al., 51 pregnant women were stratified according to their personal alignment with a Mediterranean diet, which was correlated to urinary and serum metabolites and inflammatory biomarkers at 36-weeks gestation. Demonstrable reductions in inflammatory biomarkers were notable in the women with high alignment to the Mediterranean diet compared to those with low alignment characterized by greater consumption of red meat and lower intake of fruits and vegetables. Extending such biological findings to health and developmental outcomes in both pregnant women and their infants warrants future investigation.

Among the six clinical trials reporting on Food As Medicine interventions for specific chronic diseases, Kelly et al. report on a 16-week plant-predominant fiber-rich nutrition program that was delivered to over 4,000 employees at 72 different employers across the Southwest United States over a 3-year period. This "Full Plate Living" program translated to an average 3.28 kg weight loss among the >60% of participants who lost weight during the trial, and drastically improved the daily intake of health-promoting fiber-rich foods including fruits (2.45 servings/day), vegetables (2.99 servings/day), beans (1.03 servings/day), and total fiber composites (9.07 servings/day) compared to those participants who did not lose weight. Such findings validate the role of dietary fiber in the lifestyle management of overweight and obesity.

Kirbach et al. report on the implementation and successive iteration via Plan-Do-Study-Act (PDSA) cycles of the Supervised Lifestyle Integrative Medicine (SLIM) program, which is a virtually delivered, lifestyle medicine focused shared medical appointment (SMA) program, situated within a weight management clinic of a larger health system, that served 172 participants over 2 years. The ultimate model combines one-on-one and group interactions over 12-weeks with a dedicated team including an Obesity Medicine and Lifestyle Medicine physician, registered dietician, health coach, and preventive medicine resident.

In their pilot study examining the feasibility of a 3-month lifestyle modification program based on a "Teaching Kitchen" in Japan, Baden et al. report that among 24 participants with obesity, significant post-intervention improvements were noted in weight, body mass index, diastolic blood pressure, body fat mass, and consumption of total fat and dietary sodium. Health related quality of life indices were further improved, notably on measures of bodily pain, general health, vitality, and mental wellness. Given high program completion rates and the aforementioned improvements in biometry, the program was deemed feasible.

In order to address the gap in culturally-relevant lifestyle options for blood pressure management currently available to the Filipino community, Sijangga et al. report on the development of a cookbook using participatory methods and design thinking, utilizing input from five Filipino culinary experts and a Registered Dietitian. Among 20 Filipinx participants with self-reported, physician-diagnosed hypertension included in the pilot test of the cookbook, evidence of its acceptability and feasibility emerged, with participants reporting that the recipes, nutrition labels, illustrations, and cultural aspects of the cookbook increased their motivation to pursue dietary changes aimed at reducing blood pressure, notably reducing dietary sodium intake.

Lee et al. report the findings of an 8-week whole foods plant-based (WFPB) dietary RCT in metastatic breast cancer patients on stable therapy whose intake of isoflavones and both omega-3 and omega-6 polyunsaturated fatty acids (PUFAs) were assessed both pre- and post-intervention. In the WFPB group, total daily intake of isoflavones increased from a mean of 0.8–14.5 mg/day ($p < 0.0001$), and the n-6:n-3 ratio of PUFAs decreased from a mean of 9.3–3.7 ($p < 0.0001$), providing evidence that even short courses of the WFPB diet intervention translates into meaningful changes in serum biomarkers of healthful nutrition. As with the Rowley et al. cohort, extension of the biological findings to both intermediate and long-term health outcomes through future prospective studies is warranted.

Koh et al. report on the lessons learned during the design, implementation, and evaluation of a remotely-accessible, community-based, nurse-led, culturally-tailored WFPB culinary intervention to reduce type 2 diabetes risk among Latina/o/x adults. Through their mixed-methods quasi-experimental study involving both pre- and post-evaluation and comprised of questionnaires, culinary instruction, biometry, and focus groups, the authors identify for prioritization: improved accessibility and engagement in minoritized and/or underserved communities; quality assurance and service delivery along the supply chain; sustainable study design; and interventions that are remotely accessible.

In the six studies of program feasibility or other programmatic evaluations of lifestyle-based nutrition interventions, findings were equally compelling. Albert et al. report on intermediate health outcomes—including hemoglobin A1c (HbA1c), blood pressure, body weight, and serum cholesterol—of 173 participants in a Plant-Based Lifestyle Medicine Program piloted in a New York City safety-net hospital. Over the 1-year program, the participant cohort achieved statistically significant improvements in body weight, HbA1c, and diastolic blood pressure. Among those with prediabetes, overweight or obesity, significant improvements in weight were achieved, while those with type 2 diabetes experienced significant improvements in both weight and HbA1c. Similarly, participants with hypertension achieved significant reductions in diastolic blood pressure and weight. Extending these findings to long-term health outcomes such as microvascular complications of diabetes, myocardial infarction, and cancer in larger prospective cohorts will provide even further compelling evidence of Food As Medicine for obesity and type 2 diabetes.

Understanding that persons who are deaf and hard of hearing (DHH) are at risk of developing chronic preventable diseases and have worse health outcomes when they do, Friedman et al. report on the Rochester Lifestyle Medicine Institute's adapted, online, Zoom-based, medically-facilitated "15-Day Whole-Food Plant-Based (WFPB) Jumpstart" program designed to provide this at-risk cohort the knowledge, skills, and support to undertake health-related dietary improvements. All participants lost weight, had decreases in pulse and systolic blood pressure, and reduced their total and LDL cholesterol. Participants further reported increased energy, quality sleep, and mood, and noted commensurate improvements in their knowledge and skills owing to the program.

Understanding that the African American population is disproportionately affected by many of the leading causes of preventable death, including hypertension, obesity, heart disease, stroke, and type 2 diabetes, Nyong et al. also report on the Rochester Lifestyle Medicine Institute's "15-Day Whole-Food Plant-Based (WFPB) Jumpstart" program delivered to participants recruited via a network of predominantly African American churches throughout the State of Illinois. Pre- and post-program metabolic screening of weight, vital signs, blood sugar, and cholesterol were undertaken and demonstrated: an average weight loss among 21 participants of 5.8 pounds; an average 10-point systolic blood pressure reduction; and an average 37-point total cholesterol decrease. Participants reportedly ate more vegetables, greens, fruit, whole grains, and legumes during the program and also reduced their consumption of meat, eggs and dairy, added fat, processed foods, and high-fat plant foods, thus correlating positive dietary changes to dramatic improvements in health-related biometrics.

In their qualitative case comparison study, Folta et al. report on the adoption and implementation factors related to a produce prescription program designed to close disparities in diet quality and diet-related chronic disease for persons of lower socioeconomic status. Factors such as incorporation into clinic workflow and fit with operations were raised by implementing staff as key facilitators to adoption, while the need for extra time and sustainability were cited as threats to long-term implementation.

In their online, cross-sectional survey of >6,000 individuals who downloaded the American College of Lifestyle Medicine's complimentary "Culinary Medicine Curriculum" (CMC), Staffier et al. report that while 70% of enrolled participants neither led nor created any specific sessions related to the CMC, the 30% who did, did so across clinical settings including academia, clinical establishments, and coaching practices, and represented a range of disciplines within the lifestyle medicine arena including physicians, registered dietitian nutritionists, and chefs. Future studies investigating the impact of a CMC on intermediate and long-term health outcomes for patients and clients will be a valuable extension of this work.

In their description of the development and pilot testing of a brief, dietary screener to assess the proportion of whole, unrefined plant-based foods and water relative to total food and beverage consumption, Karlsen et al. report that among 539 lifestyle medicine practitioners surveyed, >60% assess diet quality informally, and 80% report facing barriers to dietary screening in the clinical setting. As such, the newly developed screener, which consists of a 27-item diet assessment tool, can serve as a successful addition to the lifestyle medicine practitioners' clinical armamentarium.

In the first of three knowledge and nutrition assessment studies among populations targeted for dietary interventions, Quach et al. conducted a cross-sectional survey among >4,000 Vietnamese adults, over half of whom reported ongoing gastroesophageal reflux symptoms (GERS) that were troublesome. Factors associated with troublesome GERS included: eating beyond fullness, stress, insomnia, and consumption of particular trigger foods such as greasy foods, sour and/or spicy soups, citrus fruits, and carbonated soft drinks. This novel study of dietary and lifestyle factors associated with troublesome GERS in Vietnamese adults has laid the groundwork for future studies of prevention and effective lifestyle interventions.

In their exploratory analysis of nutritional knowledge, health literacy and dietary behaviors in 400 rural Chinese residents, Bai et al. report that the mean total nutritional knowledge score was 7.19 out of a maximum score of 13, indicating that declarative nutrition knowledge in this population is suboptimal. Moreover, dietary behaviors, particularly consumption of fruits, beans, and vegetables were equally poor, with male, elderly, low-income, unmarried, and persons with low-education at greatest risk of inadequate nutrition knowledge and behaviors. Such data are important to inform the design and implementation of strategies to address these disparities in health knowledge, attitude, and behaviors.

Li et al. conducted individual and small group interviews with 23 adult female caregivers of young, pre-school aged children who participated in a Texas-based produce prescription program during the COVID-19 pandemic, and noted that >80% of caregivers were Hispanic/Latino and >40% of participating families had three or more children. Thematic analysis enabled feedback to emerge around program logistics including ease of use, participant satisfaction, and desire for additional store bought options; as well as program impact including the improved ability to purchase produce, the utility of nutrition education provided, and continued challenges with preparation of produce for "picky eaters" and very young children. Understanding the facilitators and barriers to adequate produce consumption in young children, particularly those who have intersecting vulnerabilities such as neurodivergence, is critical to developing policy and programs in pediatric health.

In their description of a prospective, randomized controlled single-blind, multicenter interventional trial for a WFPB dietary intervention for the chronic neuropathic pain of leprosy, Klowak and Boggild identify that diets rich in plant-based macro- and micronutrients are likely to improve physiological and metabolic neuronal health, reduce systemic inflammation, and enhance immune responsiveness to environmental neurotoxic factors. Given that type 2 diabetes is an exceptionally common comorbidity of leprosy, the authors hypothesize that WFPB diets will mitigate progression and severity of peripheral neuropathic pain and potentially reduce the adverse events related to standard corticosteroid treatment of leprosy reactions due to their inherently anti-inflammatory nature.

Among the three topical reviews, in their scoping review of 95 articles (54% longitudinal, 37% cross-sectional, and 9% case–control) with a median sample size of >3,500 participants investigating how the quality of plant-based dietary patterns might be associated with health outcomes, Rosenfeld et al. report that higher healthful plant-based dietary index levels were associated with favorable health outcomes in over a third of comparisons, notably for obesity, mortality, diabetes, cardiovascular disease, and psychiatric disorders. On the other hand, higher levels of unhealthful plant-based dietary indices were associated with unfavorable health outcomes in a third of comparisons. The scoping review underscores how a focus on the quality of healthful diets is important to incorporate into nutrition guidance.

In their exploration of "Medicine food homology" (MFH), which acknowledges that traditional natural products have both nutritional and medicinal benefits, Qu et al. summarize the existing state of knowledge around the MFH plants that can prevent and treat periodontitis. Mechanistically, numerous MFH plant metabolites and extracts have demonstrable antibacterial action against periodontal infections. Moreover, MFH plants have been found to inhibit host inflammatory responses and bone resorption in periodontal infections. Given the severe quality of life implications of periodontal infections, MFH as a discipline has important applications in the lifestyle medicine arena.

In their review of the brain-gut-microbiota (BGM) system, Merlo et al. highlight its significant influence on cognitive processing, mood regulation and dysregulation, neuroplasticity, and other metrics of mental and neuronal health. Given that poor nutrition is linked to increased risks to brain health, mental health, and psychological functioning, the BGM system represents an important target for both preventive and therapeutic lifestyle-based interventions.

In the two perspective pieces published, Ayoob provides key insights into the concept of carbohydrate interchangeability and whether or not starchy vegetables can be considered interchangeable with grains. Given the loss of key micronutrients with interchangeability as ascertained through menu modeling analyses, the author provides an argument to categorize starchy vegetables and grains separately. Finally, McDougall argues that the dietary patterns that best support human health and that of planet Earth are underpinned by traditional starchy staples including but not limited to: rice in Asia, corn in Central and South America, potatoes in the Andes, and wheat and barley throughout the Middle East. The author further supports his argument that optimal human health requires a shift away from destructive animal-food based-diets to those centered around plant-based foods.

In conclusion, the *Food As Medicine* Research Topic provides new insights and novel data accrued through primary research into how dietary patterns, practices, and adjacent technologies can serve to improve metabolic markers of disease and biometric outcomes across different communities, life stages, and states of health and disease. Extending the data presented herein to studies of long-term health outcomes will fill existing knowledge gaps of how dietary and nutrition interventions may best be used in clinical and therapeutic environments, and as preventive public health programming.

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AB: Writing – review & editing, Writing – original draft, Data curation, Conceptualization.

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Whole-food plant-based Jumpstart for a Deaf and Hard of Hearing cohort

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Deaf and Hard of Hearing (DHH) patients are at high risk of developing chronic illness, and when they do, are at higher risk of poor outcomes than in a hearing community. Rochester Lifestyle Medicine Institute adapted its online, Zoom-based, medically-facilitated 15 Day Whole-Food Plant-Based (WFPB) Jumpstart program, to give DHH participants knowledge, skills, and support to make dietary changes to improve their health. Adaptations included having a medical provider present who is fluent in American Sign Language (ASL), is board-certified in Lifestyle Medicine, and has a Master of Science in Deaf Education; spotlighting participants when asking a question during the Q&A session; using ASL interpreters; utilizing closed captioning/automatic transcription during all Zoom meetings; and employing a Success Specialist to provide outreach *via* text and email throughout the program. Participants had significant positive changes in their eating pattern. They reported improvements in biometric measures as well as in how they were feeling. They all reported that they planned to continue to eat a more WFPB diet than they did prior to Jumpstart. All either agreed or strongly agreed that they learned important information, were confident that they knew the best eating pattern for health, and gained the skills they needed to make changes. Although this was a small pilot program, it suggests that this model can be used to provide education and support for behavior change that will lead to improved health in a DHH community.

KEYWORDS
nutrition, prevention, chronic disease, diet, lifestyle, American Sign Language

Introduction

Deaf and Hard of Hearing (DHH) patients are at high risk of developing chronic medical conditions through several causal pathways. First, hearing loss can lead to more difficulty with communication and reduced social engagement, resulting in higher risk of loneliness, depression, and dementia (1).

Second, Deaf individuals are almost 7 times more likely than hearing individuals to have inadequate health literacy, which can lead to missed opportunities for health promotion and disease prevention. Factors that contribute to lower health literacy include lack of education, as well as communication issues. The mean reading level has been reported to be grade 5.9; thus, DHH patients often have lower health terminology recognition (2). Variability in communication styles contributes to mixed comprehension: some DHH adults can read English and understand subtitles, others rely on Signed English interpretation by a qualified/licensed interpreter, and yet others rely on American Sign Language, which has its own unique grammar and syntax. Interpreters are costly and finding licensed interpreters is difficult – especially those with skills in the vocabulary and concepts of the medical field.

All of these issues lead to a high prevalence of chronic illness. DHH individuals are at increased risk of having hypertension, hyperlipidemia, pre-diabetes and diabetes, cardiovascular disease, and depression (1, 3).

Additionally, DHH patients experience many barriers to care, and are therefore at high risk for poor medical outcomes once chronic disease is established. Adults who have been deaf since birth or early childhood are less likely to have seen a physician than the general population (4). Cost can be an issue since Deaf individuals are often underemployed and, when employed, earn comparatively less than hearing people, so may struggle to afford traditional and supplementary healthcare programs (5). Suboptimal communication with their providers means that DHH patients are often unaware of their chronic conditions (3) and have poorer physical and mental health compared to hearing populations (6). This, in turn, leads to higher risk of mortality.

According to the American College of Lifestyle Medicine, Lifestyle Medicine (LM) is "a medical specialty that uses therapeutic lifestyle interventions as a primary modality to treat chronic conditions." LM clinicians "apply evidence-based, whole-person, prescriptive lifestyle change to treat and… often reverse such conditions" (7). LM focuses on six pillars: eating a whole-food, plant-predominant diet, regular physical activity, restorative sleep, stress management, avoiding risky substances, and fostering positive social connections (7). An estimated three-fourths of chronic illness in the US could be avoided if we used these pillars to help patients take charge of their health (8).

Poor diet has been identified as the leading risk factor for mortality and for disability-adjusted life-years since 2010, superseding tobacco use, which had been the leading risk factor prior to that time (9). A whole-food, plant-based (WFPB) diet has been shown to be effective in reducing the impact of many of our most common chronic conditions and diseases, such as hypertension, hyperlipidemia, diabetes mellitus, heart disease, and overweight and obesity (10–13).

Rochester Lifestyle Medicine Institute (RLMI) has developed a 15-day medically-facilitated Jumpstart program that gives participants the knowledge, skills and support to establish a WFPB lifestyle. Previously published results demonstrate that participants experience benefits in a short period of time. Program participants increase their consumption of WFPB components (fruit, vegetables, whole grains, and legumes), and decrease animal products and processed food. As a result, they experience weight loss, and improvements in blood pressure, cholesterol and blood sugar. They also report better energy, sleep, and mood, and less pain (14, 15).

Recognizing the baseline increased risk of chronic disease among DHH individuals, the barriers that they face in healthcare, and the predisposition to poor outcomes, RLMI launched a pilot project to see whether the Jumpstart program could be adapted to a DHH population, whether participants could be recruited, and whether they experienced positive outcomes from the program. The cost of participation in the program was covered through grant funding. This was the first time that this program was adapted for a DHH population, and the first WFPB educational program that we are aware of that has been provided exclusively for a DHH population.

Context

The Jumpstart program is an online, Zoom-based, medically-facilitated group program. Enrollees in the program take part in 11 h of live, interactive programming over 7 sessions. They receive menus and shopping lists, and participate in a Google Classroom that has additional teaching and support materials. Participants are counseled to eat a low-fat, whole-food plant-based diet, consisting of minimally processed vegetables, fruits, whole grains and legumes. Participants who ask about a minimum number of servings of each component are referred to the advice of Dr. Michael Greger, a nationally recognized expert in WFPB nutrition. Dr. Greger recomends at least 3 daily servings of legumes, 4 servings of whole grains, 5 servings of vegetables, and 4 servings of fruits (16).

Participants are asked to obtain and report baseline fasting cholesterol and glucose tests, as well as biometrics, including weight, blood pressure, and waist circumference. They have frequent opportunities to ask questions of a medical provider throughout the program. They participate in a cooking demonstration on the second day of the program and a "virtual potluck," in which they send in and then discuss recipes, on the eighth day of the program. Daily emails provide additional support throughout the program. Participants are asked to get follow-up labs and biometrics at the end of the program, and voluntarily share these with RLMI as part of the quality improvement (QI) program.

A convenience sample of 24 adults was recruited from nine states (USA) and Canada. Potential participants were identified through multiple contacts, including DHH networks, a Deaf nutritionist, online communities, word of mouth, non-profit organizations, social media posts, and emails and calls to colleges with large DHH communities. An email template with a coupon code was created, along with a script for phone calls. Calls were made, and targeted emails were sent to administrators of 4 US colleges and 1 high school known for their services for the hearing impaired: Gallaudet University, Washington, DC; Southwest College for the Deaf, Big Spring, Texas; California State University at Northridge, Deaf Studies Department; the National institute for the Deaf at Rochester Institute of Technology, Rochester, NY; and Lexington School for the Deaf, New York, NY. Non-profit organizations with programs for hearing impaired were targeted as well. An event flyer with links to RLMI's website page, "About Jumpstart," and an events calendar featuring the DHH cohort were included in correspondence. The Deaf nutritionist and the medical provider for the program both promoted the program widely on their social media channels, mainly Facebook; a preponderance of participants enrolled as a result of this notification. RLMI staff received inquiries from interested parties by email, text, and telephone. They responded to all inquiries with emailed instructions for registration and, when necessary, manually registered participants who needed help.

Detail

Several adaptations were made to the Jumpstart program in order to facilitate participation from a DHH population (Table 1). A grant enabled the program to be provided free of charge. An information package that included a thorough introduction to WFPB eating, including menus, shopping lists, and helpful hints on food preparation

TABLE 1 Adaptations to Jumpstart program for a DHH cohort.

Adaptation	Rationale
Program was provided free of charge through grant funding	Many DHH individuals have limited financial resources which limits access
Support materials (Jumpstart guide) sent 5 days before start of program	Provide time to read and absorb teaching materials
Use of American Sign Language interpreters and closed captioning / automatic transcription during all Zoom meetings	Multiple ways to improve communication, so that participants could use preferred method
RLMI Success Specialist outreach by text and email to participants throughout	Provide in-person support; improve feeling of connection to program
DHH participant asking question for Q + A session was spotlighted on Zoom	Improved visibility
Lifestyle Medicine board-certified physician with a Master of Science in Deaf Education provided personalized counseling	Knowledge of barriers; improved communication; improved connection between provider and participant

TABLE 2 Changes in dietary components* during the Jumpstart program (n =11).

	Beginning of program (mean (SD))	End of program (mean (SD))	p value
Measure (servings)			
Vegetables	4.66 (5.78)	7.27 (6.14)	0.003
Leafy greens	1.96 (2.73)	3.98 (2.41)	<0.001
Fruit	2.80 (2.99)	4.64 (2.95)	<0.001
Whole grains	3.05 (3.42)	3.38 (2.43)	0.65
Legumes	1.10 (1.49)	2.35 (1.43)	<0.001
High-fat plant foods	3.13 (2.77)	0.82 (2.09)	<0.001
Meat	1.09 (0.94)	0 (0)	0.003
Eggs	1.64 (1.86)	0.27 (0.47)	0.01
Added fat	2.00 (1.77)	0.09 (0.30)	0.003
Processed food	2.18 (1.33)	0 (0)	<0.001
Rating of adherence**	4.36 (3.01)	8.91 (1.38)	0.001

*Participants are counseled to eat a very low-fat, whole-food plant-based diet, consuming more vegetables, leafy greens, fruit, whole grains, and legumes, and no high-fat plant foods, meat, eggs, added fat and processed food.
**Rated adherence to a very low-fat whole-food plant-based diet on a scale from 1-10.

and eating out, was provided 5 days before the start of the program. This gave participants plenty of time to review the information and ask questions early in the program.

The medical provider for the program (KS) is board-certified in Lifestyle Medicine, has a Master of Science in Deaf Education, is fluent in American Sign Language (ASL), and understands the culture of the Deaf community. She is hearing, with Deaf and Hard of Hearing family members. Before becoming a practicing physician, she taught Deaf and Hard of Hearing students in multiple different schools in the United States and other countries. She has been a professional interpreter in many settings in the United States and internationally.

Participants in the program were asked to raise their electronic hands so that they could be spotlighted when asking a question during the Q&A session, providing better visibility for the other participants. Multiple ways of communicating were employed, including use of ASL and closed captioning/automatic transcription during all Zoom meetings. For any session lasting more than 1 h, 2 interpreters participated, to allow them time to rest, as it is physically taxing to interpret for more than an hour at a time. On days of small group "breakout" sessions, several interpreters participated so that one interpreter was available for each breakout room. All ASL interpreters were Board Certified Interpreters who had passed the National Interpreter Certification (NIC) test that is given jointly by the National Association of the Deaf (NAD) and the Registry of Interpreters for the Deaf (RID). Finally, a Success Specialist provided outreach *via* text and email throughout the program, for additional support.

Permission was given from the University of Rochester Institutional Review Board to use the data collected from RLMI as part of the QI program. The study was considered exempt.

Forty-two people registered for the program, and 24 attended. Of those, 18 provided one or more responses to questions. Changes reported from the beginning to the end of the Jumpstart were compared *via* 2-tailed paired t-tests.

The 11 participants who provided pre-post data to the QI program reported significant changes in their dietary pattern (Table 2). They ate more vegetables, leafy greens, fruit, and legumes, and less meat, eggs, added fat, processed food, and high-fat plant food. In rating how adherent their eating patterns were to a very low-fat WFPB diet, participants reported an increase from baseline to the end of the program of 4.55 points, from 4.36 to 8.91 on a scale from 1 (not very low fat WFPB at all) to 10 (every meal very low fat WFPB).

Participants who provided pre-post data also had changes in clinical and self-reported measures (Table 3). They lost weight, and had a decrease in pulse rate and systolic blood pressure, as well as in total and LDL cholesterol. They reported improvements in energy, sleep, and mood. Of the 11 participants who provided a response, all

TABLE 3 Jumpstart outcomes.

	n	Beginning of program (mean (SD))	End of program (mean (SD))	*p* value
Biometric measures				
Weight (pounds)	10	172.0 (43.5)	166.8 (41.9)	0.004
Waist circumference (inches)	8	39.1 (6.3)	37.1 (4.5)	0.13
Heart rate (beats per minute)	10	76.3 (14.8)	69.3 (9.9)	0.02
Systolic blood pressure (mm Hg)	7	129.9 (13.5)	117.4 (11.3)	0.01
Diastolic blood pressure (mm Hg)	7	76.7 (7.7)	76.6 (6.7)	0.95
Cholesterol (mg/dL)	6	204.2 (39.0)	167.2 (21.3)	0.03
LDL cholesterol (mg/dL)	6	122.8 (25.5)	100.8 (22.1)	0.03
HDL cholesterol (mg/dL)	6	67.5 (43.2)	54.7 (31.4)	0.10
Triglycerides (mg/dL)	6	139.5 (72.1)	110.5 (20.5)	0.36
Glucose (mg/dL)	4	86.8 (3.3)	88.5 (2.1)	0.24
*Self-reported measures**				
Energy	11	5.55 (2.70)	8.27 (1.56)	0.004
Sleep	11	6 (3.03)	7.91 (1.81)	0.048
Mood	11	5.91 (2.55)	8.18 (1.40)	0.004
Pain	11	3.36 (2.50)	3.27 (2.53)	0.90

*Rated on a scale from 1–10. Energy, sleep, and mood are rated from 1 (very poor) to 10 (excellent). Pain ranges from 1 (no pain) to 10 (constant severe pain).

TABLE 4 Participants' perceptions of program benefit (*n* =11).

	Strongly agree (%)	Agree (%)
"I am confident that I know about the type of eating pattern that is best for my health."	54.5	45.5
"I learned important information about the role of nutrition in health."	90.9	9.1
"I gained the skills I need to make changes to my health."	81.8	18.2

of them reported that they planned to continue to eat a more WFPB diet than they did prior to Jumpstart. All either agreed or strongly agreed that they learned important information, were confident that they knew the best eating pattern for health, and gained the skills they needed to make changes (Table 4).

Discussion

This pilot program demonstrates that an online medically-facilitated program designed to give participants the knowledge, skills and support to develop a WFPB lifestyle, can be adapted for a DHH cohort. Despite multiple potential barriers in this population, participants were identified and recruited from several networks across North America. Participants made changes to their eating pattern and expressed an intent to continue to eat a more healthy diet following the program. They noted positive changes – both in how they were feeling, and in biometric measures. Finally, they reported that they got information and gained skills needed to improve their health.

Although we are not aware of other programs that have provided education to a DHH community to help them adopt a WFPB lifestyle, many interventions have been developed to try to reduce barriers and improve access to health education in the Deaf community. A recent systematic review demonstrated that several innovations led to improved outcomes, and could serve to reduce health inequities. These included the use of online interventions, and using Sign Language during telehealth visits. However, it was noted that stronger evidence was needed to assess these interventions (6).

The adaptations to the program included multiple accommodations to improve communication, connection, and comprehension. Communication was enhanced in multiple ways: by using ASL interpreters and closed captioning/automatic transcription during all Zoom meetings, spotlighting participants during Q&A for better visibility, and having a Lifestyle Medicine physician who had a Master of Science in Deaf Education for personalized counseling. Connection was enhanced through a Success Specialist who communicated *via* email and text. Finally, comprehension was improved through giving 5 days of lead time to review written materials; multimodal communication as described above; and email responses to individual questions.

An in-person variation of this program could help to promote engagement and social support. Prior to the pandemic, the Jumpstart was run exclusively as an in-person program. Since the pandemic, all programs are run online, which enables reaching a larger and more geographically diverse group. An adaptation of the program is being developed using a shared medical visit approach, so it is feasible that practitioners with a large DHH cohort of patients could run the program in person.

Feedback was obtained through standard questionnaires on Day 15 of the program. These questionnaires are sent to all participants in the Jumpstart program, and questions were not specific to this cohort. When asked what the program could do to help participants stay on the path of a WFPB diet, responses from this cohort included sending out recipes, occasional check-in reminders, and availability of ongoing support, including a maintenance program and opportunities to communicate with program staff. When asked about barriers, none of the respondents mentioned communication issues. More qualitative feedback from DHH participants would be helpful to improve future iterations of a DHH WFPB program.

Limitations

Despite the adjustments to make the program accessible, the team still encountered some issues in running the program. Some participants preferred the interpreters to use American Sign Language, and felt the interpreters were not as skilled as desired in that language. Those participants noted that the interpreters were using a pidgin of signed English instead of ASL, which has a different and distinct grammar and syntax, making it much harder to understand (similar to someone interpreting from the French language to English by putting the English words into a French word order making the interpretation challenging to understand).

Some individuals signed up but did not participate. Since the cost of attending was covered by a grant, potential participants did not have a financial incentive to follow through with the program. Future iterations of this program could consider charging a nominal amount, so that participants are not limited by financial barriers, but still have "skin in the game" to follow through.

This was a small pilot study, designed as a "proof of concept," to demonstrate that an online Zoom-based medically-facilitated Lifestyle Medicine program with previously proven benefits could be adapted to an underserved community with barriers in both access and communication. Because this was not designed as a prospective clinical trial, demonstration of impact is limited to the responses that were voluntarily provided through an ongoing QI program. It is certainly possible that the participants who had less favorable results did not respond to the surveys.

Additionally, we used a "post-pre" analysis, in which participants were able to compare their baseline responses to their follow up. This was done so that participants could assess change during the 15 days (e.g., changes in pain or energy), and because the way in which participants measure certain outcomes (e.g., how whole-food plant-based their diet is) may change over the course of the 15 days. This approach, as well as a pre-post approach, are vulnerable to a "social desirability" bias of providing responses that are acceptable; however, this is generally a limitation of self-reported measures (17).

A larger, prospective study would reduce these biases, and yield more generalizable results. In addition, it could provide opportunities to evaluate the characteristics that are associated with positive results. However, the breadth of positive results reported by this cohort suggests that this is a model that can be used to provide education and support for behavior change that will lead to improved health in a DHH community.

Conclusion

This pilot study provides a framework for adapting an online medically-facilitated program to educate a traditionally underserved community with multiple barriers to care –namely, a Deaf and Hard of Hearing cohort –giving them knowledge, skills and support to adopt a WFPB lifestyle. Preliminary findings suggest that participants are able to make significant changes, leading to short-term health improvements. Further large-scale, prospective studies are needed to rigorously evaluate this approach, building on the "lessons learned" from the pilot program.

Data availability statement

The data analyzed in this study is subject to the following licenses/restrictions: The de-identified dataset is a subset of a quality improvement dataset managed by Rochester Lifestyle Medicine Institute. Requests to access these datasets should be directed to Bruce.pollock@roclifemed.org.

Ethics statement

The study involving human participants was reviewed and approved by the University of Rochester School of Medicine and Dentistry Institutional Review Board. Written informed consent for participation was not required for this study in accordance with national legislation and institutional requirements.

Author contributions

SF: analysis, drafting, and revision of manuscript. KS and TB: program conceptual framework, review, and revision of manuscript. BB and MD: program conceptual framework, recruitment of participants, review, and revision of manuscript. All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Increased dietary fiber is associated with weight loss among Full Plate Living program participants

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Introduction: Prior studies have demonstrated that an intake of foods rich in dietary fiber is associated with a favorable impact on health status and body weight. However, the association between fiber intake and weight loss has not been well-studied in employer settings. This research aimed to assess the relationship between dietary fiber and weight loss among individuals participating in the Full Plate Living (FPL) program.

Methods: The 16-week plant-predominant fiber-rich eating program was delivered to 72 employers, primarily in the Southwest U.S., over 3 years (2017–2019). Participants received weekly video lessons, FPL materials, and additional online resources. A retrospective analysis of repeated measures was conducted using participant data obtained from 4,477 participants, of which 2,792 (62.5%) reduced body weight. Analysis of variance with *post hoc* analysis was used to assess the statistical significance of the changes between baseline and follow-up measures of dietary fiber intake in each of the food categories, specifically the relationship between changes in individual and combined (composite) daily servings of fruits, vegetables, whole grains, beans, and nuts on body weight measures among three groups at follow-up: those who lost, maintained, or gained weight. Multilevel modeling was used to test the hypothesis that increased intake of fiber was associated with greater weight loss.

Results: The mean weight loss for the weight loss group was 3.28 kg. As compared to the two other groups, the intake of whole fiber-rich foods at follow-up was significantly higher among the weight loss group with fruits (2.45 servings), vegetables (2.99 servings), beans (1.03 servings), and total fiber composites (9.07 servings; $P < 0.001$). A significant increase in servings of grains was also noted ($P < 0.05$). Multilevel modeling demonstrated that a higher total fiber composite (Model 1), as well as higher intakes of either vegetables or fruits (Model 2), resulted in greater weight loss.

Discussion: Our findings indicate that the FPL program can be a part of a lifestyle medicine approach to healthy eating and weight loss. Delivering the program in clinical, community, and workplace settings can increase its reach as an effective and low-cost offering.

KEYWORDS

workplace, nutrition, dietary fiber, plant predominant, weight loss, whole food, intervention

Introduction

The workplace provides employers with opportunities to identify solutions to enhance employee health, wellbeing, and productivity while maintaining or reducing healthcare costs (1–6). Being overweight and obese is linked to increased healthcare expenditures across adults of all ages and body mass index ranges, particularly for individuals with severe obesity (7). Excess body weight is also linked to numerous comorbid and chronic health conditions including type 2 diabetes, heart disease, stroke, and various types of cancer. The Centers for Disease Control and Prevention Obesity (8) reports that the prevalence of obesity among adults living in the United States is 41.9%, of which ∼60% of adults in the US are working (9). With the increased prevalence of obesity in the US, recent studies have expanded our understanding of dietary contributors to weight loss. Factors associated with weight loss are multifaceted and include adjustments in dietary intake of kilocalories, macronutrients, and fiber. Previous research suggests that a higher intake of dietary fiber is a predictor of weight loss and compliance with healthy eating when combined with an overall reduction in kilocalorie intake (10–14). Intake of foods high in fiber has also been associated with improved health, quality of life, and reductions in chronic health conditions (11–19).

Full Plate Living (FPL), a multicomponent nutrition education program, was designed for individuals and groups in clinical, workplace, and community settings. The details and benefits of the FPL program have been previously described (20–22). FPL's simplified healthy eating approach emphasizes small-step habit adoption to include the consumption of plant predominant foods high in fiber, such as fruits, vegetables, beans and legumes, cooked whole grains, and nuts (21). The focus of the FPL plant-predominant nutrition program is to gradually consume 75% of a meal from nutrient-dense, low-calorie foods that are high in fiber, or ∼40 g of fiber per day, over time. FPL also emphasizes physical movement, consumption of water, and awareness of satiety cues.

The beneficial impact of FPL on improving eating behaviors and health values has been demonstrated in both community and employer settings (20, 23–25). A recent FPL analysis demonstrated significant improvements in eating behaviors and health status including increased consumption of fiber-rich foods of fruits, vegetables, whole grains, beans, and nuts; improvement in perceived health and energy values; increased confidence values of losing weight and choosing healthy foods, and overall weight loss (20). However, research gaps exist regarding our understanding of the relationship between weight modification and adherence to the FPL plant-predominant eating approach in the workplace.

This study aimed to assess the relationship between servings of whole-food plant-based foods high in fiber and the impact on body weight among employees in a workplace wellness program using the FPL program. More specifically, the present study is attempting to answer the following three questions:

(1) Does participation in the FPL program result in weight modification?
(2) As a result of participating in the FPL program, does total fiber intake or specific high-fiber foods play a role in weight loss; and
(3) To what extent does the FPL program yield differences across the following three groups: weight loss (WL), weight neutral (WN), and weight gain (WG)?

Methods

Study design

The study design, procedures, and intervention have been previously described in detail (20). The 16-week FPL program consisted of individuals receiving weekly online educational videos, FPL program curriculum materials, and online resources to include recipes and meal planning tips. A repeated measures study design was conducted using participant data from the FPL. A 20-question, self-reported confidential online health assessment was completed at both baseline and follow-up (within 3 weeks of program completion) and included questions about eating behaviors, perceived values of energy and health, and confidence values for healthy eating and weight loss. Daily servings of fiber-rich food, including fruits, vegetables, beans, grains, and nuts, were recorded by participants in a food diary. Because this study was a retrospective, *post hoc* analysis of de-identified data, IRB approval for the study was not obtained.

Subjects

The program was delivered through 72 employers located primarily in the Southwest U.S. from 2017 to 2019. Employee participants were recruited through their organization's wellness program. A total of 6,820 individuals were enrolled in the FPL program, of which 4,477 were included in the analysis as they completed the baseline and follow-up health questionnaires.

Measures

Measures of data-specific variables were previously described (20), including demographic characteristics, food intake, self-perceived health and energy values, confidence scores, and body weight.

Demographic characteristics

Available demographic details were limited to age and gender. *Gender* was coded as male or female.

Food intake

Food intake was self-reported by asking "How many actual servings of food do you consume each day over the last 2 weeks for each of the following food categories, such as fruits, vegetables, beans, whole grains, nuts?"

TABLE 1 Baseline demographic characteristics of participants by weight loss category.

Variable	Total	Weight loss (WL)	Weight neutral (WN)	Weight gain (WG)
Number	4,477	2,792	697	988
Percentage of total, %	100	62.5	15.5	22.0
Female, %	87.0	86.9	85.4	88.5
Male, %	13.0	13.1	14.6	11.5
Age, years $M \pm SD$	45.7 ± 11.7	46.0 ± 11.8	45.2 ± 11.8	45.1 ± 11.5
Baseline body weight, kg				
Female	86.3 ± 21.8	87.7 ± 22.1	83.0 ± 20.9	84.7 ± 21
Male	101.3 ± 22.0	102.1 ± 20.9	101.8 ± 25.3	98.5 ± 22.3

Data are drawn from the Full Plate Living participant survey data.

Self-perceived health

Responses were coded into five categories: excellent, very good, good, fair, and poor.

Self-perceived energy

The self-perceived energy question was assessed on a 5-point scale by asking "How would you describe your energy level in the past month?" Responses were coded into five categories: very high energy, high energy, moderate energy, low energy, and no energy.

Confidence scores

Participants recorded their confidence for each item on a 10-point scale, ranging from 0 (no confidence) to 10 (complete confidence).

Additional measures were evaluated for this study to include body weight, fiber composite, and overall water intake.

Body weight categories

Body weight was self-reported and provided a comparative measure of pre- and post-program change. Participants were divided into three groups based on their baseline and follow-up program weight change: WL, WN, and WG. Individuals recorded their weight to the nearest pound measurement. Participants who lost >1 pound or 0.45 kg of body weight were included in the WL group. Participants who maintained their weight, <1 pound or 0.45 kg, of body weight change were included in the WN group. Individuals who gained more than one pound or 0.45 kg were included in the WG category.

Fiber composite

A high-fiber food composite was developed by adding the total number of daily servings of fiber-rich foods.

Water intake

Water was assessed based on the number of cups of water consumed per day.

Analyses

Analysis of variance with *post hoc* analysis was used to assess the statistical significance of the changes between baseline and follow-up measures of dietary fiber intake in each of the food categories, specifically the relationship between changes in individual and combined (composite) servings of fruits, vegetables, grains, beans, and nuts on body weight measures among the three weight groups. The WL group was used as the reference with a comparison to both WN and WG values for the *post hoc* measures.

Multilevel modeling was used to test the hypothesis that increased fiber intake was associated with lower body weight at follow-up (i.e., weight loss). Random-intercept models were estimated with repeated measures nested in subjects. Two models were estimated. Model 1 had fiber composite as the independent variable of main interest. In comparison, Model 2 examined individual high-fiber food categories including vegetables, fruits, nuts, beans, and whole grains. Included as time-varying covariates were water intake, and a variable (time), to capture secular trends. Time-varying variables were person-mean centered to estimate their within-subject association with body weight. With two repeated measures, person-mean centering was equivalent to a change score. Age and gender were included as time-invariant covariates.

Results

The program included 6,820 program participants; of which, 4,477 individuals completed baseline and program self-reported questionnaires; therefore included in the program analysis.

Table 1 presents descriptive statistics for baseline demographic characteristics for all participants ($n = 4,447$) including subgroups based on body weight category. The average age for all participants was 45.7 (SD + 11.7). Consistent with similar nutrition and weight management studies demonstrating that women participate at rates three times greater than men (26, 27), the majority of study participants were women (87.0%). Of the three weight groups, the WL category was the largest, at 62.5% ($n = 2,792$), with an additional 22.0% gaining weight ($n = 988$) and 15.5% maintaining their weight ($n = 697$). The mean body weight for all female

TABLE 2 Change in health measures, eating behaviors, and confidence values by weight loss category.

Variable	Weight loss	Weight neutral	Weight gain
Change of body weight, kg	3.28**	0.00	2.22
Females	3.17**	0.00	2.17
Males	4.06**	0.00	2.61
Food intake (servings per day)			
High fiber food composite, servings per day			
Baseline	6.26	6.58	6.22
Follow-up	9.07**	8.51	8.09
Change	2.81	1.93	1.87
Fruit, servings per day (0–7)			
Baseline	1.54	1.64	1.53
Follow-up	2.45**	2.28	2.13
Change	0.91	0.64	0.60
Vegetables, servings per day (0–7)			
Baseline	2.03	2.09	2.08
Follow-up	2.99**	2.73	2.63
Change	0.96	0.64	0.55
Beans, servings per day (0–4)			
Baseline	0.63	0.67	0.62
Follow-up	1.03**	0.98	0.87
Change	0.41	0.31	0.26
Grains, servings per day (0–6)			
Baseline	1.27	1.35	1.22
Follow-up	1.61*	1.57	1.50
Change	0.34	0.22	0.27
Nuts, servings per day (0–4)			
Baseline	0.80	0.84	0.77
Follow-up	1.00	0.97	0.95
Change	0.20	0.13	0.18
Water intake			
Baseline	5.73	5.93	5.83
Follow-up	7.08**	6.80	6.63
Change	1.35	0.87	0.80
Health values (self-reported)			
Perceived confidence level for losing weight (0–10)			
Baseline	5.16	5.03	5.14
Follow-up	6.45**	5.71	5.39
Change	1.29	0.68	0.24
Perceived confidence level for choosing healthy food choices (0–10)			
Baseline	6.10	6.11	6.03
Follow-up	7.46**	6.96	6.77
Change	1.37	0.85	0.74
Perceived health value, 1–5			
Baseline	3.14	3.25	3.23
Follow-up	3.41**	3.39	3.31
Change	0.27	0.14	0.08
Perceived energy value, 0–6			
Baseline	2.84	2.91	2.82
Follow-up	3.33**	3.21	3.10
Change	0.49	0.30	0.28

Significant differences between groups as determined by analysis of variance and post hoc follow-up tests (Tukey). Weight loss is the reference with comparison to weight neutrality and weight gain.
**P < 0.01.
*P <0.05.
Perceived health value and water intake were only significantly different between WL and WG.

participants was 86.3 kg (SD + 21.8), while the mean body weight for male participants was 101.3 kg (SD + 22.0).

Baseline and follow-up measures of participant eating behaviors, health measures, and confidence levels among all three weight groups are presented in Table 2. Significant weight loss was demonstrated for the WL group, with a mean of 3.28 kg ($P < 0.01$) for all participants losing weight as compared to an average body weight increase of 2.22 kg in the WG group. Further segmentation by gender among the weight loss group revealed that female participants lost 3.17 kg ($P < 0.01$) of body weight as compared to male participants at 4.06 kg weight loss ($P < 0.01$). Both of the WL values were significantly different from those in the WN and WG categories.

Previous studies demonstrated that FPL participants had statistically significant improvements in eating behaviors of fiber-rich foods between baseline and follow-up (20). Unique to this study was the development of a total fiber composite. As a result of the FPL program, participants in the WL group significantly increased their daily total intake of high-fiber foods by 2.81 servings to 9.07 daily servings ($P < 0.01$) as compared to 8.51 servings for WN and 8.09 servings for the WG group.

Daily servings of fruits, vegetables, beans, and grains were also significantly higher for the WL category at follow-up as compared to the WN and WG categories. The greatest change occurred in daily servings of fruits (0.91), vegetables (0.96), beans (0.41), and grains (0.34). The WL category recorded significantly higher servings of fruits, vegetables, and beans at 2.45 ($P < 0.01$), 2.99 ($P < 0.01$), and 1.03 ($P < 0.01$) as compared to the WN and WG groups. The WL group also had a significantly higher daily intake of whole grains at 1.61 servings compared to the WN and WG groups of 1.57 and 1.50 servings, respectively ($P < 0.01$). There was no significant difference among servings of nuts at follow-up across the body weight categories.

Confidence levels in losing weight were significantly higher for the WL group at 6.45 ($P < 0.01$) as compared to the categories of WN at 5.71 and WG at 5.39. The WL group confidence levels

TABLE 3 Within-subject associations between intake of fiber-rich food composition, individuals' fiber-rich food categories, and body weight.

Variable	Model 1			Model 2		
	Estimate	SE	*P*-value	Estimate	SE	*P*-value
Water	−0.207	0.039	< 0.01	−0.193	0.39	< 0.01
Fiber composite	−0.352	0.034	< 0.01			
Vegetables				−0.658	0.094	< 0.01
Fruits				−0.355	0.101	< 0.01
Nuts				−0.126	0.147	0.392
Beans				−0.230	0.161	0.153
Grains				−0.088	0.101	0.385
Time	−2.330	0.140	< 0.01	−2.259	0.143	< 0.01

in making healthy choices were also significantly higher at 7.46 ($P < 0.01$) as compared to the categories of WN at 6.96 and WG at 6.77. The self-perceived health values for the WL group were significantly higher at 3.41 than the WG group at 3.31 but not of the WN group at 3.39. Self-perceived energy values were significantly different for the WL group at 3.33 ($P < 0.01$) as compared to the WN group at 3.21 and 3.10 for the WG group.

Table 3 shows the relationship between fiber intake and body weight through the development of two models. Model 1 demonstrates that a higher intake of total high-fiber foods (composite) at follow-up was associated with lower body weight ($P < 0.01$). Model 2 revealed that of the individual food categories of high-fiber foods (fruits, vegetables, beans, whole grains, and nuts), a higher intake of vegetables or fruits was associated with weight loss ($P < 0.01$). As a result of the multilevel modeling analysis, increases in the intake of nuts, beans, or grains were not associated with weight change during the study period ($P > 0.15$).

Discussion

Research has demonstrated that an intake of foods high in fiber is associated with a favorable impact on health status and body weight. This study adds to the body of literature examining the impact of a plant predominant fiber-rich eating approach and its relationship to weight loss in employer settings. More specifically, this study examines the relationship of dietary fiber among individuals participating in the FPL program. As demonstrated in previous studies, there is a direct relationship between the intake of dietary fiber and weight loss (10, 11, 14–17).

The initial finding confirms that the 16-week FPL program results in weight loss among the majority of participants, with 62.5% reporting weight loss. These results can help to address the adverse impact of obesity on health and productivity in the workplace and community by providing a low-cost healthy eating program (21). FPL promotes a healthy nutrition eating approach through a small-step adoption of improved eating habits through the gradual consumption of 75% of nutrients from plant-based whole foods while incorporating sustained adoption of healthy living and nutrition principles.

Further analysis evaluated the difference between three weight groups: those who lost weight, maintained weight, and gained weight. Of the WL group, there was a significant increase in total and individual servings of high-fiber foods including fruits, vegetables, beans, whole grains, and nuts. The WL group consumed 9.07 total daily servings, which was an increase of 0.56 over the WN group, and 0.98 serving more than the WG group. More specifically, the greatest intake of fiber-rich foods came from vegetables at 2.99 or 0.26 and 0.36 servings more than the WN and WG groups, respectively. As a result, our second finding demonstrated that as a result of participating in the FPL program, both the total intake of high-fiber foods, as well as select fiber-rich foods, play a significant role in body weight loss as higher daily servings resulted in greater weight loss. As with previous studies (28–30), individuals who consume higher amounts of vegetables and fruits have greater weight loss as these foods are high in fiber but lower in calories than other high-fiber foods such as beans, grains, and nuts.

The third finding of this study supports the hypothesis that dietary fiber is associated with weight loss. In our analysis, the change in fiber intake from baseline to 16 weeks was a consistent and strong predictor of weight loss. The association between increased fiber intake in the total fiber composite (Model 1) as well as and Model 2, the increased intake of vegetables or fruits, while controlling for water intake. Weight loss increases as total fiber intake, or more specifically fruit or vegetable intake increases.

Additional findings demonstrated that individuals within the WL group also had higher values of perceived energy and confidence values for losing weight and making healthier choices as compared to the other groups. Individuals who improve their health and lose weight have also been shown to have great self-efficacy (31).

There were notable limitations to the study. First, the study was 16 weeks in length and may not be reflective of long-term results. Second, as noted in previous FPL studies (20, 23, 24), self-reported survey data were used for analysis, inclusive of estimated servings of food in place of a daily food log and corresponding analysis. Third, demographic data were limited to age and gender, preventing stratification or adjustment of participant data based on race, ethnicity, and/or socioeconomic status. Finally, attrition bias is one of the major challenges in nutrition and weight management programs, consistent with this study. Future studies of the FPL program should include a longer-term program evaluation period with improved survey instruments, standardized weight measurement, comparison group, and analysis of exercise-related impact.

Despite these limitations, the study has implications for nutrition interventions. Specifically, FPL program interventions delivered at the workplace have been demonstrated to improve weight loss and therefore overall health. Due to these benefits, the FPL program may offer employers a strategy to improve both workplace productivity and healthcare costs. Programs such as FPL are also beneficial to be delivered in clinical and community settings as they may improve patient and community health. The FPL program has been found to improve overall eating habits, and for individuals who consume significant increases in fiber intake, there is corresponding weight loss. In summary, this study identified that the FPL program was effective in improving weight loss as a result of increased intake of high-fiber foods, including the consumption of total fiber and fruits and vegetables. In addition, improvements were significantly higher for confidence in losing weight, confidence in making healthy choices, and perceived health and energy values for the WL group. Future studies could focus on exploring dietary fiber intake and weight loss as part of a longer-term program in multiple settings. In addition, fiber's role in improving health through the measurement of additional clinical markers should be considered in future FPL studies.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

Ethical review and approval was not required for the study on human participants in accordance with the local legislation and institutional requirements. The ethics committee waived the requirement of written informed consent for participation.

Author contributions

RKK: conceptualization, methodology, design and formal analysis, writing, reviewing, editing, and ongoing communications. AH, JC, and RS: data collection, design analysis assistance, manuscript review and editing, and liaisons of the data and background literature. PP-F: ongoing review and edits to the manuscript. BWS: conceptualization, design analysis assistance, writing, reviewing, and editing. All authors contributed to the article and approved the submitted version.

Conflict of interest

RKK, PP-F, and BWS were paid consultants of Ardmore Institute of Health. RKK was employed by Element Health, Inc. AH, JC, and RS were employed by Ardmore Institute of Health.

Publisher's note

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Change in cardiometabolic risk factors in a pilot safety-net plant-based lifestyle medicine program

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Introduction: Interventions emphasizing healthful lifestyle behaviors are proliferating in traditional health care settings, yet there is a paucity of published clinical outcomes, outside of pay-out-of-pocket or employee health programs.

Methods: We assessed weight, hemoglobin A1c (HbA1c), blood pressure, and cholesterol for 173 patients of the Plant-Based Lifestyle Medicine Program piloted in a New York City safety-net hospital. We used Wilcoxon signed-rank tests to assess changes in means, from baseline to six-months, for the full sample and within baseline diagnoses (i.e., overweight or obesity, type 2 diabetes, prediabetes, hypertension, hyperlipidemia). We calculated the percentage of patients with clinically meaningful changes in outcomes for the full sample and within diagnoses.

Findings: The full sample had statistically significant improvements in weight, HbA1c, and diastolic blood pressure. Patients with prediabetes or overweight or obesity experienced significant improvements in weight and those with type 2 diabetes had significant improvements in weight and HbA1c. Patients with hypertension had significant reductions in diastolic blood pressure and weight. Data did not show differences in non-high-density lipoprotein cholesterol (non-HDL-C), but differences in low-density lipoprotein cholesterol (LDL-C) were approaching significance for the full sample and those with hyperlipidemia. The majority of patients achieved clinically meaningful improvements on all outcomes besides systolic blood pressure.

Conclusion: Our study demonstrates that a lifestyle medicine intervention within a traditional, safety-net clinical setting improved biomarkers of cardiometabolic disease. Our findings are limited by small sample sizes. Additional large-scale, rigorous studies are needed to further establish the effectiveness of lifestyle medicine interventions in similar settings.

KEYWORDS

plant-based diet, lifestyle medicine, chronic disease, lifestyle modification, cardiovascular risk, outcome evaluation, lifestyle intervention, cardiometabolic risk

Introduction

Chronic diseases such as heart disease, cancer, and type 2 diabetes are among the leading causes of death and disability in the United States (1). Sixty percent of adults live with at least one chronic disease and 40% live with two or more (2). Given increased prescription costs, the need for continuous care, and more frequent health care visits, the management of chronic diseases accounts for 90% of annual health care expenditures--making chronic diseases the leading drivers of healthcare costs in the U.S. (3–5) Health behaviors such as tobacco use, poor nutrition characterized by diets high in sodium and saturated fats and low in fruits and vegetables, lack of physical activity, and insufficient sleep are modifiable risk factors that contribute to the development of chronic disease (6).

There is strong evidence supporting the use of lifestyle interventions to prevent and treat chronic disease. For example, healthful, plant-predominant diets have been associated with significant reductions in the risk of ischemic heart disease, cancer, type 2 diabetes, obesity, and hypertension (7–12). This dietary pattern has also been shown to improve existing conditions such as coronary artery disease, type 2 diabetes, and obesity (12–17). In addition, other lifestyle behaviors including regular physical activity, restorative sleep, and stress management are associated with positive health outcomes (18–20). Leading medical organizations including the American Diabetes Association (21), American Association of Clinical Endocrinology (22), American College of Cardiology (23), American Heart Association (24), American Society for Preventive Cardiology (25), National Lipid Association (26), and the American Cancer Society (27) all recommend lifestyle change, including plant-predominant eating patterns, as first-line therapy.

Lifestyle medicine is a medical specialty that uses therapeutic lifestyle interventions as a primary modality to treat chronic lifestyle-related conditions (28). Trained clinicians deliver evidence-based care focused on encouraging a healthful, plant-predominant eating pattern, regular physical activity, restorative sleep, stress management, avoidance of risky substances, and positive healthy relationships. Lifestyle medicine has proliferated rapidly in recent years. More than 80 major health systems across the United States currently participate in the Health Systems Council for the American College of Lifestyle Medicine, indicating their commitment to integrating lifestyle medicine into their services (29). Lifestyle medicine interventions have been shown to improve cardiometabolic risk factors by lowering weight, blood pressure, fasting lipids, and blood sugar, while reducing angina and cardiac events (13, 30). However, there is a paucity of published data on the clinical impact of lifestyle medicine programs in traditional health care settings, outside of employee health, pay-out-of-pocket, or residential programs. Furthermore, even fewer studies have examined the impact of a lifestyle medicine program within a safety-net clinical setting that serves high-needs populations experiencing disproportionate rates of chronic diseases.

The Plant-Based Lifestyle Medicine (PBLM) Program is a pilot clinical program established in an urban public healthcare system. The program's goal is to help patients adopt a healthful plant-based eating pattern and other positive behaviors. The evaluation of the pilot program focused primarily on feasibility of implementation and demand for the program (31). We found demand for the program was high, far exceeding capacity, and patients reported joining the program in order to gain control over their lives, reduce their medication burden, and lose weight. The program's team, overall approach, and resources all were popular among patients despite reported barriers to accessing the program as well as administrative and insurance challenges. In this paper, we build on the implementation findings of the PBLM Program by assessing preliminary data on clinical outcomes including blood sugar, weight, blood pressure, and cholesterol among program patients. Our study is novel because, to our knowledge, the pilot PBLM Program is the first lifestyle medicine program operating within a traditional safety-net healthcare system to publish clinical outcomes data.

Methods

The primary goal of the pilot PBLM Program evaluation was to assess the feasibility of implementing the program and the demand for its services. A secondary goal was to assess preliminary data related to clinical outcomes. The study uses a pre/post single sample design. Approval for this study was obtained from both the New York University (NYU) Grossman School of Medicine Institutional Review Board as well as the Office of Research and Administration for Implementation at NYC Health + Hospitals/Bellevue.

Intervention

A detailed description of the 1-year pilot of the PBLM Program has been published previously (31). Briefly, the PBLM Program at NYC Health + Hospitals/Bellevue, a large public hospital in New York City, was designed to provide structured, interdisciplinary support for lifestyle changes to improve patients' cardiometabolic health. Adults with excess weight (i.e., BMI $\geq$ 25), type 2 diabetes, prediabetes, hypertension, atherosclerotic heart disease, and/or hyperlipidemia were eligible to participate. Individuals learned of the program through earned media (e.g., TV news, newspapers), social media, announcements from the office of the Brooklyn Borough President, and limited health care provider referrals from within Bellevue. Thus, most patients self-selected into the program and joined by adding their name to a waitlist. Enrollment in the program was on a first-come, first-serve basis. The program encouraged patients to transition to a healthful plant-based diet, improve sleep health, increase physical activity, improve stress management, foster positive social connections, and avoid substance use. Patients met individually with clinicians who have expertise in plant-based nutrition and lifestyle medicine, including a physician, a registered dietitian, and a health coach, to set goals and monitor progress. Group classes supplemented one-on-one visits, emphasizing education, skills-building, action planning, and peer-to-peer support. In addition, an exercise trainer offered classes focused on aerobic and strength training. Resources available to all patients included a plant-based diet starter guide, cookbook(s), HealthBucks (coupons that can be used to purchase fresh fruits and vegetables at all New York City farmer's markets), a Healthy Savings Card for grocery store discounts on fresh produce, and access to a private Facebook group for social support, advice, and recipe sharing. The frequency and duration of program engagement for each individual was determined jointly by the PBLM Program provider team and each of the patients.

Data sources

Clinical outcomes for all patients of the PBLM Program were analyzed using de-identified electronic health record (EHR) data. In total, 173 individuals had at least one visit with the program between January 16, 2019 and February 15, 2020 and had EHR data. Because data were de-identified, consent was not required. Data were pulled at one time point and contained all recorded values during the study period. Additionally, program staff maintained a separate administrative database to track the following data for all patients: (1) limited demographic data (i.e., age, gender); (2) baseline clinical diagnoses determined by the treating physician (i.e., type 2 diabetes, prediabetes, overweight or obesity, hypertension, heart disease, hyperlipidemia); and (3) medications and their dosages at baseline, three-months, and six-months. The two datasets were merged for analyses using a unique identifier.

Measures

There were six clinical outcomes of interest in this study: (1) weight (kg); (2) hemoglobin A1c (HbA1c) (%); (3) systolic blood pressure (mm Hg); (4) diastolic blood pressure (mm Hg); (5) non-high-density lipoprotein cholesterol (non-HDL-C) (mg/dl); and (6) low-density lipoprotein cholesterol (LDL-C) (mg/dl).

In order to assess the contribution of behavior change to clinical outcomes, independent of medication changes, we created a stable or reduced medication regimen variable for those with type 2 diabetes, hypertension, and hyperlipidemia diagnoses at baseline. We first calculated the total number of medications prescribed for each participant within diagnoses (e.g., total number of diabetes medications prescribed for someone with type 2 diabetes) at baseline and six-months. Then we coded changes to medications by calculating the difference in the total number of medications from baseline to six-months (+1 for new medication added, −1 for medication removed, 0 for no change in medications). For those with no change in the number of disease-specific medications, we assessed changes in dosage (+1 for increase, −1 for decrease, 0 for no change). We then combined these two factors for a medication and dosage variable where a positive number indicates a net increase (increased medication regimen), a negative number indicates a net decrease (reduced medication regimen), and 0 indicates no net change (stable medication regimen).

In addition, we created variables to represent clinically meaningful change in each of the six clinical outcomes. Clinically meaningful improvement was based on published literature and was defined as follows: ≥3% decrease in weight (32, 33), ≥0.5 percentage point reduction in HbA1c for patients with a baseline diagnosis of type 2 diabetes (34–36), no change or any decrease in HbA1c for patients with a baseline diagnosis of prediabetes (i.e., no progression to type 2 diabetes) (37), ≥3 mm Hg reduction in systolic or diastolic blood pressure (38, 39), and any decrease in non-HDL-C or LDL-C (40, 41). First, we calculated the change from baseline to six-months (positive number indicates an increase, negative number indicates a decrease, zero indicates no change). Then we created a binary variable (yes/no) to indicate whether that change was clinically meaningful for each of the clinical outcomes.

Analyses

We assessed comparability in demographic characteristics and baseline diagnoses by gender using Chi-squared tests. We conducted analyses to assess changes in patients' clinical outcomes between baseline and six-months for the full sample and then within diagnosis (i.e., overweight or obesity, type 2 diabetes, prediabetes, hypertension, hyperlipidemia) using only patients that had data at both time points; heart disease was excluded from subgroup analysis due to the small sample size. When analyzing outcomes within the baseline diagnosis subgroups, we assessed change over time only for the most relevant outcomes (e.g., non-HDL-C and LDL-C for patients with hyperlipidemia) in addition to weight because a substantial majority (i.e., ≥ 80%) of patients had a BMI ≥ 25 within each condition. We also assessed change in weight and relevant clinical outcomes for three disease-specific subgroups of patients (i.e., type 2 diabetes, hypertension, hyperlipidemia) with stable or reduced disease-specific medication regimens over the study period. Our goal in reviewing outcomes by stable or reduced medication status was to isolate, to the best possible extent, the effects of lifestyle change alone. Change in medication status was not reviewed for the prediabetes, overweight or obesity, or heart disease subgroups, given that disease-specific medications were not used for prediabetes or overweight or obesity, and the sample size of the heart disease subgroup was too small for analysis. For most patients, baseline values were established at the first appointment. In selected cases where an individual did not have clinical data from their first visit, we used lab results that were no more than 90 days before their first appointment or no more than 30 days after the first appointment. For six-month values, we used the first value 182 days or more after the baseline visit. In those instances where there were no available values at six-months or more, we used their last value as long as it was 45 days or more after the baseline value. The only exception was for HbA1c, where we increased the inclusion criteria to at least 60 days after the first appointment.

Lastly, we calculated the percentage of patients with clinically meaningful improvement in clinical outcomes between baseline and six-months for the full sample and then within diagnoses for clinically relevant outcomes. These data are shown for descriptive purposes only. We did not assess for clinically meaningful changes in HbA1c for the full sample because two-thirds of patients did not have type 2 diabetes; thus, their HbA1c levels were more likely to have been in "control" at baseline and any clinically meaningful improvement detected would not be representative of the full sample.

The sample size in analyses fluctuates due to missing outcome data. We used Wilcoxon signed-rank tests to assess changes in means of the clinical outcomes. This test is the non-parametric test used when data are not normally distributed. When sample sizes were less than 20, we did not perform statistical tests in order to avoid comparing estimates with limited statistical stability. In those cases, we present data descriptively. All analyses were conducted using SPSS version 26 (42). Results were considered statistically significant if they had a value of p less than 0.05.

Results

Demographic characteristics, baseline diagnoses, and days between measures

Table 1 shows the demographic characteristics and baseline diagnoses of all PBLM Program patients, stratified by gender. The majority of patients were female (69.4%) and were, on average, about 55 years old. The majority of patients had a baseline diagnosis of overweight or obesity (87.3%), roughly half of the sample was hypertensive or had a diagnosis of hyperlipidemia (53.2 and 49.7%, respectively), about one-third had a baseline diagnosis of type 2 diabetes (33.5%), a little over one-fifth had prediabetes (21.4%), and a small percentage of the sample had a baseline diagnosis of heart disease (12.1%). There was a statistically significant difference in heart disease among males and females. Specifically, a larger percentage of male patients had a baseline diagnosis of heart disease as compared to female patients (22.6% vs. 7.5%). The average number of days between patients' baseline and six-month measures varied: HbA1c 172 days (SD = 70), weight, systolic blood pressure, diastolic blood pressure 169 days (SD = 66); non-HDL-C 167 days (SD = 81); LDL-C 167 days (SD = 80) (not shown).

Average change in clinical outcomes over time

Table 2 displays findings for all six clinical outcomes for the full sample. We then stratified by baseline condition and show weight in addition to the measure most relevant to that condition. Among the full sample of patients, including those without overweight/obesity, type 2 diabetes, prediabetes, hypertension, or hyperlipidemia, there were statistically significant reductions in patients' weight (92.5 kg vs. 88.8 kg), HbA1c levels (6.7% vs. 6.3%), and diastolic blood pressure (76.6 mm Hg vs. 73.9 mm Hg) over time. Change in LDL-C was approaching significance (101.7 mg/dl vs. 93.0 mg/dl, $p < 0.10$). For the subgroup of patients that had a baseline diagnosis of overweight or obesity ($n = 151$), we found significant improvements in weight (95.6 kg vs. 91.7 kg). For the subgroup of patients with type 2 diabetes ($n = 58$), there were improvements in HbA1c (7.9% vs. 7.2%) and weight (98.2 kg vs. 93.3 kg). For the subgroup of patients with prediabetes ($n = 37$), only weight was evaluated for statistical significance, as there were too few patients with HbA1c measurements at both timepoints to perform statistical tests. Weight, on average, decreased from 88.1 kg to 85.0 kg ($p < 0.05$) for those with prediabetes. Statistically significant improvements were found in diastolic blood pressure among patients with a diagnosis of hypertension ($n = 92$;

TABLE 1 Sample characteristics and baseline diagnoses by gender (n=173).

Characteristic	Full sample		Males		Females	
	N	Mean (SD) or Percent	*N*	Mean (SD) or Percent	*N*	Mean (SD) or Percent
Gender	173					
Male		30.6	53	100.0		
Female		69.4			120	100.0
Age	173	55.0 (12.0)	53	54.2 (11.5)	120	55.3 (12.3)
Overweight/Obesity	173		53		120	
No		12.7		17.0		10.8
Yes		87.3		83.0		89.2
Type 2 Diabetes	173		53		120	
No		66.5		58.5		70.0
Yes		33.5		41.5		30.0
Prediabetes	173		53		120	
No		78.6		84.9		75.8
Yes		21.4		15.1		24.2
Hypertension	173		53		120	
No		46.8		47.2		46.7
Yes		53.2		52.8		53.3
Heart Disease	173		53		120	
No		87.9		77.4		92.5*
Yes		12.1		22.6		7.5
Hyperlipidemia	173		53		120	
No		50.3		50.9		50.0
Yes		49.7		49.1		50.0

*$p < 0.05$.

TABLE 2 Clinical outcomes for full sample and by baseline diagnosis.

	Full sample (*n*=173)			Overweight/Obesity (*n*=151)			Type 2 diabetes (*n*=58)			Prediabetes (*n*=37)			Hypertension (*n*=92)			Hyperlipidemia (*n*=86)		
		Baseline	Six-month		Baseline	Six-month		Baseline	Six-month		Baseline	Six-month		Baseline	Six-month		Baseline	Six-month
	N	Mean change (SD)	Mean (SD)	*N*	Mean (SD)	Mean (SD)	*N*	Mean (SD)	Mean (SD)	*N*	Mean (SD)	Mean (SD)	*N*	Mean (SD)	Mean (SD)	*N*	Mean (SD)	Mean (SD)
Weight (kg)	113	92.5 (22.1)	88.8 (22.1)*	100	95.6 (21.4)	91.7 (21.7)*	37	98.2 (23.9)	93.3 (23.0)*	24	88.1 (13.2)	85.0 (12.7)*	57	92.0 (20.2)	88.5 (19.1)*	54	93.2 (24.7)	90.0 (24.8)*
HbA1c (%)[a]	75	6.7 (1.7)	6.3 (1.2)*				32	7.9 (1.7)	7.2 (1.1)*	17	5.8 (0.2)	5.8 (0.3)[a]						
Systolic blood pressure (mm Hg)	115	126.1 (19.5)	123.0 (16.0)										60	133.8 (21.6)	128.8 (16.2)			
Diastolic blood pressure (mm Hg)	115	76.6 (10.7)	73.9 (9.8)*										60	79.1 (11.1)	75.0 (10.3)*			
Non-HDL-C (mg/dL)	70	130.8 (44.1)	121.3 (36.6)													38	140.3 (45.8)	125.3 (38.9)
LDL-C cholesterol (mg/dL)	70	101.7 (38.9)	93.0 (34.7)†													38	112.1 (42.2)	98.0 (38.9)†

Ns may vary due to missing data. The subgroups of patients by baseline diagnoses are not mutually exclusive.

[a]A statistical test assessing change in HbA1c over time was not performed for the subgroup of patients with a baseline diagnosis of prediabetes due to the small sample size.

†$p < 0.10$; *$p < 0.05$.

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79.1 mm Hg vs. 75.0 mm Hg) and weight (92.0 kg vs. 88.5 kg) between baseline and six-months. No statistically significant changes were detected in systolic blood pressure. Lastly, among individuals with hyperlipidemia ($n = 86$), the change in LDL-C was approaching significance (112.1 mg/dL vs. 98.0 mg/dl, $p < 0.10$) and weight was significant (93.2 kg vs. 90.0 kg).

Average change in clinical outcomes for those with a stable medication regimen

We assessed changes in clinical outcomes for patients with a baseline diagnosis of type 2 diabetes, hypertension, or hyperlipidemia who also had a stable or reduced disease-specific medication regimen (Table 3). Among those with type 2 diabetes, there were statistically significant improvements in HbA1c (7.8% vs. 7.1%) and weight (97.2 kg vs. 91.9 kg). For those with hypertension, we detected a significant reduction in diastolic blood pressure from 79.8 mm Hg to 75.4 mm Hg over time in addition to weight (92.0 kg vs. 88.6 kg). Changes in both non-HDL-C and LDL-C approached statistical significance (140.4 to 124.7 and 112.8 to 98.6 mg/dl, respectively) between baseline and the six-month visit for those with hyperlipidemia while there was a statistically significant improvement in weight (92.9 kg vs. 89.7 kg).

Clinically meaningful change in outcomes over time

Table 4 shows the proportion of patients who had clinically meaningful change over time for the full sample and then by baseline diagnosis. In the full sample, more than half of patients had clinically meaningful changes in four of the five outcomes assessed (HbA1c was not assessed for the full sample). Specifically, a substantial proportion of patients had improvements in their weight (50.4%), diastolic blood pressure (50.4%), non-HDL-C (54.3%), and LDL-C (55.7%); this includes patients who did not have a baseline diagnosis of hypertension or hyperlipidemia. One half of those with overweight or obesity were found to have a clinically meaningful reduction in weight. For those with type 2 diabetes, we determined that at least half of patients had clinically meaningful improvements in HbA1c (50.0%) and weight (51.4%). Among those with prediabetes at baseline, a sizable proportion had clinically meaningful outcomes in both HbA1c (76.5%) and weight (50.0%). Forty percent of those with hypertension at baseline had a clinically meaningful reduction in systolic blood pressure, 56.7% had improvement in diastolic blood pressure, and 56.1% had a clinically meaningful reduction in weight. Additionally, almost two thirds of the hyperlipidemia subgroup (60.5%) had clinically meaningful reductions in both non-HDL-C and LDL-C over time, while 51.9% had a meaningful improvement in weight.

Discussion

We have previously published findings that the pilot PBLM Program is feasible with high levels of patient satisfaction and interest (31). In this study, we now demonstrate a significant reduction in key biomarkers of cardiometabolic disease, including HbA1c, body

TABLE 3 Clinical outcomes by stable or reduced medication regimen for patients with a baseline diagnosis of type 2 diabetes, hypertension, or hyperlipidemia.

	Stable or reduced diabetes medication regimen (n=36)			Stable or reduced blood pressure medication regimen (n=55)			Stable or reduced cholesterol medication regimen (n=55)		
		Baseline	Six-month		Baseline	Six-month		Baseline	Six-month
	N	Mean (SD)	Mean (SD)	*N*	Mean (SD)	Mean (SD)	*N*	Mean (SD)	Mean (SD)
Weight (kg)	28	97.2 (23.3)	91.9 (22.5)*	47	92.0 (18.4)	88.6 (17.7)*	47	92.9 (24.9)	89.7 (25.1)*
HbA1c (%)	26	7.8 (1.5)	7.1 (1.2)*						
Systolic blood pressure (mm Hg)				48	133.6 (21.9)	128.3 (15.5)			
Diastolic blood pressure (mm Hg)				48	79.8 (10.9)	75.4 (9.6)*			
Non-HDL-C (mg/dL)							34	140.4 (48.3)	124.7 (39.0)†
LDL-C (mg/dL)							34	112.8 (44.1)	98.6 (40.0)†

Ns may vary due to missing data. The subgroups of patients by stable medication regimen are not mutually exclusive.
†$p<0.10$; *$p<0.05$.

TABLE 4 Percent of patients with a clinically meaningful improvement in clinical outcomes for full sample and by baseline diagnosis.

	Full sample (n=173)		Overweight/Obesity (n=151)		Type 2 diabetes (n=58)		Prediabetes (n=37)		Hypertension (n=92)		Hyperlipidemia (n=86)	
	N	Percent	*N*	Percent	*N*	Percent	*N*	Percent	*N*	Percent	*N*	Percent
Weight (kg)	113	50.4	100	50.0	37	51.4	24	50.0	57	56.1	54	51.9
HbA1c (%)[a]	75	n/a			32	50.0	17	76.5				
Systolic blood pressure (mm Hg)	115	42.6							60	40.0		
Diastolic blood pressure (mm Hg)	115	50.4							60	56.7		
Non-HDL-C (mg/dL)	70	54.3									38	60.5
LDL-C (mg/dL)	70	55.7									38	60.5

Ns may vary due to missing data. The subgroups of patients by baseline diagnoses are not mutually exclusive. Clinically meaningful improvement in clinical outcome was defined as follows: Weight: a minimum 3% decrease in total body weight. HbA1c for those with type 2 diabetes: a minimum 0.5 percentage point reduction. HbA1c for those with prediabetes: no change or any decrease in HbA1c, signifying lack of progression to type 2 diabetes. Systolic and diastolic blood pressure: a minimum 3 mm Hg reduction in systolic and diastolic blood pressure. Non-HDL-C and LDL-C: any decrease. [a]The percent of patients with a clinically meaningful improvement in HbA1c is not shown for the full sample because nearly half of the patients in the full sample did not have prediabetes or diabetes.

weight, lipids, and diastolic blood pressure. We report findings that are both statistically significant and represent clinically meaningful improvements related to cardiometabolic risk. While some residential, community-based, employee health, and/or pay-out-of-pocket lifestyle programs have also shown improvement in biomarkers (43–45), this study demonstrates that a lifestyle medicine program based in the primary care clinic of a resource-limited safety-net hospital, working within traditional administrative and insurance structures, can be effectively delivered to patients while also achieving clinically meaningful improvements.

The goal of identifying patients with prediabetes is to help implement healthy lifestyle behaviors to prevent the progression to type 2 diabetes and its complications. Of those identified with prediabetes in our program, 76.5% successfully reduced their HbA1c or avoided an increase. Long-term follow-up of combined diet and exercise programs has demonstrated success in preventing diabetes while also achieving cost savings (46, 47). Among the patients with type 2 diabetes, the average HbA1c reduction was 0.7 percentage points, on par with many glucose-lowering medications (48). Moreover, 50% were able to attain at least a 0.5% reduction in their HbA1c, an amount that has historically been considered clinically meaningful, especially since a positive dose–response association has been reported between HbA1c and cardiovascular outcomes and mortality (34, 35). A meta-analysis by Giugliano et al. evaluated cardiovascular outcome trials of diabetes medications and demonstrated that a 0.5% reduction in HbA1c was associated with a 20% reduction in major cardiovascular events (MACE) (36). Clinically meaningful HbA1c lowering was reported only for patients with diabetes or prediabetes, as further lowering of blood sugar among patients with normal HbA1c is less likely to occur and is of uncertain clinical benefit.

Half of the patients lost at least 3% of their body weight, an amount that is clinically meaningful as it has been shown to translate into meaningful improvement in obesity-related comorbidities (33). Notably, the weight loss occurred without prescribed calorie restriction. The program emphasizes the consumption of unprocessed or minimally processed plant-foods – which are high in fiber and nutrient density, and low in energy density – while encouraging patients to limit or avoid animal products, saturated fats, sodium, added sugars, and ultra-processed foods. Several factors may contribute to the weight-management benefits of a healthful plant-based diet: higher fiber, lower energy density, gut microbiome effects, and increased thermogenesis (49).

We used a 3-mm Hg drop in either systolic or diastolic blood pressure as clinically meaningful as this aligns with the FDA's criteria for approval of blood pressure lowering medications (38, 39). Moreover, evidence suggests that even modest reductions in blood pressure have the potential to result in meaningful decreases in cardiovascular risk (50, 51). In the entire study population, including those without a diagnosis of hypertension, 43% of patients achieved at least a 3-mm drop in systolic blood pressure and 50% achieved at least a 3-mm drop in diastolic blood pressure. Among those with a diagnosis of hypertension, 40% of patients attained this clinically meaningful drop in systolic blood pressure and 57% attained this clinically meaningful drop in diastolic blood pressure, signifying an important reduction in cardiovascular risk (52, 53).

The baseline LDL-C of patients with hyperlipidemia in our pilot program was 112 mg/dl, with the majority already on statin therapy to lower cholesterol. Long-term drug treatment studies have shown that there is a continuous relationship between LDL-C and MACE, even at low levels of LDL-C (41, 54). For this reason, any LDL-C lowering appears to be clinically meaningful. In this pilot program, 60.5% of patients with hyperlipidemia experienced a decrease in their LDL-C and non-HDL-C. Among those on a stable or reduced cholesterol medication regimen, the average LDL-C was lowered by 14.2 mg/dl to 98.6 mg/dl.

A key finding in this study is that clinical improvements occurred among patients with stable or reduced medication regimens for diabetes, blood pressure, or cholesterol. This strongly suggests that the noted improvements in glycemic control, diastolic blood pressure, lipids, and body weight were due to lifestyle changes themselves, rather than to increases in medications. Typically, healthy lifestyle behaviors are synergistic with medications, resulting in clinical improvements and lower cardiometabolic risk without higher medication burden (21–25). In some cases lifestyle changes may allow for the reduction or cessation of medication. These benefits extend not only to patients' short- and long-term health, but to lower cost of prescription medications and lower risk of medication side effects.

There are limitations to this study worth noting. First, the majority of patients of the PBLM Program were highly motivated individuals who self-referred into the program. Consequently, the findings may be biased upwards if these individuals were more earnest in their attempts to adhere to program recommendations than a typical patient. Second, some patients reported they were already following a healthful plant-based diet at baseline. Therefore, it is also possible that the study did not fully capture the clinical benefits of transitioning from a less-healthful dietary pattern; this would bias the findings toward the null. Third, findings for the full sample includes patients with a variety of baseline conditions potentially obscuring changes for individual outcomes when only a subset of patients would be expected to improve. Fourth, without a comparison group, we cannot be certain that improvements in clinical outcomes were a result of participation in the PBLM Program. Fifth, certain clinical measurements used in this study may be unreliable. For example, in-office blood pressure measurements are known to be unreliable due to "white-coat" effects and improper measurement technique (55, 56). Additionally, lipid measurements may have been impacted by inconsistency in whether patients fasted prior to measurement. However, this limitation does not apply to non-HDL-C measurements which are not significantly affected fasting status. Sixth, it is also important to note that at times sample sizes were rather small, particularly when evaluating subgroups. Small sample sizes result in reduced power to detect statistically significant differences, as well as increased margin of error. However, because the primary goal of the evaluation was to assess implementation and demand, this study was not designed or powered to assess the PBLM Program's impact on clinical outcomes and can only provide a preliminary signal as to the effectiveness of the program. Despite these limitations, this study is novel and to our knowledge, the first of its kind to include an under-resourced and vulnerable population in a public healthcare setting.

Given the burden of chronic disease and the high cost of health care, it is essential that the care delivery system move beyond merely managing lifestyle-related illnesses, but rather, addressing their key root causes. Lifestyle medicine, where providers help build a foundation for healthful eating, active living, and emotional resilience, is a promising approach for reaching this goal. The findings from this pilot study are encouraging and may have implications for healthcare practitioners and health systems. Further study is needed to demonstrate additional health benefits over time and the potential for cost-savings to society.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

Approval for this study was obtained by the NYU Grossman School of Medicine Institutional Review Board and the Office of Research and Administration for Implementation at NYC Health + Hospitals/Bellevue. Written informed consent was not required for this study in accordance with the national legislation and the institutional requirements.

Author contributions

SLA and MM co-designed the study. SLA led the study and drafted the manuscript. REM led data management and performed data analysis with LK. LC and MM led data acquisition. HEA advised data analyses. All authors contributed to the interpretation of the results, writing the manuscript, and approved the final draft.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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Culturally-tailored cookbook for promoting positive dietary change among hypertensive Filipino Americans: a pilot study

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Introduction: Among all Asian American subgroups, Filipino-Americans have consistently been shown to have the highest rates of hypertension, raising risks of heart attack and stroke. Despite this alarming fact, little has been done to investigate culturally-sensitive interventions to control hypertension rates in this vulnerable population. To address the lack of culturally-relevant lifestyle options for blood pressure management currently available to the Filipino community, this exploratory pilot study used a design thinking approach informed by culinary medicine to develop a culturally-tailored, heart-healthy, and low sodium recipe cookbook for Filipino Americans with hypertension and evaluate its feasibility as a hypertension intervention.

Methods: Our team developed a cookbook using participatory methods and design thinking, utilizing input from five Filipino culinary experts and a Registered Dietitian. The cookbook incorporates traditional Filipino recipes, excerpts from community members' interviews, and nutrient analyses. Twenty Filipinx-identifying individuals* who self-reported physician-diagnosed hypertension were recruited from Filipino community-based organizations, enrolled into this study, provided with the cookbook, and asked to cook at least one recipe. Pre- and post-intervention surveys were conducted and centered around behavior change and features of the cookbook.

Results: This study provided evidence for the cookbook's acceptability and feasibility, with participants' open-ended responses revealing that the recipes, nutrition labels, illustrations, and cultural aspects of the cookbook increased motivation to achieve dietary change, including reducing sodium in their diet to improve their blood pressure. Participant responses also indicated positive behavior change as a result of using the cookbook, with participants reporting increased likelihood of adopting recommended actions to lower their BP after utilizing the cookbook ($\bar{x}$ = 80.83%), compared to before ($\bar{x}$ = 63.75%, $p < 0.008$), according to Hypertension Self-Care Management scaled scores.

Discussion: In conclusion, the results of this pilot study demonstrated acceptability of this unique cookbook and provide preliminary findings consistent with increased motivation in participants to make dietary changes and improve personal health, drawing attention to the importance of considering future culturally-tailored health interventions. Next steps should include a robust, randomized controlled trial design comparing measured blood pressure outcomes of an intervention vs. control group. *Filipinx is an inclusive term representing the gender identities of all participants in our study.

KEYWORDS

hypertension, dietary change, culturally-tailored intervention, lifestyle change, cardiovascular disease, culinary medicine, cardiometabolic disease, Filipino cookbook

1. Introduction

Filipino Americans account for the third largest Asian American population in the U.S (1, 2). For consistency in this paper from here on, we will refer to this specific Asian subgroup as Filipino Americans. This population consistently shows disproportionately higher rates of hypertension in comparison to non-Hispanic White adults in the US (3, 4). Within the U.S. population, non-Hispanic Asian males and females have a prevalence of high blood pressure of 51.0 and 42.1%, respectively (5). However, when data are disaggregated by subpopulation, among all Asian American subgroups, Filipino Americans suffer from the highest rates of hypertension (3, 4). Studies have estimated that three in five Filipino American adults have a diagnosis of hypertension (6) and that more than half of Filipino Americans aged 50 and over will develop hypertension (7). Despite this alarming disparity, little research has been done to investigate culturally sensitive interventions to help control high blood pressure or to reduce rates of hypertension in this community. A recent study also found that hypertension awareness, treatment, and control rates among Filipino Americans were shockingly low, indicating that a majority of Filipino Americans with hypertension experience poor hypertension management (8).

Poor medical management and control of this chronic condition, as well as a variety of cultural factors, may contribute to the high rates of uncontrolled hypertension in Filipino Americans. These cultural factors include the traditional custom of sharing meals contributing to difficulties in reducing caloric intake (9) and limited medical visits due to patients not visiting until their condition is more advanced (9). Furthermore, there is a high prevalence of smoking among Filipino Americans (17%) (10), paired with a decreased likelihood of smoking cessation in a social setting due to the Filipino value of *pakikisama* (desire to get along with others to prevent conflict) (11). One major factor contributing to high prevalence of hypertension among Filipino Americans is dietary intake. The "westernized" Filipino diet consists of foods high in sodium which can exacerbate hypertension, foods high in fats, and readily digestible, refined carbohydrates, which can contribute to worsening cardiometabolic conditions (12, 13). Studies have found that the Filipino diet consists of an average of 12 g of sodium–eight times higher than recommended by the American Heart Association (10). In an attempt to help reduce and control blood pressure in hypertensive Filipino Americans, many physicians may recommend generic lifestyle modifications. Furthermore, physicians recommend dietary modifications that gravitate toward traditional American cuisine, such as the widely recommended Dietary Approaches to Stop Hypertension (DASH) diet that discourages intake of refined carbohydrates, such as white rice (14), that is reported to be a central part of the daily Filipino diet (15, 16). Existing literature has also found that patient-centered, culturally-sensitive patient-physician communication is severely lacking for ethnic minority populations (17, 18), with multiple case studies highlighting the tendency of providers to recommend the removal of cultural foods from patients' diets completely (19). As a result, many Filipino Americans struggle with making modifications to their diet because they do not know how to, or simply do not want to modify their diet in this way. Certain dietary changes may compromise the taste of traditional Filipino food that could make adherence more difficult (16). In addition, some patients express they want to eat the same foods as family members or are concerned that making changes in diet will of necessity exclude other family members (20). These modifications are thus perceived to reduce what is a critical family joy of eating all together, a value that is especially prevalent within the Filipino American community (15). Therefore, there is a need for more culturally-tailored approaches to encourage dietary change in hypertensive Filipino Americans struggling with blood pressure management, especially support for adopting lifestyle changes.

Despite the clear necessity for more culturally nuanced dietary approaches to address high rates of hypertension in the Filipino community, few studies have been conducted to help solve this problem. While culturally-nuanced training has been provided by the Filipino American Cardiovascular Health Conference on best practices for physician interaction and counseling for Filipino patients, it has not been published (21). In our review of existing literature, we were able to find only one study in which the researchers demonstrated that a culturally-tailored educational intervention that promotes physical activity and reduces dietary sodium intake among Filipino Americans resulted in a significant reduction in blood pressure in comparison to the control (22). Other culturally-sensitive dietary interventions for Filipino Americans found were focused on non-heart related diseases, including cancer (23) and diabetes (24). Other interventions which apply a cookbook as part of their dietary intervention include ones that targeted African Americans for healthy dietary change (25), or Mexican-Americans for decreased sodium consumption and increased fruits and vegetable intake (26). Similarly, single recipes or cooking demonstrations have been part of multi-component interventions to decrease meat consumption (27) or increase purchasing of produce, including for Latino/a populations (28). The positive dietary change results from these dietary interventions, along with specific evidence from the DASH trial

(29) showing diets which emphasize fruits, vegetables, and low sodium foods reduce blood pressure in hypertensive patients, serve as the rationale behind our intervention design to target a unique population and support the promise of culturally-tailored interventions.

Culinary medicine interventions include clinical and public health approaches for food-based education and skill training to increase access to disease-preventing and higher quality foods (30–32). It encompasses the aforementioned dietary change principles and may positively impact hypertension outcomes. Studies have found that culinary medicine approaches are low-cost and high-impact (33), have improved dietary attitudes, culinary skills, and dietary intake, and can increase self-efficacy and competence in nutrition knowledge (32, 34)–all of which are found to be important for blood pressure control (35, 36). While this intervention type has been shown to be successful, studies have also highlighted the need for cultural competency in this setting, with findings of higher diet adherence, improvements in disease management, and lower chronic disease burden when cultural elements are incorporated (37). Similar to other dietary intervention studies found in our review of existing literature (23, 24, 28), culturally-focused culinary medicine studies have predominantly been conducted in Hispanic/Latinx populations and in populations with diabetes (75%) (30, 37). Despite its importance, studies have highlighted a gap in culinary medicine interventions focused on Asian populations–despite recognition of this population's increased cardiovascular disease risks (37). Despite this lack of literature, a nascent culinary medicine movement is seen to be rising in popularity within the Filipino community, with an established group of more than 2,000 members predominant on social media (38). These findings further highlight the need for the implementation and robust study of similar interventions in hypertensive, Filipino-based communities. Overall, the successes from these prior studies further support applications of design thinking to create a culturally-appropriate culinary medicine cookbook intervention for Filipino-Americans with hypertension.

In addition to the previously mentioned desire to reduce the gap in this field of heart-healthy nutrition research, the personal connection of one of our first authors (D. Pack) to this specific topic serves as inspiration for this project and the writing of this manuscript. Within the cookbook, Pack recounts a specific personal story involving his grandfather (or Lolo in Tagalog) that served as inspiration for the creation of this unique cookbook intervention; we share a summarized version of that with readers here:

"Mr. Bianes, your blood pressure is extremely high. I am going to recommend that you modify your diet and perhaps cut Filipino food out completely because it's too unhealthy." I remember my Lolo's (grandfather's) physician saying this as I sat in on one of his doctor's appointments. I simply could not come to terms with the notion that cutting out ALL Filipino food from our diets is the solution to improving diet-related chronic health conditions like hypertension, diabetes, or cardiovascular disease. I felt determined to explore culturally sensitive solutions that allow Filipino patients to continue eating foods that are true to their roots of Filipino culture and cuisine while simultaneously improving their health. My hope is that this cookbook will provide others with the tools needed to embark on their own journey of improving health and rediscovering Filipino roots, culture, and cuisine.

This current study will help address the identified gap in interventions by applying design thinking to culinary medicine approaches including creation of this prototype cookbook, and gathering formative implementation data. Here, we explore the design and piloting of a culturally-tailored cookbook intervention aimed at helping Filipino Americans make modifications in certain less healthy aspects of Filipino foods, by incorporating more plant-based foods, reducing sodium in cooking, and applying other heart-healthy eating strategies, while preserving attention to cultural cuisine and flavor. An additional goal is to empower individuals with hypertension to improve their blood pressure control through dietary change, ultimately helping to reduce the disproportionately high rates of hypertension that exist amongst Filipino Americans.

2. Methods: intervention design and pilot study

2.1. Human subjects ethics statement

This pilot study was added as an amendment onto a larger IRB approved study, "Comparative Effectiveness Study of Technologies to Promote Blood Pressure Control" conducted by Dr. Susan L. Ivey (PI). After discussion with The Committee for Protection of Human Subjects (CPHS), at the University of California, Berkeley, this pilot study did not require further approval from CPHS to proceed (IRB Protocol 2019-04-12136).

2.2. Formative work: applying design thinking

In this phase of the research project, Pack and team used an iterative design process (39) and culinary medicine approaches to create a prototype heart-healthy Filipino recipe book (going forward, we refer to this as the cookbook). First, the decision to use a recipe-based intervention was rooted in the culinary medicine principles of reducing the food knowledge gap (40), increasing development of food agency (41), and encouraging healthy food enjoyment (in replacement of enforcing unhealthy food avoidance) (33), through providing healthy ingredient choices, flavoring techniques, and cooking methods in these recipes (42). A key culinary medicine recommendation is to seek collaboration between nutrition experts, Registered Dietitians (RD), and specialists with culinary training (42). Thus, the first step was to engage several Filipino culinary experts from whom to seek advice, while also assembling a team of advisors including fellow students, a physician faculty expert in hypertension and lifestyle change, and an RD, who would provide input on design, development of recipes, dietary analysis of dishes based on average portion size, and basic dietary cardiovascular risk reduction principles for lowering blood pressure.

The team examined possible ways to make modifications to classic Filipino recipes, exploring potential ingredient substitutes, alternative cooking methods, and plant-based alternatives. The ultimate goal was to develop and/or identify existing recipes that would be heart-healthy, defined as lower sodium, lower fat, lower cholesterol, and higher fiber foods, while still being flavorful and culturally acceptable.

After networking and connecting with Filipino culinary experts in this field, Pack and team chose a diverse group of five Filipino individuals to contribute recipes and unique stories to the cookbook. In the selection process of choosing the five Filipino individuals to contribute to the cookbook, we carefully selected individuals who would add different perspectives on various themes that the team ultimately wanted to convey throughout the cookbook. There were no specific inclusion/exclusion criteria other than that the individuals had to identify as culturally Filipino and/or Filipino American and be in a "culinary and/or food related" career. The definition of a "culinary and/or food related" career was not strict, and ultimately diverse careers were represented in the individuals that were selected ranging from commercial chefs, herbalists, food justice advocates, business owners, and public health advocates. Ultimately, Pack and team reached out to five individuals to contribute to the cookbook through email and all five accepted to be interviewed and agreed to contribute a recipe to the cookbook.

In order to gather stories, each contributing individual met with Pack virtually through Zoom and was asked a subset of semi-structured interview questions pertaining to topics curated based on three major themes: (1) Topics focused on deconstructing and reversing the damaging narratives that portray Filipino cuisine as "unhealthy," (2) Topics highlighting the importance of reconnecting with the land and foodways of our ancestors, and (3) Questions highlighting how to make healthy modifications to the Filipino cuisine, without compromising flavor profile. Questions for each contributing individual were tailored to the interviewee's background and expertise. Interviews lasted around 30 min, were recorded, and subsequently transcribed. Each contributing individual was asked to donate a recipe to the cookbook and to describe their inspiration for the specific recipe they donated.

Once recipes were submitted by each culinary expert, an RD conducted nutrient analyses to evaluate the nutritional quality of each recipe and determined if they could be categorized as heart-healthy. To do this, the RD utilized ESHA Research's Food Processor Nutrition Analysis software, which contained a food and nutrition database with information from the Food and Nutrient Database for Dietary Studies (FNDDS), the USDA Standard Reference database, manufacturer's data, USDA FoodData Central Brands (43), among others, to create a nutrition label delineating the total calories, total fat, sodium, cholesterol, total carbohydrates, protein, vitamin D, calcium, iron, and potassium contained in a set portion of each recipe (as determined by the culinary expert). Based on this analysis, the RD ensured that each recipe was appropriate for people with cardiometabolic disease, and suggested heart-healthy modifications for recipes deemed to be out of specification. Specific nutrients focused on were total calories, total fat, and sodium, with the RD providing recommendations of decreasing serving size, decreasing ingredient amount, and replacing certain ingredients with healthier ones. Examples of these included recommending intake of a smaller portion size, decreasing the amount of sugar added, and utilizing low sodium soy sauce or light coconut milk instead of their calorically dense counterparts. Once adjustments were implemented and approved by the RD, an official nutrition label was created to be easily displayed and interpreted by cookbook readers.

2.3. Intervention design

The team then applied design thinking to structure the contents of the cookbook. Design thinking is an "applied research and innovation framework that prioritizes *empathy* for users of a service or product, involves highly diverse and collaborative project teams, and encourages an action-oriented rapid prototyping of user-derived insights rather than top down hypotheses" (44). This process involves five key components: the Empathize mode (observing and learning about the population of interest), the Define mode (framing a specific meaningful problem to address), the Ideate mode (collaborating with key stakeholders and brainstorming ideas to resolve the issue), the Prototype mode (creating tangible prototypes users can interact with), and the Test mode (refining prototypes through user feedback) (45). Applying this framework to our project, this prototype stage consisted of developing, testing out, and photographing the recipes, then compiling the text (including stories and chef information) and photos into a visually appealing, cohesive cookbook. This cookbook was created in Canva under a Pro Content License. The cookbook was designed with themes of tradition and "reconnecting to our roots" in mind, and with a goal of making each recipe inviting and less daunting to follow. This was conveyed through culturally relevant textiles and colored backgrounds, as well as floral and plant-based imagery applied throughout each page to evoke a sense of authenticity and familiarity (**Figure 1**). Complementary colors, ingredient graphics, and images of each recipe provided an enticing representation of each dish and demonstrated its feasibility to a proposed target audience. These recipes' authenticity was supplemented with a foreword by each culinary expert, explaining their background, cultural significance of each dish, and rationale of their ingredient choices (**Figure 2**). In addition to the recipes, specific dietary education on the health benefits of each dish was included and written in a manner that was likely to be understandable to our population of interest. The nutrition facts of each recipe were similarly positioned to be more readable and less complex, through continued use of an inviting background, supporting graphics, and clear labeling (**Figure 3**). Overall, we created our cookbook with a story-telling framework, incorporated anecdotes and imagery, and paired recipes with health information to create a culturally competent heart-healthy Filipino cookbook. The prototype cookbook was reviewed by chefs, dietitians, and team members, and assessed to be ready to test out in a sample population. In addition to featuring classic Filipino recipes, priority was also placed on utilizing traditional Filipino ingredients, such as tamari, garlic, calamansi, coconut vinegar, and spicy peppers, and employing culturally-appropriate terminology throughout the cookbook, like *ampalaya* (in lieu of their westernized counterpart of bitter melon) and *patis* (fish sauce), paired with graphics that highlighted these ingredients (**Figure 4**).

2.4. Pilot study phase

Eligibility criteria for the pilot study included being over the age of 18, self-identifying as Filipino/a/x, self-reporting physician-diagnosed high blood pressure, and living in the San Francisco Bay Area. In order to screen for physician-diagnosed high blood

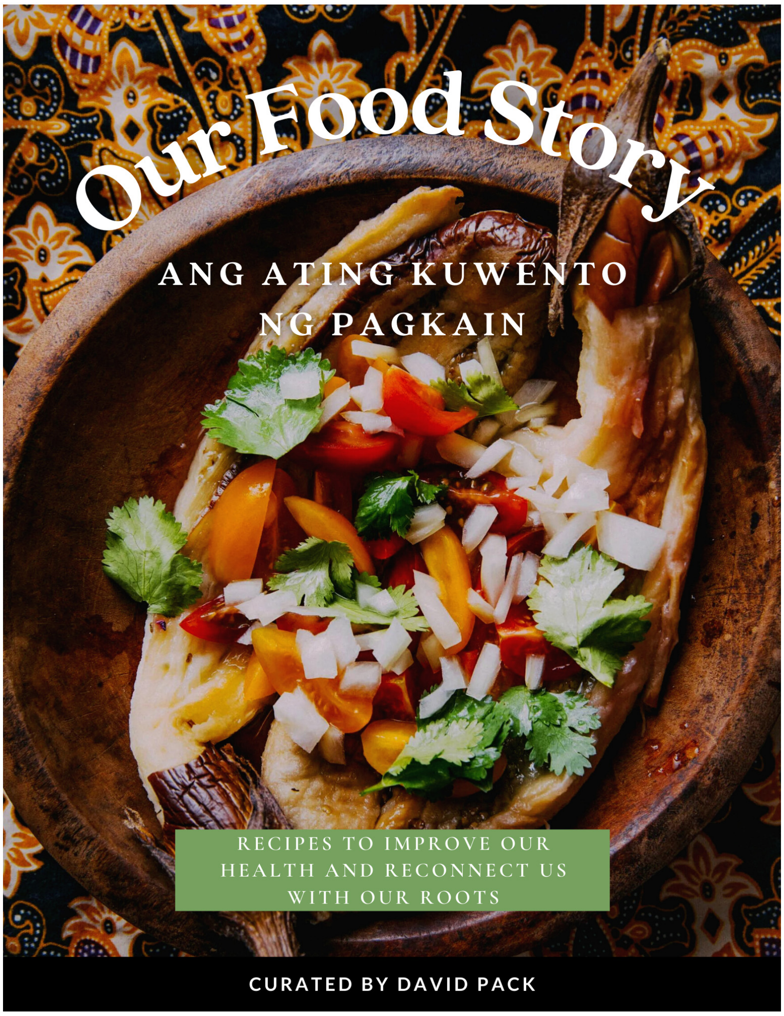

FIGURE 1
Introductory page of the cookbook, containing a floral and plant-based background. Extends an invitation to readers to start their culinary journey while reading the text.

pressure, potential participants were asked the question, "Have you previously been told by a physician that you have high blood pressure?". The sampling frame for recruitment included community members drawn from local community free clinics, cultural-based organizations, and Filipino-serving community-based organizations. Ultimately, recruitment was done through presentations to these various organizations, virtual flyering, and through word-of-mouth. The recruitment process took place June 7th–June 18th, 2021. Once we developed the intervention, the team set a target goal to enroll at least 20 participants into the pilot study. We chose this target sample size of 20 participants due to the time and budget constraints of this small pilot study. A total of 22 participants were initially screened; however, two participants did not meet the eligibility criteria. Thus, twenty people who met the eligibility criteria were ultimately enrolled into the pilot study. We then asked the enrolled participants to use a copy of the cookbook prototype for 3 weeks, to cook at least one of the recipes in that period, and to complete a pre- and post-use survey including providing feedback on use of the recipes and cookbook, ease of cooking different dishes, and acceptability of the recipes.

Dietary change was assessed in the post-intervention survey through questions pertaining to fruit and vegetable consumption, sodium intake, and likelihood of using specified recommended actions to lower blood pressure, as well as through direct questions related to perceived motivation and success in achieving these dietary change behaviors.

2.5. Data collection

Participant data were gathered through structured surveys conducted using Qualtrics (Qualtrics, Provo, UT, USA) between June 19th and July 21st, 2021, for the baseline survey and August 4th–August 15th, 2021, for the post-intervention survey. The baseline survey was centered around topics of age, gender, educational attainment, living situation, self-rated general health status, fruit and vegetable intake, access to fresh and affordable foods, blood pressure medication use, COVID-19 impact, and contained questions from the Self-Care of Hypertension Inventory scale (SC-HI) (v. 2.0, March 2016) related to maintenance,

FIGURE 2
Culinary expert introduction and recipe forward, providing readers with the cultural background of the dish and importance of its heart-healthy modifications.

confidence, and management for persons with hypertension, to obtain an understanding of their current health behaviors (46). This SC-HI scale instrument underwent content and scale validation in a sample of hypertensive individuals drawn from multiple outpatient clinical settings across the United States. This sample was gender and ethnically diverse (70% female, 60% Black, 32% White, and 6% Latino) with a mean age of 56.4 ± 13 years (46). Comparatively, our sample was 45% female, the mean age is 44.5 ± 14.5 years, and our sample was ethnically Filipino. The physician on the team (S. L. Ivey) had used these scales successfully in a local California population of diverse patients (∼20% API) with high blood pressure. The authors of the scale we used have successfully used this scale in Brazilian populations (47, 48) and have worked on a hypertension self-care scale in Filipino-Americans (49).

The post-intervention survey contained a mixture of closed and open-ended questions and was focused on dietary behavior change and usability and acceptability of the cookbook, with the first block containing questions about perceived health status, blood pressure control, motivation and success in dietary change, and questions from the Self-Care Management subscale from the SC-HI. The other two subscales of the SC-HI, the Self-Care Maintenance subscale and Self-Care Monitoring subscale, were not part of this survey as this intervention focused on promoting hypertension management behaviors, and we sought to increase participant engagement on this survey by using the survey instrument most relevant to our study. Given that each subscale is intended to be scaled and standardized separately, as per scale instructions provided by its authors, and noted to have good internal consistency (46), the removal of these two subscales from the survey does not impact the overall interpretation of participants' hypertension management behaviors (50). The second block contained questions specifically related to the cookbook,

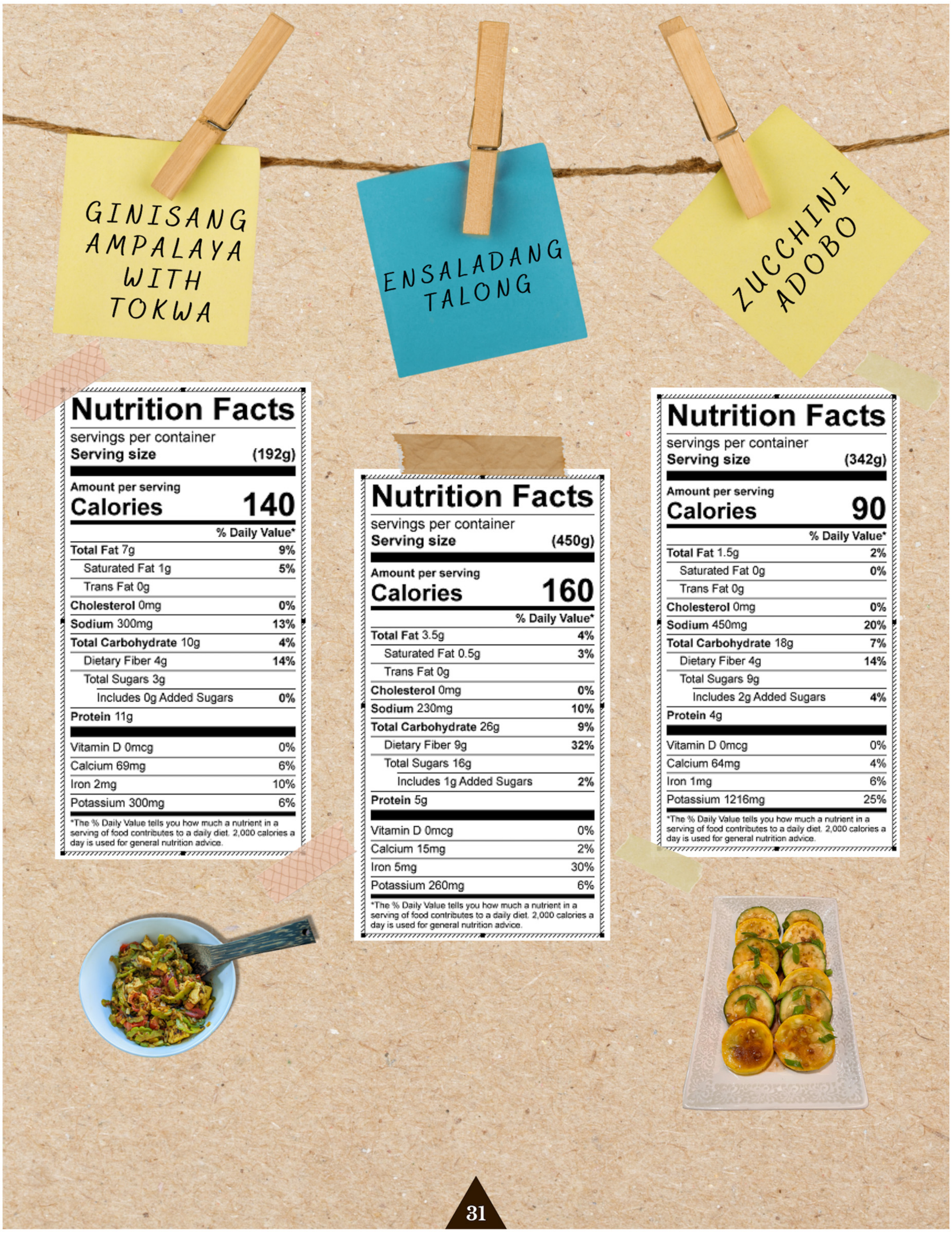

FIGURE 3
Nutrition labels of three recipes created by a Registered Dietitian. The page was formatted with images of the dish and casual design elements to be more approachable and understandable for our readers.

with closed-ended questions about the ease of following recipes, affordability of ingredients, and their likelihood of recommending this cookbook to others. This block also utilized six open-ended questions that asked participants to share their opinions on each section of the cookbook–the story-telling approach, the text sections before and after each recipe, and the illustrations included–as well as their general thoughts on their experience using the cookbook, favorite aspects of the cookbook, and suggestions for improving it. All instruments and questions were in English, and interviews were conducted in English.

ZUCCHINI ADOBO

This recipe is Chef Dominic's Filipino take on a simple Chinese style eggplant dish he learned while working at his first restaurant. He decided to choose zucchini instead for this recipe because it is a very versatile ingredient that works well roasted, steamed, or fried. He then "Filipino-ized" it by tossing it in a homemade adobo sauce that is bright, tangy, and most importantly tasty!

PREP TIME	COOK TIME	SERVINGS
10 - 15 mins	15 - 20 mins	1

INGREDIENTS

1 Zucchini (medium size, about 9 oz)
2-3 green onions
Adobo Sauce (enough for 4-5 servings):
- **1** tsp vegetable oil
- **1** tbsp ginger
- **1** tbsp garlic
- **1/4** cup water
- **1/4** cup soy sauce/Tamari
- **3/4** cup vinegar
- **2** tsp black ground pepper
- **1** tbsp sugar

Slurry:
- **1** tbsp cornstarch
- **1** tbsp water

INSTRUCTIONS

Adobo Sauce:

1) In a small saucepan on medium, add the oil and sauté garlic and ginger until tender.

2) Add the soy sauce, vinegar, water, black pepper and sugar in the garlic/ginger mixture; let simmer for a few minutes to bring all the flavors together.

3) After a few minutes of simmering, bring up the temperature to a beginning boil, then slowly add the cornstarch slurry (1 tbsp water mixed with 1 tbsp cup cornstarch) to thicken. Mix well. Not too thick. You should see all the ingredients begin to float within the soy/vinegar and not fall to the bottom. Then remove from heat and set sauce aside.

Zucchini Adobo:

1) Cut Zucchini into 3/4" rounds, roast on 375°F to al dente. This is about 10-12 minutes.

2) Remove from oven and add the roasted zucchini in a separate bowl and toss with the adobo sauce.

3) Pour the combined ingredients onto a plate and top with sliced green onions as garnish.

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FIGURE 4
Zucchini adobo recipe featuring traditional ingredients and their accompanying graphics, as published in the cookbook.

2.6. Data analysis: quantitative and qualitative

After the implementation phase, twenty pilot participants completed an exit survey to share their thoughts on the cookbook. In our analysis of the data, we compared participants' closed-ended responses related to dietary and lifestyle behaviors before and after the 3 weeks period to evaluate changes in these factors that could be attributed to the intervention. These direct comparisons were made possible through the verbatim utilization of the same behavioral questions in both the pre- and post-intervention surveys.

First, we checked the normality of participants' quantitative scaled scores through the Shapiro-Wilk normality test utilizing RStudio (version 4.2.2), to determine if a parametric test could be used to compare for significant differences in score before and after intervention. As this test resulted in a non-significant p-value ($p > 0.05$), we proceeded with a paired T-test to assess individuals' scores for differences in behaviors. For Likert scale-based items, we conducted a proportion-based analysis to understand if the overall intervention group had shifted their perspectives toward specific aspects of hypertension-based behaviors. A Pearson's chi-square test was conducted in RStudio to understand whether these shifts in proportion of each response were statistically significant. A proportion-based analysis was also conducted for qualitative, closed-ended responses in the post-intervention period that did not have a comparison counterpart in the pre-intervention survey, to understand attitudes of participants toward components of the cookbook. Graphical representations were created using RStudio for clearer presentation of this data.

To conduct qualitative data analysis, we utilized participants' open-ended responses, in which participants disclosed how they felt toward the recipes, the design, the excerpts from the culinary experts, and any other suggestions or closing thoughts. These responses were evaluated and divided into these related categories: participant acceptability and satisfaction with intervention, and hypertension-based behavior changes following intervention. Two designated study team members worked together on this content analysis with thematic coding of participant responses, then the entire study team reviewed these categorizations and contributed to their interpretation. No inter-rater reliability was calculated given the very small number of interviews (n = 20). Through the categorization and analysis of responses, in conjunction with data from the quantitative analysis, we were able to organize interpretation of results.

3. Results

We first cover our qualitative results from the formative interviews, followed by results from the pilot participants.

3.1. Results of culinary expert interviews

Our team conducted formative individual interviews with the Filipino culinary experts who each provided a recipe for the cookbook. In these interviews, they shared their thoughts on the topics of authenticity, home, tradition, health, and inspiration for their recipes. We include exemplary quotes from the culinary experts here, illustrating their approach to making modifications to recipes in order to create lower sodium, plant-based, or higher fiber dishes – all examples of changes that might reduce cardiovascular risks.

When asked about what authentic Filipino food means to them, many of the culinary experts shared similar sentiments that Filipino food is ever evolving and cannot be constrained by a singular concept of what "real" Filipino food is. As one culinary chef noted:

> *Authenticity changes. Food culture is not frozen in time, it changes. It's not static. We need to leave room for change and for growth. We need to look back at the roots, and honor them, (but) also know that the ideas of (what is) authentic will shift, that we are part of making culture.*

This idea is reflected upon further by two other culinary experts, who provided the example of adobo, the national dish

TABLE 1 Sociodemographic characteristics of participants.

	Overall (N = 20)
Age	
Mean (SD)	44.5 (14.5)
Median (min, max)	42.5 (23.0, 71.0)
Gender	
Female	9 (45.0%)
Male	10 (50.0%)
Non-binary	1 (5.0%)
Living alone?	
No	17 (85.0%)
Yes	3 (15.0%)
Currently working at a job?	
No	7 (35.0%)
Yes	13 (65.0%)
Providing care work?	
No	12 (60.0%)
Yes	8 (40.0%)
Unemployment	
Refused	1 (5.0%)
No	16 (80.0%)
Yes	3 (15.0%)
Currently searching for work?	
No	18 (90.0%)
Yes	2 (10.0%)
Number of hours working at a job or providing care work	
Mean (SD)	48.6 (18.7)
Missing	6 (30.0%)
Number of primary care visits (12 months)	
Mean (SD)	1.40 (0.940)
Number of years living in the US	
Mean (SD)	40.4 (11.8)
Missing	10 (50.0%)
Primary language spoken	
English	15 (75.0%)
Tagalog	5 (25.0%)
Education level	
High school or lower	2 (10.0%)
2 years junior or community college	2 (10.0%)
4 years college or university	12 (60.0%)
Graduate or professional school	4 (20.0%)
Born in the US?	
No	10 (50.0%)
Yes	10 (50.0%)

(Continued)

TABLE 1 (Continued)

	Overall (*N* = 20)
Number of times eating fruit per week	
Mean (SD)	6.15 (5.45)
Median (min, max)	4.00 (0, 21.0)
Number of times eating vegetables per week	
Mean (SD)	7.71 (7.30)
Median (min, max)	5.00 (0, 28.0)
Missing	1 (5.0%)
How often fruits and vegetables are affordable	
Always	7 (35.0%)
Sometimes	2 (10.0%)
Usually	11 (55.0%)
Never	0 (0%)
How often fruits and vegetables are accessible	
Always	14 (70.0%)
Sometimes	0 (0%)
Usually	6 (30.0%)
Never	0 (0%)
High blood pressure within the last month	
Don't know	8 (40.0%)
No	5 (25.0%)
Yes	7 (35.0%)
Currently taking blood pressure medication	
Don't know	1 (5.0%)
No	10 (50.0%)
Yes	9 (45.0%)
Had experienced lifestyle changes due to COVID-19	
No	8 (40.0%)
Yes	12 (60.0%)
Eating habits changes due to COVID-19	
Don't know	2 (10.0%)
Much more healthy	7 (35.0%)
Somewhat more healthy	8 (40.0%)
Somewhat less healthy	3 (15.0%)
Much less healthy	0 (0%)
Hypertension self-care management scaled score (%)	
Mean (SD)	63.8 (22.7)
Median (min, max)	66.7 (8.33, 91.7)
Hypertension self-care maintenance scaled score (%)	
Mean (SD)	50.9 (13.2)
Median (min, max)	51.5 (15.2, 75.8)
Missing	1 (5.0%)
Hypertension self-care confidence scaled score (%)	
Mean (SD)	60.8 (17.9)
Median (min, max)	61.1 (27.8, 94.4)
Missing	1 (5.0%)

of the Philippines. One culinary expert explained how different regions of the Philippines may use different techniques and ingredients to create the same dish depending on what is readily available to them, yet both are still adobo. Another expert described how adobo was once considered not authentic since it popularly includes soy sauce, an ingredient with Chinese origins, but now adobo is the national dish. She went on to bring up other Filipino dishes that are Chinese influenced, such as pancit, siopao, lumpia, and how these are now indigenized. She also stated what she is trying to capture with her recipes:

> *I am trying to recreate Filipino classics with plant-based ingredients. It is trying to capture the essence. It is not about re-writing the narrative.(They might feel) my nostalgia is not there because (I) changed the dish. But then in the Philippines, I realized the more different the better. They actually celebrate. "They put cheese in their pancit! Let's go there." But in the US, we feel like "how dare you put cheese in the pancit." All I can do is have the best intentions. I hope they understand that I veganize with high respect. It boils down to intention and execution.*

Here, we gain insight into the approach of this culinary expert for creating plant-based Filipino dishes while retaining authenticity. She acknowledged that some may not find vegan Filipino food to be authentic, but believes that they are not questioning its authenticity, but rather what is personal and familiar to them. Knowing this, she highlighted the importance of being intentional with her recipes as well as embracing a non-static attitude toward authenticity. In her words, *"saying that Filipino food can only be made one way is going against the grain of what Filipino food is."*

On the topic of health and how it relates to Filipino cuisine, one culinary expert discussed how "*the word 'healthy' can be charged*," as it "*depends on everyone's relationship to cooking, their class, our ancestral lineage, what was passed down to us, both the trauma and resilience.*" Given that in many communities, foods considered "*healthy*" may not be easily available or accessible, the concept of "*health*" may "*create some type of ableism.*" She explained that "*health does not have to be a binary construct or provoke polarization*," and suggested, for example, that rather than directly asking people to remove meat from their diet, to ask them to add more vegetables. Many of the culinary experts emphasized that the association between food and health is complex and not one-dimensional, paralleling their attitudes toward authenticity.

As another culinary expert recounted:

> *Food nourishes us in more than one way. Food nourishes us physically but also mentally, emotionally, and spiritually. Our traditional foods are ways in which we can illustrate those connections. Without these dishes, without access to these dishes, without access to ingredients, it also has a corollary effect on our overall health, not just physically but emotionally, mentally, and spiritually. There is a direct connection there.*

This culinary expert explained how food is related to various aspects of health and how the food we consume represents and embodies our relationships. He later shared how the recipe he provided was his lola's (grandmother's) recipe, and likely passed down by her lola before her, *"as a way to pass on that generational wisdom around how our foods are healing. It comes from our relationship with one another, our relationship with the earth, and our relationship with our ancestors and our culture,"* encapsulating his beliefs in the direct connection between food and our relationships.

These interviews provided valuable insight into the approaches of the project's culinary experts for developing their recipes. We also included their words throughout the cookbook in order to provide these personal stories about their connection to food, ancestral roots, and how to make changes with respect for authenticity so readers might follow along during their culinary journey. Overall, the interviews with the culinary experts effectively allowed each of them to provide more details about their backgrounds and experiences, and how that has translated into their attitudes toward these crucial topics surrounding food and nutrition.

3.2. Results: participant pre- and post-intervention surveys (closed and open-ended results)

Here we detail the participants' results following use of the cookbooks. All except two participants (of 20) noted they used one or more recipes, indicating a 90% participation rate.

3.2.1. Sample characteristics and baseline behaviors

The sociodemographic characteristics of the participants ($n = 20$) are presented in **Table 1**. Among participants, 10 identified as male, nine identified as female, and one identified as non-binary; their age ranged from 23 to 71 years old (mean = 44.5). The majority of participants had obtained a degree from a 4 years college or university or higher (80%). While all participants spoke both Tagalog and English, a majority of participants identified English as their primary language spoken (75%). There was an even proportion of participants who were born in the US (50%) and not born in the US (50%), with a mean number of years living in the US of 40.4 years (22.0–52.0). No dropouts occurred across this 3 weeks intervention, with all twenty participants fully participating in the study and pre-post data collection.

At baseline, participants reported consuming fruits and vegetables an average of 2.76 and 3.53 times per week, respectively. Adequate access and affordability of fruits and vegetables in their current food environments were observed, with 70% reporting that they always could find fruits and vegetables and 30% reporting that they could usually find them, as well as 35% reporting that they were always affordable, 55% reporting that they were usually affordable, and 10% reporting that they were sometimes affordable. The COVID-19 pandemic was also perceived to cause lifestyle changes among a majority of participants (60%), with 35% reporting that their eating habits became much healthier, 40% reporting that they were somewhat more healthy, and 15% reporting that they were somewhat less healthy.

When assessing hypertensive self-care behaviors through the three SC-HI sub-scales at baseline, participants had an average hypertension management score of 63.8%, maintenance score of 50.9%, and confidence score of 60.8%, indicating moderate levels of self-care.

3.2.2. Participant acceptability and satisfaction with intervention

Participants expressed that they highly resonate with the level of detail incorporated in both the recipes and the explanations behind their cultural aspects by the culinary experts, as it brought forth shared feelings of connection and empathy that encouraged them to try these heart-healthy recipes. As one participant wrote, "*I really loved the story telling aspect of this cookbook because it gave deeper meaning and connection to the food.*" Another participant reciprocated this positive feeling of having an understanding of the goal of the cookbook and shared how this was a motivating factor in sparking dietary change: "*I understand your approach. Food is medicine. The flavor profile was definitely there. The stories, along with the pictures made it compelling enough for me to try the recipes. It's a start. we all must have a beginning.*" It is evident that the intentional design of including the stories from the culinary experts had a beneficial impact on motivation levels for pilot participants and promoted familiarity with the recipes as participants tried them for the first time.

Furthermore, participants reported that the culturally tailored aspects of this cookbook helped shift their perspective on the feasibility of managing their hypertension by changing their dietary habits while still retaining their culture, with one participant describing their prior perception of being unable to feel healthy while eating Filipino foods: "*It felt nice to eat Filipino food and not feel very guilty about it*!" This optimistic sentiment of having a unique culturally-tailored invention was echoed by other participants, with another stating that "*Filipino cooking, as we know, is not the healthiest. But if there are recipes with healthier options available, we can continue to perpetuate our culture through food and feel good about ourselves at the same time.*" Such feedback from participants demonstrated how they understood and embraced a major goal of the cookbook and the culinary experts–to begin transforming fixed, negative thoughts on the healthiness of Filipino food by introducing a dynamic, multi-faceted, growth mindset toward health and food.

Thus, the inclusion of excerpts from these interviews into the cookbook enabled participants to obtain a deeper understanding of the stories and the roads traveled by the cookbook's culinary experts to provide a more intimate and guided culinary experience. This design element empowered readers to embark on dietary change as they tried out these novel heart-healthy recipes themselves.

Overall, participant responses from the post-intervention surveys highlighted the practical applications of this cookbook and suggest the preliminary feasibility of circulating the cookbook to a wider audience. All participants reported a positive degree of likelihood of recommending this cookbook to someone else–85% of participants stated that they were "very likely" to recommend, 10% of participants reported they were "somewhat likely" to, and zero participants reported that they would not recommend it.

3.2.3. Improvements in hypertensive self-care behaviors

While two of twenty participants reported they did not cook any recipes, all twenty participants were noted to have read through and thus understood the contents of the cookbook through their detailed open-ended responses. Furthermore, this high instruction compliance rate of 90% indicates that a majority of this group of Filipino American hypertensive individuals were willing to test one or more recipes.

Comparing participants' average Self-Care Management subscale scores from before ($\bar{x}$ = 63.75%) to after intervention ($\bar{x}$ = 80.83%) revealed an average increase of 17% across the study population (**Figure 5**). Assessing individuals' scores for differences in behaviors yielded significant results ($p < 0.008$), indicating that each individual participant was more likely to implement recommended actions to reduce their blood pressure after using the cookbook for 3 weeks. This behavior change is supported by an increased proportion of participants reporting they always eat fruits and vegetables (10% increase), an increase in participants reporting that they eat a low salt diet daily or frequently (10% increase), and an increased proportion of participants reporting that they frequently ask for low salt items when eating outside of their household (5% increase) after completing the intervention, as seen in **Table 2**. Although increases are non-significant ($p > 0.05$), these positive changes across multiple behaviors essential for hypertensive lifestyle change indicate a trend to follow in future rigorous studies.

This trend in improving hypertensive self-care behavior change was also observed in participants when they were asked to reflect on their motivation to achieve dietary change during their 3 weeks with the cookbook; 95% of participants responded that they felt at least somewhat motivated to achieve dietary change, and no participants reported being "*unmotivated*" (**Figure 6**). All participants reported varying levels of success in achieving dietary change within their 3 weeks of using the cookbook, with 10% reporting that they were extremely successful, 25% reporting that they were very successful, 35% reporting moderate success, and 30% reporting that they were somewhat successful (**Figure 7**). This cookbook was also seen to inspire further dietary change, with 80% of participants agreeing or strongly agreeing with the statement "*I intend to continue to work to achieve dietary behavior change to improve my blood pressure*" (**Figure 8**). These results are summarized in **Table 3**.

Participants also expressed appreciation for how the recipes were tasty, easy to follow, and overall appealing. This valuable feedback indicates the cookbook was well-received by participants, suggesting the practicality of distributing this intervention in a larger, more diverse population. Participants' open-ended answers about their experiences during the intervention phase further supports this idea, with one participant stating: "*The recipes were accessible and not very daunting.*" Another participant previously believed making heart-healthy dietary changes equated to a trade-off with taste, but shares how this cookbook helped transform their attitude: "*The recipes were easy to follow and tasteful even when the recipes only ask for a small portion of salt, oil, etc. They were delicious.*" Participants also attributed the effectiveness of this cookbook to its design elements, with its illustrations and photographs playing a large part in both understanding the recipe and motivating them to use the recipes. A participant explicitly pointed out that the images "*made me want to try out the recipes,*" while another described their thoughts on the functionality of the design:

> *I thought the illustrations and pictures were a nice addition and a necessity with any recipe book. Some people may not be familiar with some of the vegetables featured in the recipes, plus it gives us a guide on how the dishes are supposed to look like, at the end.*

Overall, the design thinking approach used to create this cookbook, paired with the comprehensibility of materials fostered by the culinary experts and dietitian expert, were observed to encourage positive health behavior change, further emphasizing the need for incorporation of culturally tailored dietary/cooking instruction into hypertension-based interventions.

Although participants' blood pressures were not measured in this pilot study, the exit survey revealed participants reported lower perceived blood pressure post-intervention. Specifically, 71% of participants who stated their blood pressure was high during the month prior to the study, reported their blood pressure was not high within the month of receiving and using the cookbook. This finding points to the preliminarily positive physiological effects of this intervention, which could be investigated in a larger study with a more rigorous design.

4. Discussion

This research project included a design phase paired with a small feasibility pilot assessing the effects of a unique culturally-tailored cookbook on dietary changes with hypertensive Filipino Americans. Using design thinking principles, the team worked with culinary experts, chefs, and advisors to create a cookbook that would reach our population of interest. The cookbook integrated storytelling with cultural recipes to better engage this population. The cookbook also featured selected information in Tagalog. The recipes were created in partnership with culinary experts and chefs to incorporate more plant-based foods and reduce sodium in traditional Filipino American dishes while retaining preferred flavors. This study demonstrated that the tailored cookbook was well-accepted by the population of interest and was effective in encouraging dietary change, with a future goal of reducing blood pressure.

The input received from culinary experts, paired with positive acceptance and behavior change reported by participants, provides a starting point for further hypertension intervention developments in the space of culturally-sensitive approaches for this underserved population. While existing literature highlights the disproportionate rate at which Filipino Americans are impacted by hypertension (3, 4, 6, 7), the lack of disaggregated data (3), and minimally available culturally-specific studies (22) conducted on this subpopulation underscores the necessity of this pilot study. Furthermore, multiple studies conducted on understanding health promotion beliefs and attitudes in the Filipino American population have emphasized the importance of incorporating these cultural considerations into healthcare practices and recommendations (9, 11, 15, 16, 20), as this formative study is focused on developing. Published studies focused on the Filipino American population that have utilized these cultural

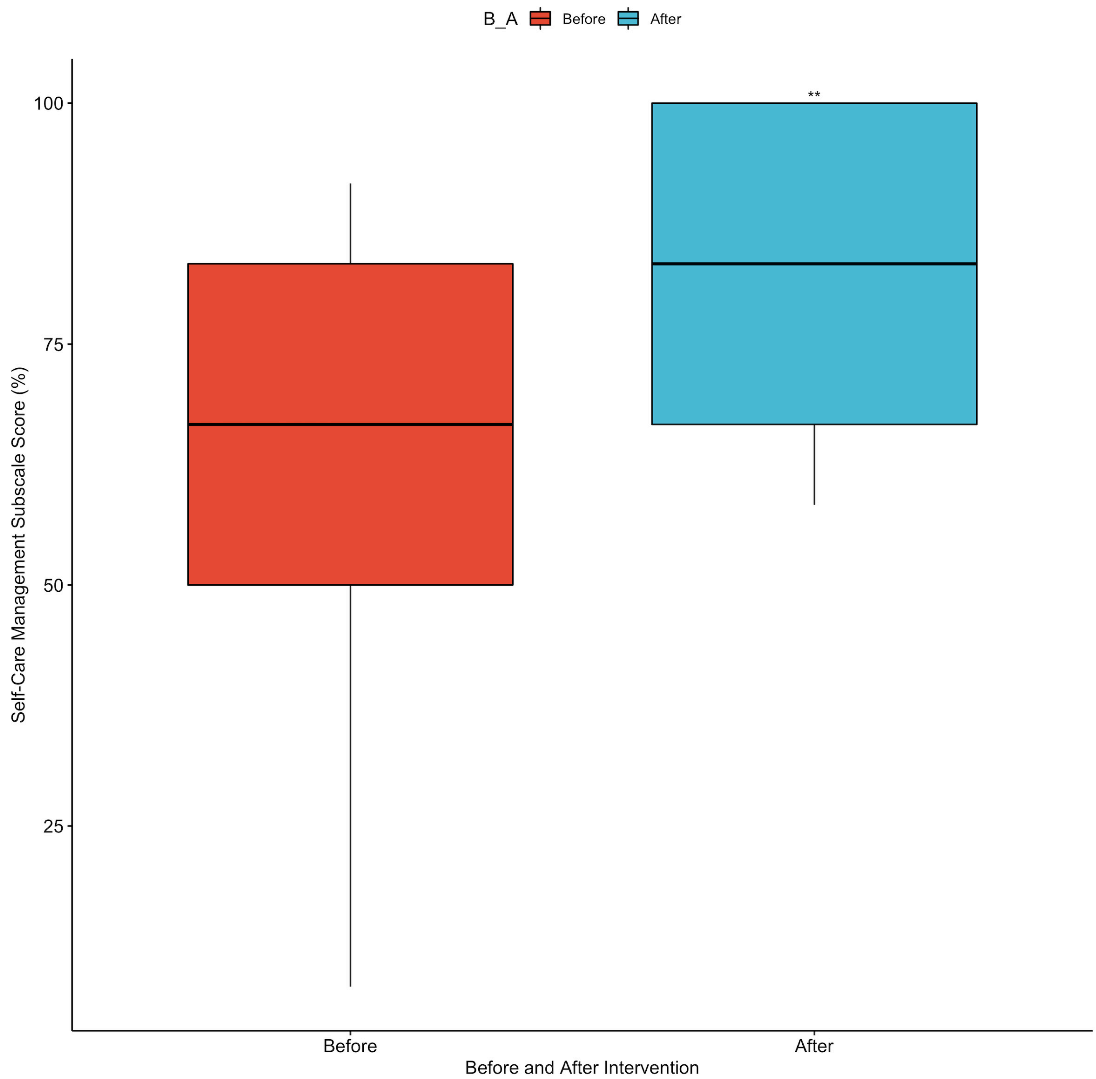

FIGURE 5
Boxplot of Self-Care Management subscale scores before and after intervention. **Indicates statistically significant difference, $p < 0.008$.

TABLE 2 Categorical sum of participant responses to selected Self-Care Maintenance subscale questions, before and after receiving intervention.

Self-Care Maintenance subscale questions		Response (%)				
		Never or rarely	Sometimes	Frequently	Always or daily	Missing
How routinely do you eat lots of fruits and vegetables?	Before	5	25	40	25	5
	After	0	30	35	35	0
	Net change	−5	+5	−5	+10	−5
How routinely do you eat a low salt diet?	Before	10	75	10	5	0
	After	25	50	15	10	0
	Net change	+15	−15	+5	+5	0
How routinely do you ask for low salt items when eating out or visiting others?	Before	65	30	5	0	0
	After	55	35	10	0	0
	Net change	−10	+5	+5	0	0

factors in their interventions have only included diet as an aspect of a multi-component hypertension-based intervention (22) or have only focused their interventions on non-hypertension conditions (23, 24). The results of our study also align with results observed in other culinary medicine-based studies, with the increase in self-efficacy, improved dietary attitudes, and improved dietary

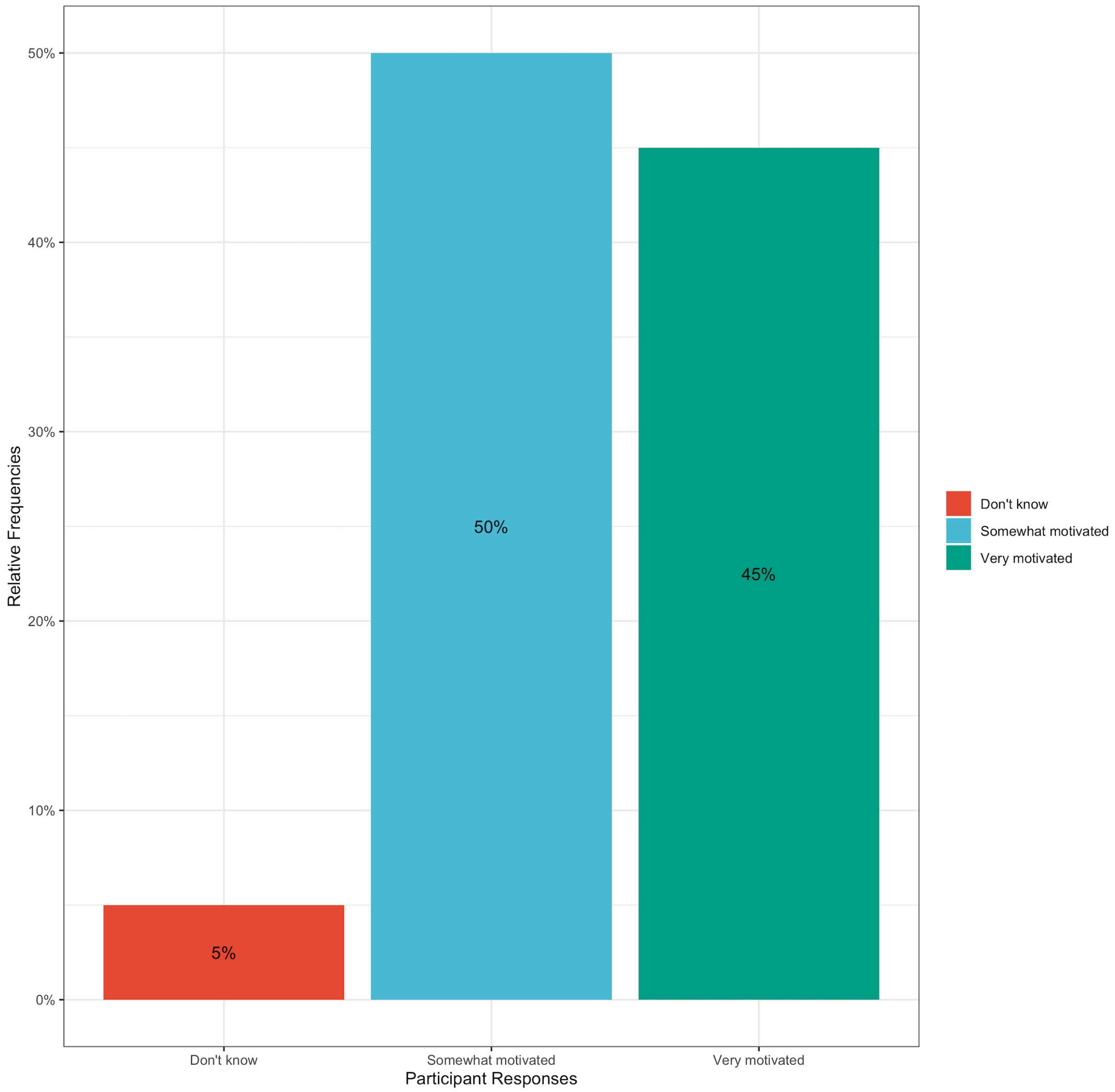

FIGURE 6
Bar graph of percentage of participant responses to post-intervention survey question: How motivated would you say you have felt during the past 3 weeks to achieve dietary change? Answer choices included: Very motivated, somewhat motivated, neither, somewhat unmotivated, and very unmotivated.

behavior change reported in literature (32, 34), as well as a significant increase in participants' Self-Care Management scores, following our culinary medicine intervention. Thus, this study addresses the lack of robust literature on culturally-nuanced dietary approaches developed to reduce hypertension in the Filipino American population and demonstrates the appeal of specifically tailored interventions for high risk groups.

4.1. Strengths

Strengths of this study include extensive front end processes to connect with Filipino American culinary experts, who would have interest and capability to provide heart-healthy recipes, and a student design team with caring connections to heritage and visual design that would appeal to the target audience, as well as a registered dietitian who volunteered time to conduct nutritional analyses. While the pilot is small, by engaging with a local Filipino-serving community clinic, we were able to recruit individuals who reported a prior diagnosis of hypertension. First author (D. Pack) also brought "in language" resources to translate sections into Tagalog, given this was a very low budget student-driven project of the heart. This is one of just a handful of studies conducting research pertaining to cardiometabolic-based interventions for Filipinos, with only one published paper to date investigating culturally-relevant dietary modifications for this large, underserved subset of the population. Furthermore, the results of this study corroborate the positive dietary change

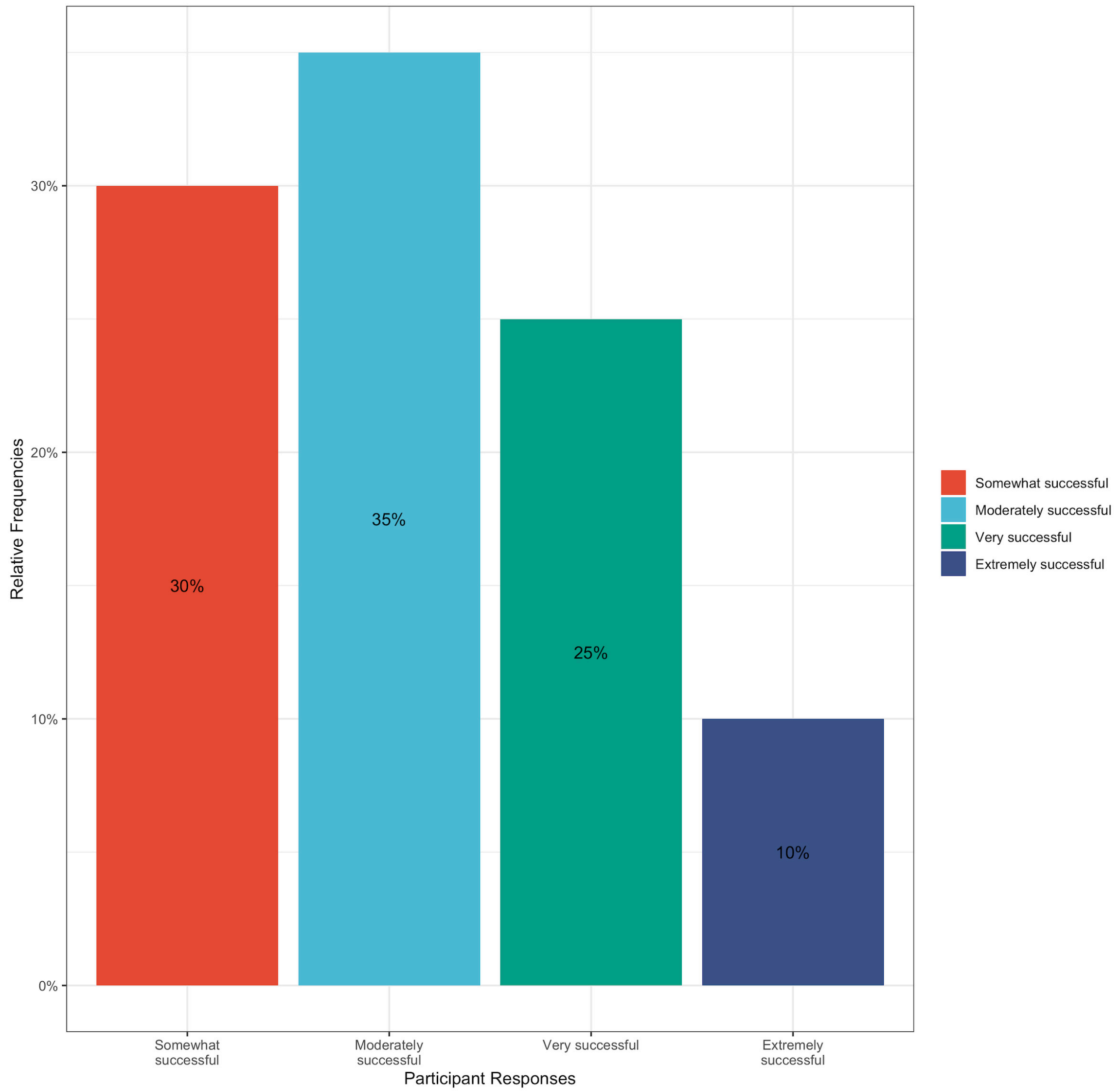

FIGURE 7
Bar graph of percentage of participant responses to post-intervention survey question: Thinking about the past 3 weeks, how successful would you say you have been in achieving dietary change? Answer choices included: Extremely successful, very successful, moderately successful, somewhat successful, and not at all successful.

findings observed in culinary medicine interventions conducted in other populations, indicating a high likelihood of success in applicability to hypertension. Thus, the novel approach of this study, focused on culturally-tailored culinary medicine, will help fill gaps in the literature and greatly augment this field of study.

4.2. Limitations

Limitations of this study included recruiting challenges, small sample size, and challenges finding resources to scale the intervention. Participants were recruited through snowballing and community flyering. These methods were restricted in reach and may bias who participates. While this was a pilot study, the small sample size and lack of a control group impacts power to detect changes and generalizability of findings. This was a low budget student-driven project and lacked the personnel and funding to scale the intervention including inability to recruit a larger number of participants, and challenges in funding cookbook printing (estimated at $12.50/cookbook). Analytic approaches were confined to univariate and bivariate analyses of survey data by students.

Additionally, participants were provided with an electronic version of the cookbook, instead of being sent a physical copy. Given that this study population included older adults, a digital "only" format could lead to decreased usability of all elements of the cookbook and lower adherence to its comprehensive applications. Limited resources also led to constraints in language use, with the cookbook only utilizing Tagalog and English languages available to the student team, despite the diverse range of dialects spoken by the larger Filipino American community.

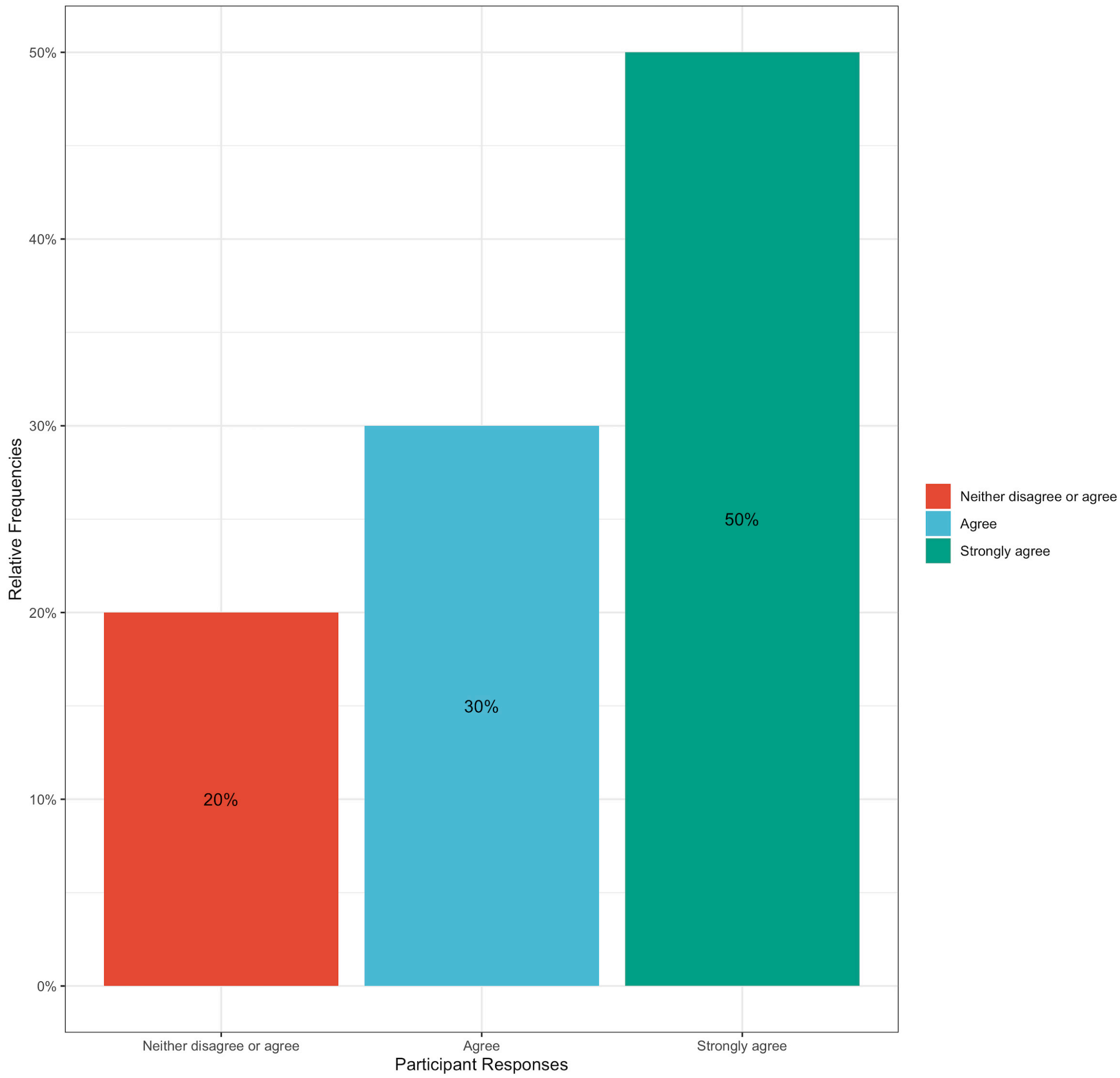

FIGURE 8
Bar graph of percentage of participant responses to post-intervention survey question: How much do you agree that the following statement is true for you: "I intend to continue to work to achieve dietary behavior change to improve my blood pressure"? Answer choices included: Strongly agree, agree, neither agree or disagree, disagree, and strongly disagree.

TABLE 3 Participant responses to post-intervention survey questions related to dietary behavior change.

Post-intervention survey questions	Likert scale responses (%)						
	1	2	3	4	5	Don't know	Refused
How motivated would you say you have felt during the past 3 weeks to achieve dietary change? You can answer: "Very unmotivated" (1), "Somewhat unmotivated" (2), "Neither" (3), "Somewhat motivated" (4), or "Very motivated" (5)	0	0	0	50	45	5	0
Thinking about the past 3 weeks, how successful would you say you have been in achieving dietary change? You can answer: "Not at all successful" (1), "Somewhat successful" (2), "Moderately successful" (3), "Very successful" (4), or "Extremely successful" (5)	0	30	35	25	10	0	0
How much do you agree that the following statement is true for you: "I intend to continue to work to achieve dietary behavior change to improve my blood pressure" You can answer: "Strongly disagree" (1), "Disagree" (2), "Neither disagree or agree" (3), "Agree" (4), or "Strongly agree" (5)	0	0	20	30	50	0	0

5. Conclusion and next steps

The post-intervention survey revealed additional insights on the usability of the cookbook, as well as the feasibility of implementing this unique intervention in the wider population. All but two of the twenty participants tried at least one recipe in the cookbook and many found the ingredients were accessible and affordable. Participants also expressed appreciation for how the recipes were tasty, easy to follow, and overall appealing. This valuable feedback indicates the cookbook was well-received by participants, suggesting the practicality of distributing this intervention in a larger, more diverse population. Participants' open-ended answers about their experiences during the intervention phase further support this idea, with participants noting that recipes were easy to use, as well as that recipes they tried were found to be flavorful. Participants also enjoyed the design elements including illustrations and stories. These statements highlighted the importance of incorporating a design-thinking approach and cultural considerations in fostering motivation toward positive behavior change, which was also seen through significant improvements in each participant's hypertension-based Self-Care Management score. Thus, this study contributes to existing literature on the importance of understanding health promotion beliefs in ethnic minority populations and prioritizing these cultural factors in best healthcare practices and providing recommendations. As this study is one of the first to examine a culturally-focused dietary approach as an exclusive intervention for hypertensive Filipino-Americans, this serves as a potential starting point for the expansion of robust literature on specific culturally-tailored dietary interventions for similar high risk groups.

In conclusion, this unique intervention applied design thinking and culturally imbued knowledge of cuisines to provide a culturally-tailored intervention that helped encourage dietary change in hypertensive Filipino Americans struggling to control and manage their blood pressure. While small in scale, the results achieved through this pilot study provided knowledge about feasibility, acceptability, and positive dietary change which serve as grounds for scaling up the study into a more robust, follow-up randomized controlled trial comparing measured blood pressure outcomes of a control vs. intervention group. In a subsequent follow-up study, a larger sample size would be recruited, blood pressure changes would be assessed by monitoring measured blood pressure before and after the intervention, and a longer study period would be used in order to better measure the impact of the intervention. In addition, to fully evaluate this cookbook's impact on hypertensive behavior change, data related to potential external confounding factors would be measured at both baseline and post-intervention. Lastly, the creation of different cookbook versions in other Filipino language dialects would be beneficial to test in a larger sample size that encompasses participants from a wider variety of Filipino American subgroups. This culturally-tailored intervention was seen to be extremely meaningful to participants from the Filipino American community, a minoritized ethnic population. In addition, the positive changes observed in dietary behavior are promising. Such an intervention can change the landscape of dietary change for hypertensive individuals who seek a more diverse selection of culturally nuanced cuisines with heart health goals in mind.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by the Committee for Protection of Human Subjects (CPHS) at the University of California, Berkeley. The patients/participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

DP and SI contributed to the conception and design of the study. NY contributed to the design of the intervention. DP, MS, and AD performed the survey analysis. DP wrote the manuscript. SI edited the first draft of the manuscript. MS, DP, MV, NY, AD, and SI wrote sections of the final manuscript. All authors contributed to manuscript revision, read, and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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"Medicine food homology" plants promote periodontal health: antimicrobial, anti-inflammatory, and inhibition of bone resorption

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"Medicine food homology" (MFH) is a term with a lengthy history. It refers to the fact that a lot of traditional natural products have both culinary and therapeutic benefits. The antibacterial, anti-inflammatory and anticancer effects of MFH plants and their secondary metabolites have been confirmed by numerous research. A bacterially generated inflammatory illness with a complicated pathophysiology, periodontitis causes the loss of the teeth's supporting tissues. Several MFH plants have recently been shown to have the ability to prevent and treat periodontitis, which is exhibited by blocking the disease's pathogens and the virulence factors that go along with them, lowering the host's inflammatory reactions and halting the loss of alveolar bone. To give a theoretical foundation for the creation of functional foods, oral care products and adjuvant therapies, this review has especially explored the potential medicinal benefit of MFH plants and their secondary metabolites in the prevention and treatment of periodontitis.

KEYWORDS

medicine food homology plants, periodontitis, antibiosis, virulence factor, anti-inflammatory, bone resorption

1. Introduction

A multifactorial microbial infectious disease known as periodontitis is characterized by gingival bleeding, swelling, attachment loss and bone absorption, as well as other destructive changes in the periodontium that finally lead to tooth loss, decreased chewing function, changes in food intake or eating habits and a reduction in the quality of the patient's life (1). Simply put, the intricate interaction between subgingival microorganisms and the host immune system leads to periodontitis. The incidence of periodontitis has increased by 83.4% in the last 10 years, and population growth and aging are raising the disease's global burden (2). In addition, studies have revealed that periodontitis is linked to several different health conditions throughout the body, including atherosclerosis (3), diabetes (4), cancer (5) and respiratory problems (6).

Traditional Chinese medicine has used the term "MFH" since the beginning of time. Eating when one is hungry is treated as taking medicine and given to the patient as medicine, which is a statement that reflects the concept of "MFH" made in "*Huang Di Nei Jing*" (7). The term "MFH plants" alludes to the fact that many Chinese medicines double as food and medication. In addition, many traditional Chinese medicines can also be used in functional foods that are suitable for specific groups. Although functional food cannot replace medicine, it can regulate human bodily functions and help maintain and promote human health (8). Furthermore, many secondary metabolites found in MFH plants have been demonstrated to have anti-inflammatory

(9), antibacterial (10) and anticancer (11)effects, indicating the potential use of MFH plants in disease prevention and medical care.

The idea of "food therapy" has recently been used in the preservation of periodontal health. Several studies have noted that the body can get anti-inflammatory and antioxidant substances from the diet, like polyphenols and flavonoids, that the body cannot generate on its own (12). Several MFH plants are now useful against periodontitis in a variety of ways, including antibacterial action against periodontal pathogens, decreasing host inflammatory response and improvement of alveolar bone loss (Figure 1). In order to offer a theoretical framework for the use of pharmacological and food homology in periodontitis, the mechanism and research progress of MFH plants and their secondary metabolites against periodontitis were categorized and explained in this paper.

2. Pathogenic mechanism of periodontitis

The most prevalent form of bacteria in the oral microenvironment is plaque biofilm. It is primarily present on the outside of oral soft and hard tissues or prostheses and is made up of a very complex extracellular polymeric matrix community. Subgingival plaque is a crucial contributor to the etiology of periodontitis and is distinguished from supragingival plaque by the gingival margin. The rich substances in the gingival fluid serve as the essential nutrient supply for bacteria, and the gingival sulcus offers a rather stable dwelling environment for bacteria. The amount and makeup of the bacterial population in plaque vary dynamically depending on the host's state of health or sickness so that the environment in plaque is not constant (13). In contrast to the healthy condition, the subgingival bacterial community will be much more diverse and abundant in diseased periodontal tissue. The proportion of some populations, such as those pathogens linked to periodontitis, will also be relatively higher (14). Studies have shown that *Porphyromonas gingivalis* (*P. gingivalis*), *Tannerella forsythia*, *Treponema*, *Fusobacterium nucleatum* (*F. nucleatum*), *Prevotella intermedia* (*P. intermedia*), *Actinobacteria*, *Pseudomonas aeruginosa* (*P. aeruginosa*) and so on (15–17), has been confirmed to have a strong correlation with the onset of periodontitis. *P. gingivalis*, *Tannerella forsythia*, and *Treponema*, also known as the red complex, have the strongest correlation with periodontitis (18). Even at low concentrations, these bacteria can cause inflammatory reactions in the periodontal tissues, yet these reactions are consistent with the tissues' defensive capabilities, allowing the periodontal tissues to continue to function normally (19). However, when this balance is upset by some factors, such as poor host oral hygiene, bad habits like smoking, or systemic diseases, the host periodontal tissue's defensive capability is significantly diminished, which promotes the growth of some periodontal pathogens and makes them absolutely dominant in quantity and abundance, as well as has an impact on the host-microbial crosstalk (20). The microbiota is encouraged to change into a more pathogenic state when the host's periodontal tissues experience an inflammatory reaction (21). Additionally, some bacterial structural elements, biomacromolecules and byproducts are cytotoxic and aid in bacterial colonization, copolymerization, biofilm formation, nutrient uptake, host cell invasion and escape ability, among other processes that are thought to participate in the inflammatory response of periodontitis (22–24). According to certain studies, a healthy, stable biological community is less likely to cause an inflammatory response in periodontal tissue than an ecologically unbalanced population rich in virulence factors (25). Moreover, the etiology of systemic disorders may be influenced by the ectopic colonization or circulation of periodontal bacteria, virulence factors, or specific mediators (26, 27).

Although bacteria are the initial causes of periodontal tissue inflammation and injury, they are not the primary component driving the development of the disease (28). When some cells and receptors in the host periodontal tissue recognize and kill invading pathogens, they also cause damage to the periodontal tissue. The equilibrium between tissue breakdown and regeneration is upset when the immune response is overactive and activates to levels above what is considered normal. This intensifies organizational destruction. Host immunity consists mainly of congenital and acquired immunity (29). Bacterial metabolites stimulate epithelial cells to produce

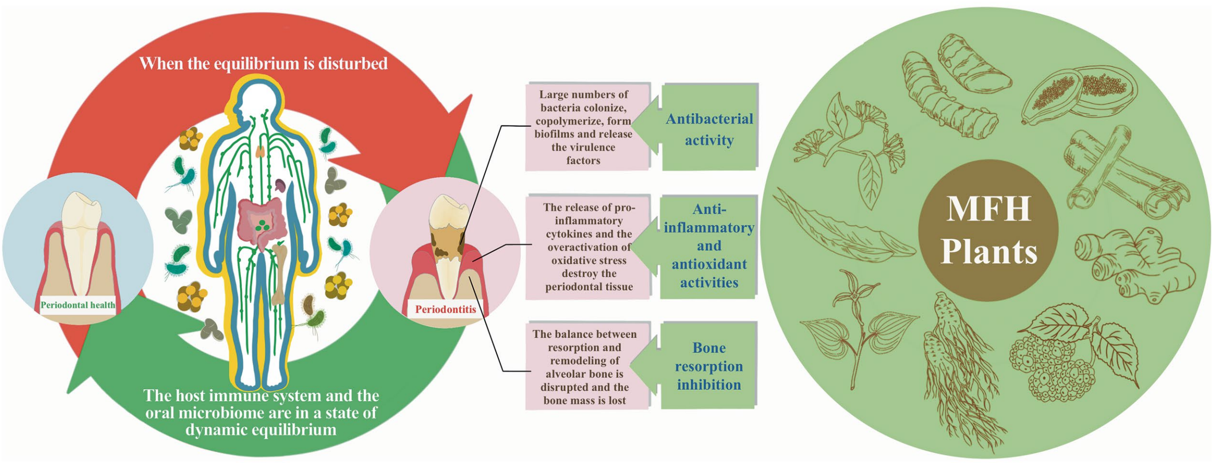


FIGURE 1
The etiology and pathogenic process of periodontitis as well as MFH plants' anti-periodontitis effects.

pro-inflammatory cytokines and neurons release neuropeptides to induce vasodilation and promote neutrophil migration to the inflammatory site of the periodontal tissue to resist pathogen invasion. If the infection is not eliminated, it can lead to early lesions, mainly characterized by gingival hyperplasia, bleeding and increased crevicular fluid flow. Innate immunity progressively changes into acquired immunity as the severity of gingivitis rises, and this process is mediated by macrophages, plasma cells and T and B lymphocytes. Blood circulation is hampered and collagen fibers keep dissolving. Mild gingivitis now advances to moderate to severe gingivitis, and it also appears to change color and shape at this stage. Gingivitis develops into periodontitis as the inflammation progresses deeper into the deep tissues, leading to loss of attachment and dental bone resorption (30). In the aforementioned process, cytokine release has the potential to directly destroy periodontal tissues in an irreversible manner as well as indirectly destroy them by altering intracellular signaling and gene expression (31). Aside from killing harmful bacteria, the respiratory burst of neutrophils can result in excessive production of reactive oxygen species (ROS) and matrix metalloproteinases, which can cause an oxidative imbalance in periodontal tissues and permanent tissue deterioration (32). The many immune response mechanisms used by the various cell types in the periodontitis immune response intersect and overlap, eventually generating the immunity/inflammation cascade reaction process, which leads to the complexity and multi-level pathogenesis of periodontitis.

3. Dietary intervention in periodontitis

Many researchers have supported the fact that diet quality can either promote or inhibit periodontal health. A healthy plant-based diet decreased the incidence of periodontitis and was favorably correlated with antibody levels, according to a cross-sectional study (33). Anti-inflammatory diets may help people with periodontitis improve their periodontal condition and reduce tooth loss, according to some research (34, 35). Cross-sectional research of Hispanic or Latino populations between the ages of 18 and 74 years revealed that those who consumed more whole grains, fruits, and vegetables and less red or processed meat had lower incidences of severe periodontitis (36). Sugar, snacks, and fast food, especially those high in processed carbohydrates, may promote the development of periodontitis by affecting the biofilm formation in the mouth (37). The buildup of oral biofilms is not decreased by a healthy diet, which includes fruits, dietary fiber, vegetables, and dairy products, but a good diet can encourage the growth of non-pathogenic microbial communities by controlling oral microbial populations. For instance, in saliva samples from obese people, the Mediterranean diet decreased the relative abundance of *P. gingivalis*, *P. intermedia*, and *Treponema* but did not affect the makeup of the overall salivary microbial community (38). However, there are difficulties in determining a causal link between dietary variables and periodontitis from the above-mentioned cross-sectional investigations. Several theories on the connection between diet and periodontitis have also been advanced by researchers. The Western diet, which predominantly includes processed meat, butter, high-fat dairy products and so on, was only linked to an increased risk of periodontitis among obese individuals, according to a prospective study of 34,940 men (39). Systemic inflammation, insulin resistance, and metabolic disorders associated with obesity may be key factors in the increased risk of periodontitis (40). In addition, obesity is significantly associated with diabetes, and numerous studies have shown that diabetes has a significant bidirectional promoting relationship with periodontitis (41). As everyone knows, dietary intervention is one of the most fundamental forms of treatment for diabetes and obesity. Therefore, we hypothesize that dietary intervention influences periodontal health through many mechanisms and has the ability to prevent periodontal damage brought on by diabetes and obesity. In recent years, significant advancements have been made by MFH plants in the treatment and management of diabetes and its complicating disease (8). MFH plants also have great potential in the prevention and treatment of periodontitis which is one of the complications of diabetes. Its dual use as medicine and food makes it safe, widely available, low cost and remarkable effect, which gives a fresh concept and approach to periodontitis dietary intervention.

4. Antibacterial effects and the inhibition of bacteria-related virulence factors of MFH plants and their secondary metabolites

Many secondary MFH plant metabolites or extracts have demonstrated direct antibacterial action against periodontal infections. The most popular evaluation index is minimum inhibitory concentration (MIC). The MIC is the minimum concentration of an antibacterial agent required to totally prevent test strains of organisms from growing visibly under tightly controlled *in vitro* circumstances. It serves as an indicator of how sensitive bacteria are to antibiotics (42). Table 1 displays the findings of the MIC analysis for the MFH plant extract, secondary metabolites and associated products. The main mechanisms by which MFH plants exert their antibacterial effects on bacteria include the breakdown of bacterial cell walls or membranes as well as interference with the synthesis of DNA and other vital biological macromolecules. The key bioactive components of MFH plants' basic chemical structure are directly related to this inhibitory function.

Additionally, MFH plants and their secondary metabolites can reduce bacterial viability. Instead of immediately killing and suppressing bacteria under the sub-MIC concentration, MFH plants are more likely to influence bacterial copolymerization, adhesion, biofilm formation, signal transmission, and nutrition intake by decreasing virulence factors associated with their survival and invasion. A specific component or metabolite of the bacteria may be the source of the virulence factor they create. It can encourage the inflammatory response of periodontal tissue and ultimately result in tissue loss in addition to aiding bacterial survival (23). Table 2 displays the correlational researches of the MFH plant extracts, secondary metabolites and associated products inhibiting the virulence factors of *P. gingivalis*. *P. gingivalis*, a kind of gram-negative anaerobic bacteria, has been linked to the etiology of periodontitis, which is the primary subject of investigations on the virulence factors connected to periodontal infections at the moment. Animal models exposed to *P. gingivalis* develop inflammatory reactions and lose alveolar bone. The virulence factors present in *P. gingivalis* include pili, gingipains, outer membrane vesicles (OMVs) and hemagglutinin (56, 57). The

TABLE 1 Antibacterial effects of MFH plants, secondary metabolites and related products.

MFH plants	Extracts, essential oils or secondary metabolites and derived materials	Bacteria	MIC	Ref.
Clove	Clove essential oil	*P. gingivalis*	6.25 μg/mL	(43)
	Eugenol	*P. gingivalis*	31.25 μM	
Ginseng	Ginsenoside Rh4	*P. gingivalis*	31.3 μg/mL	(44)
		F. nucleatum	16 μg/mL	
		P. aeruginosa	125 μg/mL	
	Ginsenoside Rk3	*P. gingivalis*	62.5 μg/mL	
		F. nucleatum	16 μg/mL	
		P. aeruginosa	125 μg/mL	
	Ginsenoside Rg5	*P. gingivalis*	16 μg/mL	
		F. nucleatum	16 μg/mL	
		P. aeruginosa	62.5 μg/mL	
	Ginsenoside Rh2	*P. gingivalis*	16 μg/mL	
		F. nucleatum	16 μg/mL	
		P. aeruginosa	62.5 μg/mL	
	Ginsenoside Rd	*P. gingivalis*	400 μM	(45)
Cinnamon	CBEO	*P. gingivalis*	6.25 μg/mL	(46)
	Cinnamaldehyde	*P. gingivalis*	2.5 μM	
Licorice	Glabridin	*P. gingivalis*	1.562 μg/mL	(47)
	Licochalcone A	*P. gingivalis*	1.562 μg/mL	
	Isoliquiritigenin	*P. gingivalis*	12.5 μg/mL	
Roselle calyx	Extract	*F. nucleatum*	7.2 mg/mL	(48)
		A. naeslundii	14.4 mg/mL	
		A. actinomycetemcomitans	28.8 mg/mL	
		P. gingivalis	7.2 mg/mL	
		P. intermedia	14.4 mg/mL	
Aloe	Fresh aloe gel	*A. actinomycetemcomitans*	50 μg/mL	(49)
		P.gingivalis	50 μg/mL	
		S.mutans	25 μg/mL	
	Extracts of *Rheum palmatum* root and *Aloe vera*	*P. gingivalis*	2 mg/mL	(50)
Mulberry	Resveratrol	*P. gingivalis*	78.12–156.25 μg/mL	(51)
Turmeric	Curcumin	*P. gingivalis*	62.5-125 μg/mL	(52)
Psoraleae	Psoralen	*P. gingivalis*	6.25 μg/mL	(53)
	Angelicin	*P. gingivalis*	3.125 μg/mL	

fimA gene encodes the protein FimA, which can be polymerized to produce pili and is involved in bacterial invasion of host cells, copolymerization, colonization and biofilm formation (58). By destroying periodontal tissue's constituents, gingipains, such as the two kinds of arginine-specific gingipains (RgpA, RgpB) and the lysine-specific gingipains (Kgp) encoded by *rgpA*, *rgpB* and *kgp*, can hasten the start and progression of periodontitis (59). The *P. gingivalis* hemagglutinin may bind heme and hemoglobin, which is helpful for bacterial survival and the spread of infection. The hemagglutinin-encoding genes, *hagA* and *hagB*, are also strongly linked to the development of biofilms (60). Furthermore, A variety of virulence factors are enriched in OMVs, which include outer membrane proteins, lipopolysaccharide (LPS), phospholipids, DNA and cytoplasm (61).

4.1. Phenolic compound

Phenolic compounds are a typical class of active ingredient found in a variety of natural plants. They have at least one aromatic ring structure linking one hydroxyl group. Three categories are frequently used to categorize phenolic compounds: lignans and tannins, which are polyphenols; low phenolic oligophenols including flavonoids, stilbenes, and coumarins; and

TABLE 2 The ingredients from MFH plants and their inhibitory mechanism against virulence factors of *P.gingivalis*.

Bioactive ingredient	Type of compounds	Source	Related mechanism	Ref.
Eugenol	Phenolic compounds	Cloves, Cinnamon	Inhibition of the expression of pili-related genes *fimA*, *hagA*, *hagB* and gingipains-related genes *rgpA*, *rgpB* and *kgp*.	(43)
Resveratrol	Phenolic compounds	Mulberry	Inhibition of bacterial degradation and adhesion of typeIcollagen; down-regulation of the expressions of *fimA II* and *IV* and gingipains-related genes *rgpA* and *kgp*.	(51, 54)
Curcumin	Phenolic compounds	Turmeric	Inhibition of gene expression of *fimA*, *hagA* and *hagB* and gingipains-related genes *rgpA*, *rgpB* and *kgp*, thereby inhibiting biofilm formation and reducing bacterial adhesion.	(52)
Petroselinic acid	Fatty acid	Fennel	Triggers the formation of OMVs-like particles that enrich RagA and RagB on the surface of bacteria, which can trigger explosive bacterial degradation and spillage of cell contents and DNA.	(55)
Ginsenoside Rd	Saponin	Ginseng	Reducing bacterial surface hydrophobicity and blocking the expression of virulence genes (*fimA* and *kgp*), which has an impact on bacterial adhesion, copolymerization, and biofilm formation.	(45)

monophenols (62, 63). Numerous studies have established that phenolic compounds have an antibacterial impact, and some researchers have outlined the antibacterial mechanisms in detail. The current generally held beliefs can be summed up as follows: 1. The phenolic compounds alter cell permeability and causes leakage of cellular contents by interacting with bacterial cell walls or membranes, as well as surface proteins; 2. Reactive oxygen species (ROS) are produced by phenolic chemicals, which enhances oxidative stress in bacterial cells; 3. Phenolic compounds prevent the synthesis of bacterial-related biological macromolecules, which inhibits the bacteria's development and metabolism; 4. Phenolic substances prevent DNA and ATP from being synthesized; 5. The production of proteins or virulence factors necessary for bacterial survival and biofilm formation are weakened by phenolic chemicals (64). The positions and amounts of the hydroxyl and methoxy groups (65–67), as well as the amounts and locations of hydrophobic substituents such as isopentenyl, alkylamino, and alkyl chains (68, 69), are all intimately related to the aforementioned activities. Figure 2 depicts the chemical composition of phenolic compounds found in MFH plants that have antibacterial properties.

The primary active component of the essential oils of several MFH plants, including *Syringa aromaticum* (cloves) and *Cinnamomum cassia* (cinnamon), is eugenol, a widely available monophenol molecule (70, 71). At MIC concentrations, eugenol can reduce the planktonic activity of *P. gingivalis* in a time-dependent manner. After being exposed to eugenol, *P.gingivalis* cells exhibited atrophic changes and severe cell membrane destruction, as revealed by a scanning electron microscope(SEM). In addition, leakage of nucleic acids and proteins within cells can be observed, indicating that eugenol interferes with cell membrane permeability and integrity. The hydrophobicity of eugenol and the impact of hydroxyl groups are closely related to the aforementioned actions (43). The extremely reactive hydroxyl groups in eugenol can create hydrogen bonds with a specific target enzyme of bacteria, which can disrupt the activity of the enzyme and result in a malfunction of the cell membrane system (72). Besides that, eugenol can indirectly inhibit the production of bacterial virulence factors by *P. gingivalis* by down-regulating the expression of the *fimA* genes, the hemagglutinin encoding genes *hagA* and *hagB* and the gingipain genes *rgpA*, *rgpB* and *kgp*, thereby affecting bacterial colonization, copolymerization, biofilm formation and nutrient uptake (43).

As a traditional Chinese medicine, *Glycyrrhiza glabra* (licorice) has high medicinal value in its dry roots and rhizomes and can also be used in the daily diet (73). The research demonstrated that the licorice extract's flavonoid known as glabridin had a potent antibacterial effect against *P. gingivalis*. Furthermore, glabridin and the antibacterial peptide -poly L-lysine work together to kill bacteria (47). Glabridin has a high affinity for DNA gyrase and dihydrofolate reductase (DHFR) and can be utilized as inhibitors of two enzymes, even though the antibacterial mechanism is still unknown. Glabridin's phenolic hydroxyl generates two hydrogen bonds with certain amino acids at DNA gyrase's ATP binding site, preventing the synthesis of nucleic acids, and the affinity is higher than ciprofloxacin. Glabridin's affinity for DHFR is primarily mediated *via* a hydrogen bond and other factors and is slightly weaker than trimethoprim's (74).

Fructus mori (mulberry), the fruit clusters of the mulberry tree, are juicy and delicious fruits rich in the polyphenolic compound resveratrol (75). Resveratrol is a common stilbene compound, which can kill *P.gingivalis* and can be found that the size and shape of bacteria are damaged to varying degrees through SEM (51). Despite the fact that there is currently no agreement on resveratrol's antibacterial capabilities (76), the double bond between the two benzene rings and the location and number of hydroxyl groups in the resveratrol structure, according to some researchers, may be important components in resveratrol's ability to inhibit bacteria (77, 78). Other studies have demonstrated that following resveratrol therapy, the expression of the *P. gingivalis* pili-related genes *fimA II* and *IV* decreased by more than 50%, and the expression of the gingipains-related genes *rgpA* and *kgp* also decreased (51). Resveratrol can impair *P.gingivalis*' adhesion to the basement membrane model and prevent *P.gingivalis* from degrading type I collagen in a dose/time-dependent manner (54).

Curcuma longa (turmeric) is an ancient Chinese medicinal plant of the ginger family, whose dried roots can be used in everyday cooking as well as for medicinal purposes. Curcumin is a phenolic compound extracted from turmeric (79). At concentrations below the MIC, curcumin can considerably limit the activity of six different strains of *P. gingivalis* and reduce its adhesion ability (52). Similarly, the researchers stressed the significance of aromatic hydroxyl groups in curcumin's antibacterial effect (80, 81). Studies have shown that curcumin can downregulate the gene expressions of *fimA*, *hagA*, *hagB*, *rgpA*, *rgpB*, and *kgp*, inhibit the formation of *P. gingivalis* biofilm and reduce bacterial adherence (52).

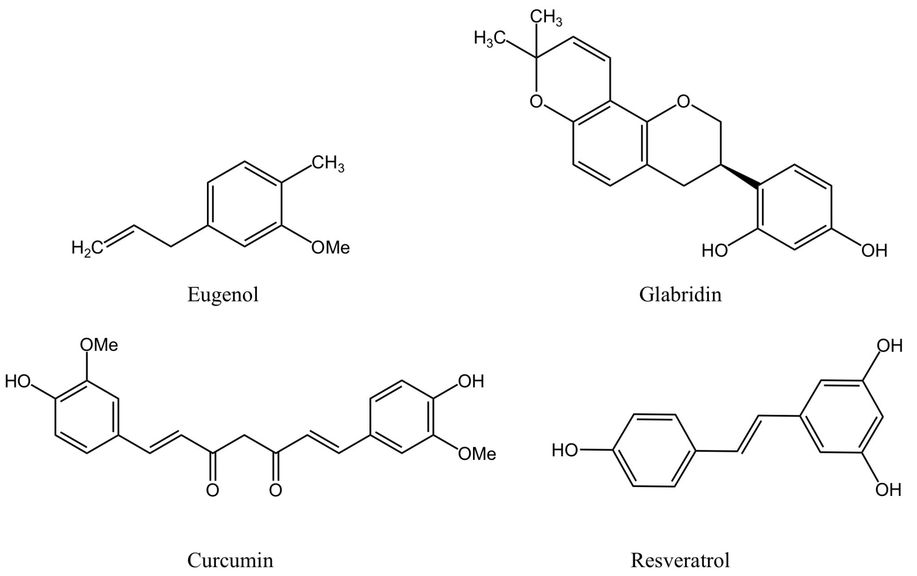


FIGURE 2
Phenolic compounds derived from MFH plants with antibacterial properties (created with KingDraw chemical structure editor).

4.2. Saponin

Saponins are composed of oligosaccharides partially linked with triterpenoids or steroidal aglycones, which can be divided into Triterpenoid saponin and steroidal saponin (82). They are prevalently present in plants as active compounds and have important pharmacological activities. Similar to surfactants, saponins include both hydrophilic and lipophilic groups. By lowering surface tension in aqueous solutions and producing micelles at crucial locations, these chemicals can alter the structure of biological macromolecules (44). Figure 3 displays the saponins from MFH plant sources that can be employed as antibacterial agents.

In China, *Panax ginseng Meyer* (ginseng) has an extended tradition of use in both food and medicinal. Ginsenosides are triterpenoid saponins isolated from ginseng (83). According to research, ginsenosides' primary antibacterial targets are bacterial cell membranes, and their amphiphilic characteristics are essential for membrane binding and permeability (84). *P. gingivalis* treated with ginsenosides can show the damage of cell membrane system and the outflow of cell contents, and the membrane binding characteristics of ginsenosides also depend on the polarity of ginsenosides, that is, the number of polar sugar groups in the structure (85). High-polarity ginsenosides can be decalcified and dehydrated employing high temperature or biotransformation to reduce polarity and enhance affinity with bacterial cell membranes (44, 86, 87). According to studies, less polar ginsenosides, which contain just one glycosyl group, such as Rk3, Rh2, Rh4 and Rg5, exhibit a better bactericidal action than highly polar ginsenosides, which contain three glycosyl groups and include Rg1, Re, Rb1, Rb2, Rc and Rd. (MIC >500 g/mL). According to TEM images of *F. nucleatum* treated with ginsenoside Rh2, the cell membrane had been destroyed and the contents of the cell had leaked (44). Through experimentation, some researchers have demonstrated that high polar ginsenoside Rd can likewise have a lethal effect on *P. gingivalis* (MIC = 400 µM), but this concentration is quite considerable. Intriguingly, *P. gingivalis* might be limited or even destroyed after treatment with modest concentrations of ginsenoside Rd (100 and 200 µM). Low concentrations of ginsenoside Rd can also drastically reduce bacterial surface hydrophobicity and block the expression of *fimA* and *kgp*, which has an impact on bacterial adhesion, copolymerization, and biofilm formation (45).

4.3. Aldehyde

The dried bark of the cinnamon tree, known as cinnamon, is a common element in Chinese cuisine and traditional herbal remedies. Cinnamaldehyde is an organic compound of olefine aldehydes extracted from cinnamon essential oil (Figure 4) (88). According to several researchers, the main cause of cinnamaldehyde's antibacterial effects is the destruction of bacterial cell walls and membranes, which causes the contents of the cells to leak out. The interaction of hydrocarbons with hydrophobic bacterial cell membranes is thought to be the cause of this effect, but the antibacterial mechanism is not just restricted to this. It may also be connected to how cinnamaldehyde permeates bacteria and how it affects genetic material (89). In comparison to other chemicals lacking an aldehyde functional group, cinnamaldehyde had the strongest effect on removing *Escherichia coli* biofilm, leading Kot et al. to conclude that the antibacterial action of cinnamaldehyde may be derived from the aldehyde functional group it carries (90). The major component of cinnamon bark essential oil (CBEO), cinnamaldehyde, has been shown in experiments to have a substantial antibacterial impact on the cell wall and membrane of *P. gingivalis*. When *P. gingivalis* was exposed to CBEO and cinnamaldehyde, it developed uneven surfaces, folds, or damage that allowed intracellular proteins, DNA and RNA to leak out. Cinnamaldehyde at the sub-MIC level can inhibit the formation of 67.3% biofilm of *P. gingivalis* (46).

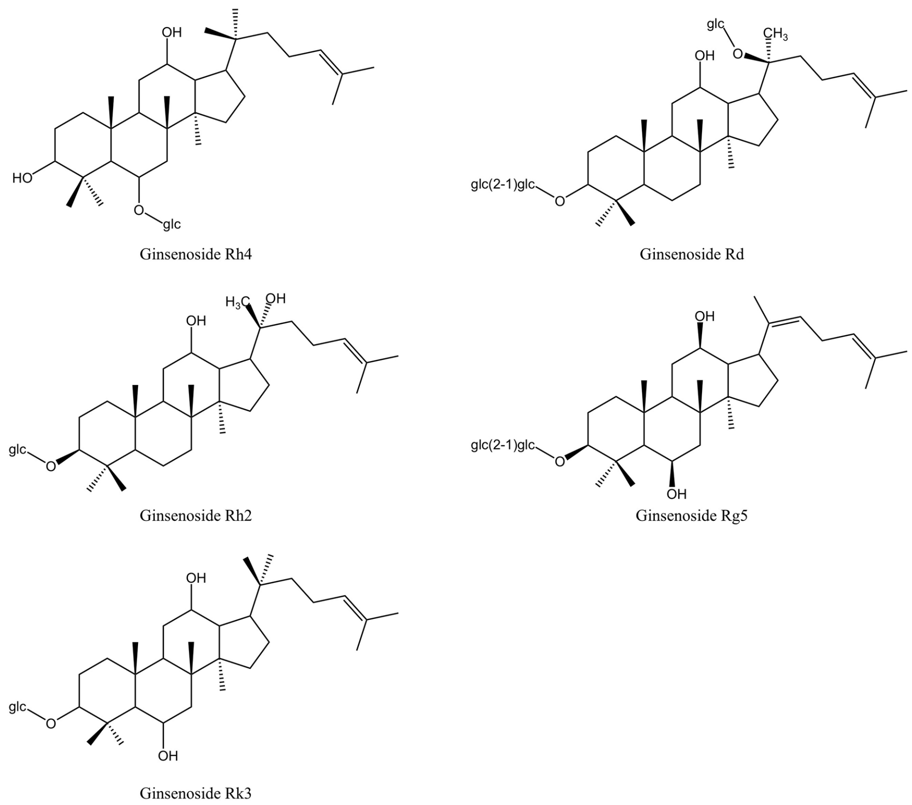


FIGURE 3
Saponins derived from MFH plants with antibacterial properties (created with KingDraw chemical structure editor).

4.4. Anthraquinone

Aloe vera (aloe) is an edible herb of the lily family. Studies have shown that the gel prepared from mature fresh aloe leaf has an inhibitory effect on pathogens extracted from patients with subgingival stones, periapical abscesses, and periodontal abscesses, but only at a higher concentration. A low concentration of aloe gel does not show an antibacterial effect (91). In other studies, fresh aloe gel has an inhibitory effect on *P. gingivalis*, *A. actinomycetemcomitans*, and other periodontal pathogens, but the effect is not significant compared with *S. mutans* (49). However, both studies lack an analysis of the main active ingredients. When researchers used dried aloe powder extract, the outcomes were very different from those of fresh aloe gel and did not demonstrate any antibacterial activity against *P. gingivalis*. The reason might be that the dried aloe powder contains so little of the anthraquinone component aloe-emodin (Figure 4) (50). Anthracene and two carbonyl groups make form the chemical molecule known as anthraquinone. It is a typical chemical found in numerous plants. Its antibacterial activity primarily consists of impeding DNA synthesis and replication, compromising the integrity of cell membranes, preventing bacterial virulence factors, and preventing the development of biofilm (92–94). However, some academics have also asserted that Aloe-emodin is more likely to attach with peptidoglycan to destroy bacterial membranes and damage cell membrane permeability. Aloe-emodin consequently has more antibacterial effect against gram-positive bacteria than against gram-negative bacteria (95). This may also be one of the reasons why the outcomes of some studies on the bacteriostasis of aloe-emodin on *P. gingivalis* are not ideal. Aloe-emodin's chemical composition also contributes to its antibacterial properties. According to several researchers, the antibacterial impact is directly tied to the aromatic hydroxyl groups on the anthracene core, and the antibacterial activity is further increased by the hydroxyl methyl groups the compound carries (96).

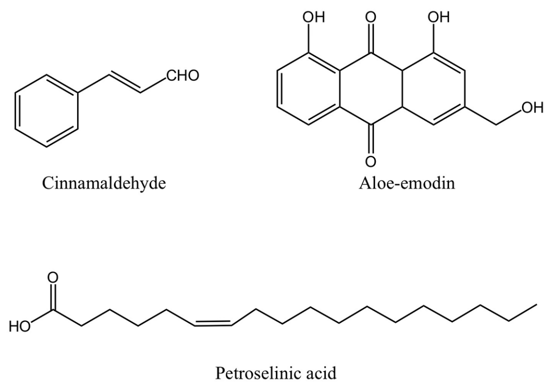


FIGURE 4
The structure of other antibacterial active ingredients from MFH plants including cinnamaldehyde, aloe-emodin and petroselinic acid (created with KingDraw chemical structure editor).

4.5. Fatty acid

Foeniculum vulgare (fennel) is a traditional medicinal and culinary plant. Petroselinic acid extracted from fennel is an unsaturated fatty acid (Figure 4). Petroselinic acid induced the formation of moniliform OMVs-like particles on the surface of *P. gingivalis*, which, unlike naturally occurring OMVs, induced explosive degradation of the bacteria and leakage of cell contents and DNA. The accumulation of RagA and RagB in OMVs-like particles can lead to the reduction of RagA and RagB in *P. gingivalis* (55). RagA and RagB proteins are believed to have a part in the uptake of macromolecules like polysaccharides or glycoproteins (97, 98). In addition, fennel extract and petroselinic acid also showed inhibitory effects on gingipains (55). However, the relationship between the anti-*P. gingivalis* and its virulence factor effect of petroselinic acid and its molecular structure has not been elaborated. Some scholars have found that the antibacterial activity of unsaturated fatty acids can be affected by the length of the carbon chain, the degree of unsaturation, and the position and configuration of the double bond. Moreover, the virulence factor and its gene expression of *Staphylococcus aureus* were significantly inhibited by petroselinic acid, suggesting that there may be targets between petroselinic acid and these virulence factors, but this part has not been confirmed by molecular docking research (99).

4.6. Others

In addition, some MFH plants have antibacterial activity. Some researchers have proposed that ethanol extract of *Hibiscus sabdariffa* L. (roselle calyx) has inhibitory effects on a variety of periodontal pathogens (48), but this study did not discuss the key active elements or the precise processes of roselle calyx. However, other researchers have hypothesized that protocatechuic acid, which, by generating ROS, damages DNA and causes lipid peroxidation in bacteria, changing the redox equilibrium (100), may be in charge of the roselle calyx's antibacterial properties (101). More research is necessary to determine whether proto-catechuic acid has the same antibacterial impact against periodontal infections. Ethanol extract of *Morus alba* leaves can reduce the growth of periodontal pathogens in a dose-dependent manner (102). Similarly, diosgenin extracted from *Trigonella foenum-graecum* L. (fenugreek) also showed dose-dependent inhibition of *P. gingivalis* and *P. intermedia* (103). Yet neither study provided information on effective doses.

In conclusion, periodontitis-related bacteria have been found to be significantly inhibited by MFH plants and their active ingredients. In contrast to the direct killing of bacteria, the majority of MFH plants and their active ingredients appear to be more effective at preserving the stability and balance of the periodontal microenvironment by inhibiting bacterial accumulation, copolymerization, biofilm establishment, and the production and activity of bacterial virulence factors. Based on the aforementioned studies, several academics stress the significance of these active components' chemical structures for their antibacterial activity. Each active ingredient's antibacterial effect can be attributed to a unique bond or functional group in its chemical structure that can interact and bind with a particular bacterial structure or enzyme, disrupt the physiological function of bacteria result in abnormal bacterial activity or metabolism, and ultimately produce the desired antibacterial effect.

The aforementioned research still has some incomplete aspects in several areas, though. First off, rather than being primarily linked to the pathogenic properties of a specific bacterium, periodontitis tends to be more susceptible to abnormalities in the oral microbial ecosystem. The mouth cavity contains about 1,000 bacteria. Other microbes outside bacteria exist as well, including fungi, viruses, and archaea (104). Distinct strains of microbes can produce distinct active components due to differences in their surface properties and functional groups. Future research should take into account the variations between the harmful bacteria because the aforementioned tests mostly consider one or two of them. In addition, the aforementioned studies did not address whether the active components of some MFH plants can achieve the ideal antibacterial effect *in vivo*, whether the bactericidal effect is particular, or whether it can affect the stability of the overall microenvironment of the oral flora. Therefore, more research is required.

5. Medicine food homology plants inhibit host inflammatory response and bone resorption

Although the development of early periodontal tissue lesions requires the presence of bacteria, their significance should not be overstated. As was previously stated, bacteria alone cannot predict how periodontitis will develop. Recent studies have also highlighted the importance of the role of host inflammation and the immune system as opposed to particular bacteria in the etiology of periodontitis. To take part in the inflammatory response, immune cells react to bacterial stimuli by triggering a number of signaling pathways and producing a range of inflammatory cytokines.

The oxidative stress in periodontal tissue and the absorption of alveolar bone may be directly related to the inflammatory response of periodontal tissue. The development of oxidative stress is attributed to an imbalance between the immune system's capacity to eradicate ROS produced by tissues and the ROS's actual creation. Some researchers have hypothesized that inflammation and oxidative stress are interconnected and can be mutually causative, causing and boosting one another in terms of their relationship (105). The oxidative stress environment in periodontal tissue, which is created by neutrophil hyperactivity and excessive ROS generation, is critical in causing periodontitis to develop, as was previously discussed. Additionally, the high production and ongoing stimulation of pro-inflammatory cytokines appear to be intimately linked to this excessive activation (106). Therefore, the development of oxidative stress can heighten the periodontal tissue's inflammatory response, causing substantial harm to the tissue. Similar to this, because of the intricate relationships and dynamic interplay between inflammatory cells and bone cells, inflammatory reactions can significantly alter bone homeostasis and bone remodeling (107). Firstly, cytokines activated during the inflammatory response process, such as IL-1β, IL-6, and TNF- α, and signal pathways, especially nuclear factor kappa B (NF- κβ), have been shown to be closely related to the differentiation and activity of osteoclast, and can promote the process of bone absorption by promoting the differentiation of osteoclast; Secondly, numerous inflammatory mediators can further inhibit the differentiation of osteoblasts and affect bone remodeling. The above two points are important mechanisms for bone mass reduction caused by inflammation (108, 109). In other words, an inflammatory response can undermine the stability of the bone microenvironment, upset the delicate balance between bone creation and absorption, and is inextricably linked to periodontitis' symptoms of bone absorption. Numerous studies have demonstrated that MFH plant extracts and secondary metabolites can inhibit the production of proinflammatory cytokines, decrease the inflammatory response and oxidative stress of periodontal tissue, and affect the process of osteoclast formation, thereby inhibiting alveolar bone absorption by regulating the aforementioned signal pathways or by altering the transcription and translation of specific regulators (Table 3).

5.1. Aldehyde

It has been demonstrated that cinnamaldehyde is a very effective anti-inflammatory medication (136). Cinnamaldehyde was found to diminish the *P. gingivalis*-activated NF-κβ signal pathway, which in turn reduced the expression of inflammatory factors and ROS generation in RAW264.7 cells. The same anti-inflammatory function has also been confirmed in Human periodontal ligament cells (HPDLCs). Cinnamaldehyde inhibits *P. gingivalis*-induced upregulation of pro-inflammatory cytokines in HPDLCs, including IL-6, IL-8, TNF-α and IL-1β. Downregulation of immune cell chemokines including monocyte chemoattractant protein 1 (MCP1), intercellular adhesion molecule 1 (ICAM1) and vascular cell adhesion molecule 1 (VCAM1) is also observed. Meanwhile, cinnamaldehyde also promotes the expression of osteogenic differentiation markers in HPDLCs and improves oxidative stress status. Cinnamaldehyde also inhibits the phosphorylation of P65 and Iκβ and inactivates the NF-κβ signaling pathway (110). According to academics, the impacts of cinnamaldehyde can be summed up as follows: 1. Cinnamaldehyde can chelate metal ions and alter several signaling pathways; 2. The aldehyde functional groups carried by cinnamaldehyde can give hydrogen ions to neutralize free radicals, lowering oxidative stress and inflammatory reactions in tissues (137). Cinnamaldehyde can be given orally to mice with ligation-induced periodontitis to slow the rate of alveolar bone loss and the levels of inflammatory cells and oxidative stress in periodontal tissue (110).

5.2. Phenolic compound

Phenolic compounds are electron or hydrogen atom donors with aromatic rings and multiple hydroxyl groups, which can eliminate free radicals through hydrogen ion or proton transfer, inhibit lipid peroxidation, and inhibit the activation of pro-inflammatory cytokine-mediated inflammatory signaling pathways, reducing oxidative stress and inflammatory response (138, 139). They have developed into one of the areas of research that has received a lot of attention lately. MFH plant-derived phenolic compounds with anti-inflammatory, antioxidant, and bone resorption inhibition properties are shown in Figure 5.

In-vitro studies have demonstrated that resveratrol blocks the activation of human monoblastic leukemia cell transcription factors induced by *P. gingivalis*, and interfere with the NF-κβ signal pathway in a dose-dependent manner (54). Triggering receptor expressed on myeloid cells-1 (TREM-1) is closely associated with the production of IL-1β and TNF-α that contribute to the persistence of inflammatory pathways (140). Resveratrol significantly down-regulates the expression of TREM-1 mRNA and reduces the inflammatory response in THP-1 cells induced by *P. gingivalis* (54). Toll-like receptor-4 (TLR-4) is an LPS-specific cell sensor that inhibits LPS-induced osteoblast differentiation and bone remodeling (141). Resveratrol down-regulates LPS-stimulated elevated levels of TLR-4 in human gingival fibroblasts (HGFs), thereby reducing the inflammatory response (111). Matrix metalloproteinase (MMP) is a family of zinc-dependent endopeptidases whose main function is to cleave extracellular matrix proteins, reshape tissues and degrade extracellular matrix under physiological and pathological conditions, and is considered to be an important substance involved in periodontal tissue collapse and inflammatory response during the development of periodontitis (142). Cyclooxygenase-2 (COX-2) promotes the disease process of periodontitis by mediating the inflammatory process in periodontal tissues (143). Nuclear factor erythroid 2-related factor 2 (Nrf2) and its downstream anti-invertases, such as heme oxygenase-1 (HO-1), are essential in resisting cellular oxidative stress and down-regulating the inflammatory response (144). Resveratrol has been shown to help reduce the inflammatory response and oxidative stress of rat periodontal tissue *in vivo* studies, decrease the protein levels of COX-2, MMP-2, and MMP-9 in rats with periodontitis, prevent the reduction of HO-1 and Nrf2, and effectively prevent alveolar bone loss by inhibiting osteoclast production (111).

Similarly, curcumin has shown superior anti-inflammation and antioxidant potential *in vitro* and *in vivo*. Curcumin downregulates COX-2 mRNA and protein expression in HGFs by inhibiting LPS-activated NF-κβ activation (112). Based on this, additional researchers have discovered that LPS can greatly upregulate IL-1β and TNF-α in rat gingival fibroblasts, and that curcumin can counteract this rise. In addition, the ratio of osteoprotegerin (OPG)/nuclear factor B receptor activator ligand (RANKL) increased in LPS-induced rat gingival fibroblasts treated with curcumin, and this bone protection feature was also demonstrated in rats with ligation-induced periodontitis (113). To treat rats with LPS-induced periodontitis, some researchers gave them an oral dose of the corn oil carrier that diluted curcumin each day. In periodontal tissue, downregulation of the expression of the IL-6, TNF-α, and prostaglandin E2 (PGE2) synthase genes was seen after 15 days. But curcumin can only block the pathway at a dose of 30 mg/kg (114). Additionally, more investigators discovered that the curcumin gel shell can minimize inflammatory infiltration and restrict bone absorption similarly to tetracyclines when used as an antibacterial supplementary treatment for scaling and root planning (SRP). Contrary to tetracyclines, interestingly, curcumin-treated rats showed iron deposits in their bone trabeculae, suggesting that curcumin may have the ability to encourage bone growth (145).

Zingiber officinale Roscoe (ginger) is a kind of herb of the ginger genus. Its rhizome is used as an essential cooking spice in the home and has a high medicinal value. Volatile phenolic compounds 6-Gingerol are the main irritating compounds present in ginger rhizomes. After heat treatment, they are prone to dehydration reactions to form 6-shogaol, which is also the source of the spicy flavor of ginger (146). Hyperglycemia in diabetes patients can induce protein glycosylation, and produce the advanced glycation end products (AGEs) that can damage periodontal tissue by increasing the oxidative stress of periodontal histiocytes and the expression of

TABLE 3 Inhibitory effects of secondary metabolites derived from the plant MFH on the inflammatory response and bone resorption.

MFH plants	Secondary metabolites	Type of compounds	Related mechanism	Ref.
Cinnamon	Cinnamaldehyde	Aldehyde	Diminishing the *P. gingivalis*-activated NF-κβ signal pathway and reducing the expression of inflammatory factors and ROS generation in RAW264.7 cells. Inhibiting *P. gingivalis*-induced upregulation of pro-inflammatory cytokines in HPDLCs. Downregulation of immune cell chemokines including MCP1, ICAM1, and VCAM1. Promoting the expression of osteogenic differentiation markers in HPDLCs and improving oxidative stress status. Inhibiting the phosphorylation of P65 and Iκβ and inactivating the NF-κβ signaling pathway.	(110)
Psoraleae	Psoralen and angelicin	Phenolic compounds	Blocking the release of IL-1β and IL-8 from monocyte-like THP-1 cells stimulated by *P. gingivalis* LPS. Boosting the expression of osteogenic proteins as well as the activity of alkaline phosphatase in HPDLCs.	(53)
Mulberry	Resveratrol	Phenolic compounds	Inhibiting the activation of transcription factors of the human monoblastic leukemia cell induced by *P. gingivalis*, and interfering with the NF-κβ signal pathway in a dose-dependent manner. Downregulation of the expression of TREM-1 mRNA and reduction of inflammatory response in THP-1 cells induced by *P.gingivalis*. Improving the inflammatory response and oxidative stress of rat periodontal tissue. Decreasing the protein levels of COX-2, MMP-2, and MMP-9 in rats with periodontitis, preventing the reduction of HO-1 and Nrf2 and alveolar bone loss by inhibiting osteoclast production.	(54, 111)
Turmeric	Curcumin	Phenolic compounds	Downregulation of COX-2 mRNA and protein expression in HGFs by inhibiting LPS-activated NF-κβ activation. Counteracting rise of IL-1β and TNF-α induced by LPS in rat gingival fibroblasts. Decreasing the ratio of OPG/RANKL in LPS-induced rat gingival fibroblasts.	(112–114)
Licorice	Glycyrrhizin (Glycyrrhizic acid)	Saponin	Inhibiting the expression of HMGB1, IL-6, and IL-1β in PDLSCs induced by TNF-α. Suppressing the production of HMGB1 and RAGE mRNA in the gingiva and serum and lessening the inflammatory response of the periodontal tissue.	(115, 116)
	Glycyrrhetinic acid	Saponin	Preventing the rise in vascular endothelial permeability brought on by *P. gingivalis* LPS. Impacting vascular endothelial permeability by preventing *P. gingivalis* LPS-promoted the internalization of VE-cadherin of HMECs, which is the cause of the rise in vascular endothelial permeability. Reducing the expression of IL-8, which increases vascular endothelial permeability in HMEC by preventing the activation of NF-κβ.	(117)
	Isoliquiritigenin	Phenolic compounds	Inhibiting the expression level of RANKL-induced osteoclast related genes and transcription factors in RAW264.7 and BMMs, and inhibiting the differentiation of osteoclast. Inhibition of the activation of NF-κβ pathways and blocking the initiation step of osteoclast formation process by inhibiting the binding of RANK and TRAF6. The expression of the c-Fos protein and NFATc1 has also been found to decrease.	(118)
Aloe	Aloe-emodin	Anthraquinone	Down-regulation of AMcase.	(119)
	Aloin	Anthraquinone	Inhibition of phosphorylation of p38 and ERK and downregulation of IL-1β Induced IL-8 expression level.	(120)
Ginseng	Ginsenoside Rd	Saponin	Downregulation of the expression levels of osteoclast marker genes Acp5, Nfatc1 and Mmp9 induced by RANKL to inhibit osteoclast formation, and downregulating the expression levels of inflammatory cytokines such as IL-1β, IL-6, and IL-8 in LPS-induced HGFs. Inhibiting alveolar bone resorption and destruction in mice models of periodontitis.	(45)
	Ginsenoside Rb3	Saponin	Inhibiting the mRNA expression of Nfatc1, Mmp9, Ctsk and Acp5 and decreasing the protein expression levels of MMP-9 and CTSK by inhibiting the RANKL-activated MAPK and NF-κβ signaling pathway in RAW264.7 cells. ERK pathway may be the target of ginsenoside Rb3	(121)
	Ginsenoside Rg1	Saponin	Inhibiting Drp1-mediated mitochondrial fission by activating AMPK and blocking NLRP3-mediated pyroptosis of HPDLCs.	(122)
Papaya	β-cryptoxanthin	Terpenoid	COX-2 and mPGES-1 are downregulated by β-cryptoxanthin in osteoblasts. And β-cryptoxanthin also decreases the NF-κβ transcription activity.	(123)
Ginger	6-Shogaol	Phenolic compounds	Inhibiting the production of ROS in AGEs-induced HGFs, and upregulating the expression levels of two antioxidant factors HO-1 and NQO1. Inhibiting the phosphorylation of MAPK p38, ERK, and NF-κβ p65, as well as the production of pro-inflammatory cytokines. Blocking the MAPK signal transduction caused by RANKL in BMMs.	(124, 125)

(Continued)

TABLE 3 (Continued)

MFH plants	Secondary metabolites	Type of compounds	Related mechanism	Ref.
Schisandra chinensis	Gomisins G and gomisins J	Phenolic compounds	Inhibiting the activation of NF-κβ, downregulating the expression levels of TNF-α, IL-1β and IL-6, and inducing HO-1 production by blocking the nuclear translocation of NF-κβ in RAW264.7 cells induced by *P. gingivalis*	(126)
	α-Iso-cubebenol	Terpenoid	Mediating nuclear translocation and transactivation of Nrf2 in THP-1 cells by promoting the PI3K/Akt and ERK pathways, inducing HO-1 mRNA and protein expression. Inhibiting the nuclear translocation of NF-κβ and its activity. Inhibiting the production of *P.gingivalis* LPS-stimulated pro-inflammatory cytokines.	(127)
	Schisandrin	Phenolic compounds	Enhancing Nrf2 nuclear translocation and HO-1 expression by inducing PI3K/Akt and ERK signaling pathways.	(128)
Pueraria	Puerarin	Phenolic compounds	Suppressing the activation of Akt, downregulating the expression of genes involved in osteoclast formation, and blocking the differentiation of RAW264.7 cells into osteoclasts and the release of proinflammatory substances. Preventing the ubiquitination degradation of Nrf2.	(129, 130)
Eucommia ulmoides	Geniposidic acid	Iridoid glycoside	Down-regulating MAPK phosphorylation and TLR2 expression in HGECs induced by *P. gingivalis*, inhibiting IL-6 production. Blocking the expression of genes linked to osteoclast differentiation in BMMC.	(131)
Magnolia officinalis	Magnolol	Phenolic compounds	Activation of the Nrf2/HO-1 signaling pathway to reduce the oxidative stress and inflammatory response of RAW264.7 caused by LPS. Inhibiting the expression of COX-2 and iNOS protein in gingival tissue, reduced the ratio of MMP-1/TIMP-1 and MMP-9/TIMP-1.	(132, 133)
Epimedium	Icariin	Phenolic compounds	Increasing OPG in human periodontal cells and downregulated the expression level of RANKL. Increasing the mRNA expression of Cbfa1 and OC. Increasing the protein and gene expression levels of alkaline phosphatase, which is downregulated by LPS in HPDLCs.	(134, 135)

inflammatory-related factors (147). *In vitro* experiments showed that 6-shogaol can inhibit the generation of ROS in AGE-induced HGFs and upregulate the expression levels of two antioxidant factors, HO-1 and NAD(P)H quinone dehydrogenase 1 (NQO1). In addition, 6-shogaol can also inhibit the phosphorylation of mitogen-activated protein kinases (MAPK) p38, ERK, and NF-κβ p65, as well as the production of pro-inflammatory cytokines (124). Other studies discovered that 6-shogaol blocked the MAPK signal transduction caused by RANKL in mice bone marrow macrophages (BMMs), which prevented the development of mice osteoclasts in a dose-dependent manner. Additionally, this research showed through *in vivo* tests that 6-shogaol can successfully stop bone loss and inflammation in the periodontal tissue of periodontally ligated mice (125).

Licorice isoliquiritigenin is a flavonoid compound. Some studies have suggested that isoliquiritigenin may reduce the levels of expression of RANKL-induced osteoclast-related genes and transcription factors in RAW264.7 and BMMs, and inhibit the differentiation of osteoclasts. And isoliquitigenin inhibits the activation of NF-κβ pathways and blocks the initiation step of the osteoclast formation process by inhibiting the binding of RANKL-stimulated receptor RANK and signal adapter molecule TRAF6. The expression of the c-Fos protein and nuclear factor of activated T cells c1 (NFATc1) has also been found to decrease. Animal studies have also supported isoliquiritigenin's inhibitory effect on bone resorption. When isoliquiritigenin was administered intraperitoneally to mice, their bone loss was significantly reduced (118).

The dried rhizome of *Pueraria lobata* is a kind of traditional medicinal and edible plant. An isoflavone substance called puerarin is derived from *P. lobata*. Puerarin has been shown to suppress the activation of Akt, downregulate the expression of genes involved in osteoclast formation, and block the differentiation of RAW264.7 cells into osteoclasts caused by LPS and the release of proinflammatory substances. Puerarin can greatly reduce LPS-induced bone loss and the number of osteoclasts in the mice skull in later animal trials (129). According to an intriguing study, signaling pathways connected to Nrf2 may be able to shield periodontal tissue from oxidative stress in hypoxic conditions, preventing damage to the tissue. In typical conditions, Nrf2 can be weakened by Kelch ECH-associating protein 1(Keap1). Nevertheless, p62 and Nrf2 are regulated by a positive feedback loop. By strengthening its association with Keap1, p62 can prevent the degradation of Nrf2 by that protein, and the Akt/mammalian target of the rapamycin(mTOR)signaling pathway influences the production of p62. Puerarin can indirectly prevent the ubiquitination degradation of Nrf2 mediated by Keap1 and enhance the nuclear translocation of Nrf2 in HPDLCs. It can also upregulate the production of p62 *via* stimulating the Akt/mTOR signaling pathway. Puerarin has additionally demonstrated *in vivo* studies that it can successfully stop alveolar bone loss in animals with periodontitis (130).

Magnolia officinalis is a member of the magnolia family whose dried stem bark, root bark and branch bark used in ancient Chinese medicine and can also be incorporated into the diet. Magnolia officinalis is the source of the plant polyphenol known as magnolol. According to studies, magnolol can trigger the Nrf2/HO-1 signaling pathway to reduce the oxidative stress and inflammatory response of RAW264.7 caused by LPS (132). In addition, magnolol significantly reduced the inflammatory response of periodontal tissue and alveolar bone loss and decreased the number of osteoclasts and the expression level of RANKL in experimental periodontitis rats. Magnolol also inhibited the expression of COX-2 and iNOS protein in gingival tissue, reduced the ratio of MMP-1/tissue inhibitor of metalloproteinases-1

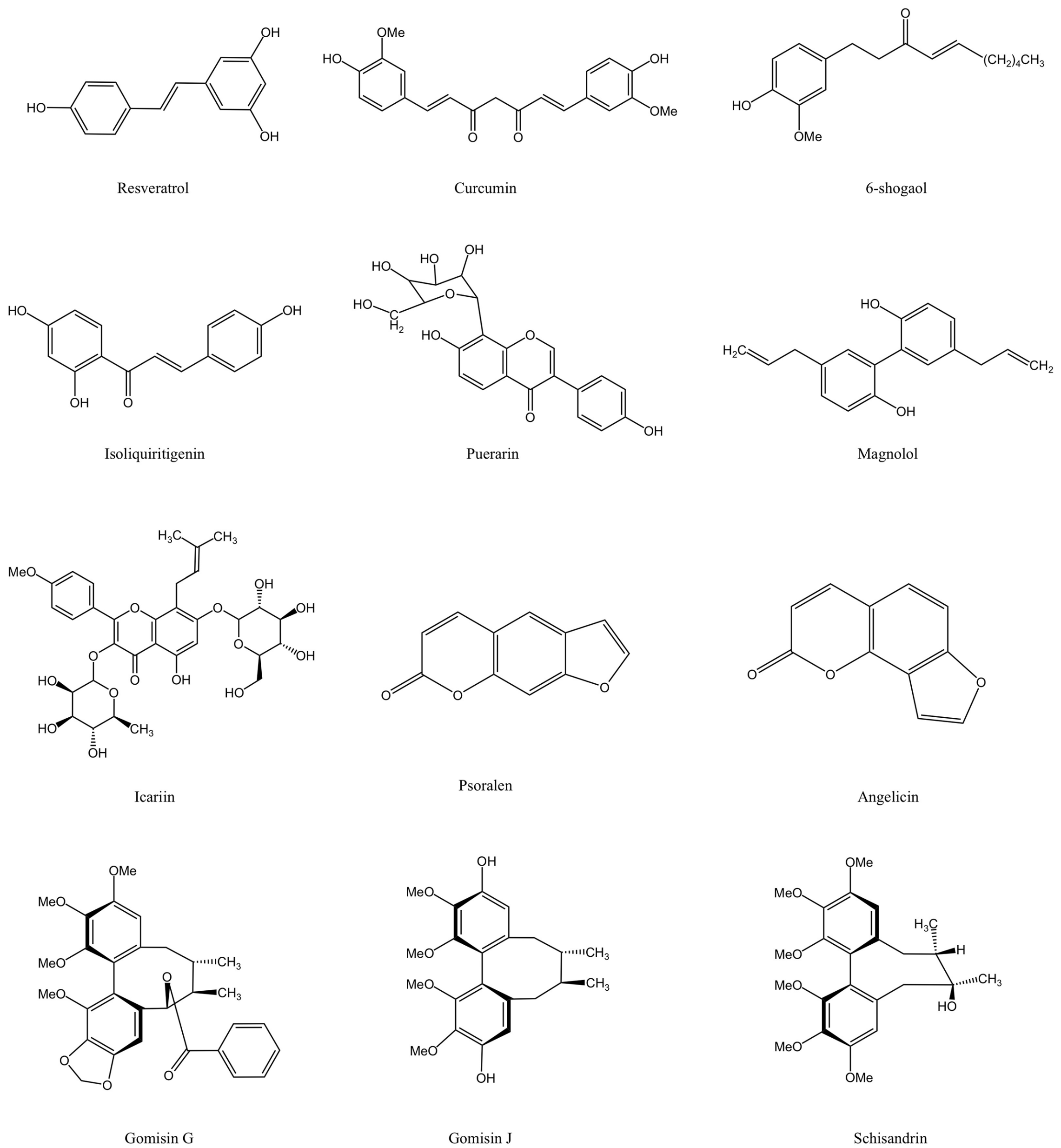


FIGURE 5
Phenolic compounds derived from MFH plants with anti-inflammatory effects (created with KingDraw chemical structure editor).

(TIMP-1) and MMP-9/TIMP-1, and inhibited the destruction of periodontal tissue (133).

Epimedium brevicornu Maxim. (epimedium) is a Ranunculus Berberis plant whose dried leaves are used both medicinally and for food. Icariin is a flavonoid compound that is the main active ingredient in epimedium. 0.01 μg/mL icariin increased OPG in human periodontal cells and downregulated the expression level of RANKL, leading to a decrease in the RANKL/OPG ratio. In addition, icariin also increased the mRNA expression of core binding factor alpha1 (Cbfa1) and osteocalcin (OC) in a dose-dependent manner, and the icariin group at 0.01 μg/mL showed the highest expression, which had a bone-promoting effect; however, when the icariin concentration was greater than 0.1 μg/mL, the expression of Cbfa1 and OC was decreased (134). Icariin can also increase the protein and gene expression levels of alkaline phosphatase, which is downregulated by LPS in HPDLCs (135). Local injection of icariin can attenuate the inflammatory process in minipig periodontitis models, and levels of the pro-inflammatory cytokines IL-1β and IFN-γ were lower in the icariin group than in the control group. In addition, icariin can effectively promote the regeneration of periodontal fibers and bone tissue (148).

Psoralea corylifolia (psoraleae) is a traditional plant whose fruits can be eaten and used medicinally. Psoralen and angelicin, which are active components of psoraleae and are coumarin compounds, can, in a dose-dependent manner, block the release of IL-1β and IL-8 from monocyte-like THP-1 cells stimulated by P.gingivalis LPS. Additionally, psoralen and angelica can boost the expression of osteogenic proteins as well as the activity of alkaline phosphatase in HPDLCs. The osteoprotective activities of angelicin on the alveolar bone of periodontitis-affected mice were further supported by this work, although the *in vivo* effects of psoralen remain unaccounted for (53).

Schisandra chinensis (Turcz.) Baill is a traditional Chinese medicine in the magnolia family. Its fruit can be used as a medicine or as a daily food. The active ingredient of *Schisandra chinensis* is lignans, including gomisins and schisandrin (149). Gomisins G and J inhibit the activation of NF-κβ, downregulate the expression levels of TNF-α, IL-1β and IL-6, and induce HO-1 production by blocking the nuclear translocation of NF-κβ in RAW264.7 cells induced by *P. gingivalis* (126). HO-1 expression is mainly regulated by the phosphoinositide 3-kinase (PI3K)/Akt pathway. In RAW264.7 cells induced by LPS of *P. gingivalis*, schisandrin can enhance Nrf2 nuclear translocation and HO-1 expression by inducing PI3K/Akt and ERK signaling pathways (128). However, there have been no reports on the *in vivo* anti-inflammatory effects of the active ingredients of Schisandra chinensis mentioned above.

Chaenomeles sinensis (Papaya) is a plant of the genus Papaya in the family of rosaceae. Its fruits are very common in daily life and can be eaten raw or used as a cooking ingredient and, after drying, can also be used as a medicine. β-cryptoxanthin is a carotenoid extracted from Papaya. In LPS-induced mice, β-cryptoxanthin can considerably reduce the amount of cranial bone resorption. Additionally, COX-2 and membrane-bound PGE synthase-1 (mPGES-1), two related enzymes that induce to production of PGE2 in the body, are downregulated by β-cryptoxanthin in osteoblasts. And β-cryptoxanthin also decreases the NF-κβ transcription activity. Molecular docking showed that β-cryptoxanthin competitively binds to the ATP-binding domain of inhibitor of NF-κβ kinase (IKKβ), inhibiting its activity and attenuating the activity of the LPS-induced NF-κβ pathway. In addition, β-cryptoxanthin inhibited RANKL-induced osteoclast differentiation and significantly reduced cathepsin K (CTSK) expression levels in RAW264.7 cells (123).But the effects of β-cryptoxanthin also lack proofs of *in-vivo* experiments.

5.3. Terpenoid

The class of active compounds known as terpenoids, which are abundantly present in nature, is made up of isoprene structural units. They can be categorized as monoterpenes, sesquiterpenes, diterpenes, triterpenes, tetraterpenes, and polyterpenes based on how many isoprene units they contain. Terpenoids have been proven to have significant anti-inflammatory benefits (150). Terpenoids can suppress the development of osteoclasts and the oxidative stress on periodontal tissue as well as operate on a variety of targets in the signal pathway and diminish the generation of inflammatory cytokines. Figure 6 displays the MFH plant terpenoids having anti-inflammatory properties reported in this paper.

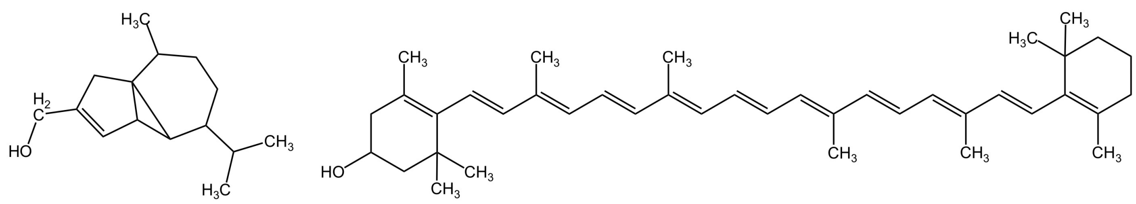
α-Iso-cubebenol is a cubebene sesquiterpene compound extracted from *Schisandra chinensis* (151). α-Iso-cubebenol mediated nuclear translocation and transactivation of Nrf2 in human macrophage THP-1 cells by promoting the PI3K/Akt and ERK pathways, induced HO-1 mRNA and protein expression in a time- and dose-dependent manner, and the anti-inflammatory effect of α-Iso-cubebenol can be reversed by the selective inhibitor tin-protoporphyrin of HO-1. In addition, α-Iso-cubebenol can also inhibit the nuclear translocation of NF-κβ and its activity, as well as inhibit the production of *P.gingivalis* LPS-stimulated pro-inflammatory cytokines (127). However, *in-vivo* research has not been done to further support the effects of α-Iso-cubebenol mentioned above.

5.4. Iridoid glycoside

Iridoid is a natural compound that often combines with sugars in plants to form iridoid glycoside. *Eucommia ulmoides* Oliv. is a plant whose bark is used in traditional medicine and food. Geniposidic acid (Figure 7), an iridoid glycoside extracted from *Eucommia ulmoides*, down-regulates MAPK phosphorylation and TLR2 expression in human gingival epithelial cells (HGECs) induced by *P. gingivalis*, inhibits IL-6 production. Additionally, Geniposidic acid can block the expression of genes linked to osteoclast differentiation in Bone marrow mononuclear cells (BMMC) in a concentration-dependent way. However, Geniposidic acid has no impact on IL-6 levels in BMMC, even though IL-6 is also linked to osteoclast differentiation. Geniposidic acid taken orally can reduce the inflammation of periodontal tissues and alveolar bone absorption in the mice of periodontitis caused by *P.gingivalis* (131).

5.5. Anthraquinone

Both the periodontitis inflammation response and bone resorption are improved by aloe-emodin and aloin derived from aloe (Figure 8). In rat models of periodontitis, aloe emodin has been suggested to lessen alveolar bone loss and periodontal inflammation. The mechanism may be the downregulation of aloe-emodin on acidic



a-iso-cubebenol b-cryptoxanthin

FIGURE 6
Terpenoids derived from MFH plants with anti-inflammatory effects (created with KingDraw chemical structure editor).

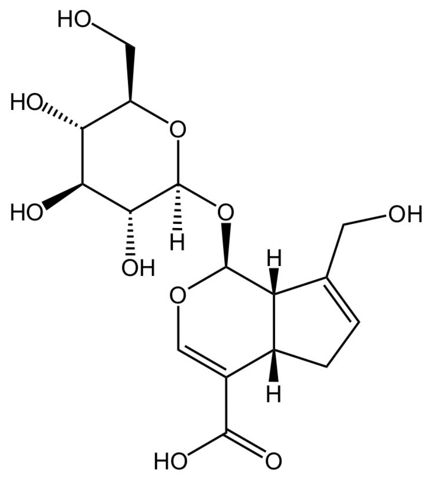


FIGURE 7
The structure of geniposidic acid (created with KingDraw chemical structure editor).

mammalian chitinase (AMcase) (119). AMcase is a hydrolase that cleaves glycoside saccharide bonds in chitin. Although humans cannot synthesize chitin, the expression level of AMcase is higher in inflammatory periodontal tissues than in normal periodontal tissues and is associated with the immune response to various inflammatory diseases (152). Aloin is also an anthraquinone compound extracted from aloe, composed of two types of diastereomers (153). Research has shown that aloin down-regulates IL-1β-induced IL-8 expression by inhibiting the phosphorylation of p38 and ERK in KB cells (120), but the anti-inflammatory mechanism *in vivo* has not been elucidated.

5.6. Saponin

The saponin components derived from MFH plants also have anti-inflammatory effects (Figure 9). Ginsenoside Rd can downregulate the expression levels of osteoclast marker genes Acp5, Nfatc1 and Mmp9 induced by RANKL to inhibit osteoclast formation *in vitro* and downregulate the expression levels of inflammatory cytokines such as IL-1β, IL-6, and IL-8 in LPS-induced HGFs. Furthermore, *in vivo* experiments have shown that ginsenoside Rd can significantly inhibit alveolar bone resorption and destruction in mice models of periodontitis (45). Ginsenoside Rb3 inhibited the mRNA expression of Nfatc1, Mmp9, Ctsk and Acp5 and decreased the protein expression levels of MMP-9 and CTSK by inhibiting the RANKL-activated MAPK and NF-κβ signaling pathway in RAW264.7 cells. Besides that, ginsenoside Rb3 has the most significant inhibitory effect on the MARK/ERK pathway, suggesting that the ERK pathway may be the target of ginsenoside Rb3 (121). In experimental periodontitis rats stimulated by *P. gingivalis* LPS, Ginsenoside Rb3 inhibits alveolar bone loss and osteoclast differentiation as well (154). Activation of NLRP3 inflammasomes plays an important role in the production of pro-inflammatory cytokines and pyroptosis. Mitochondria are the key regulators of NLRP3 inflammasome activation. Mitochondrial homeostasis is closely linked to AMP-activated protein kinase (AMPK) and dynamin-related protein 1 (Drp1). Ginsenoside Rg1 can inhibit Drp1-mediated mitochondrial fission by activating AMPK, as well as block NLRP3-mediated pyroptosis of HPDLCs in a variety of ways (122). However, the *in-vivo* activity of ginsenoside Rg1 still needs further investigation.

High mobility group protein 1(HMGB1) is a group of non-histone chromosomal proteins that can be released from necrotic or damaged cells. It is highly expressed in periodontitis and can mediate bone resorption by promoting the differentiation of osteoclasts (155, 156). Glycyrrhizin, also known as glycyrrhizic acid, is a triterpenoid saponin isolated from the root of licorice (157). Glycyrrhizin can inhibit the expression of HMGB1, IL-6, and IL-1β in human periodontal ligament stem cells (PDLSCs) induced by TNF-α, according to *in vitro* investigations. *In vivo* test using a rat periodontitis model treated with glycyrrhizin revealed the downregulation of HMGB1, IL-6, and IL-1β in the gingival crevicular fluid and periodontal tissue (115). AGEs receptors (RAGE) in tissues and plasma of diabetic patients bound to HMGB1 are key in the association between periodontitis and diabetes (158). In diabetic mice with periodontitis, glycyrrhizic acid can suppress the production of HMGB1 and RAGE mRNA in the gingiva and serum and lessen the inflammatory response of the periodontal tissue (116). Glycyrrhetinic acid is the main metabolite of glycyrrhizin with two residues of glucose acid (157). According to the *in-vivo* Miles vascular permeability assay, glycyrrhetinic acid can prevent the rise in vascular endothelial permeability brought on by *P. gingivalis* LPS. Studies conducted *in vitro* have demonstrated that glycyrrhetinic acid impacts vascular endothelial permeability by preventing *P. gingivalis* LPS-promoted internalization of VE-cadherin of human microvascular endothelial cells (HMECs), which is the cause of the rise in vascular endothelial permeability. Additionally, by preventing the activation of NF-κβ, glycyrrhetinic acid can reduce the expression of IL-8, which increases vascular endothelial permeability in HMEC (117). Some researchers applied glycyrrhetinic acid locally to the gingival sulcus of the rat periodontitis model and found that glycyrrhetinic acid could effectively inhibit the formation of LPS-stimulated immune complex and inflammatory cell infiltration, and no loss of attachment was observed (159).

5.7. Others

In addition to the secondary metabolites from MFH plants outlined above, several MFH plant extracts also have notable inhibiting impacts on periodontal tissue inflammation and bone resorption, such as *Angelica dahurica*, *Ginkgo biloba*, *Houttuynia cordata*, *Chrysanthemum morifolium* Ramat. (chrysanthemum), and *Evodia rutaecarpa* (160–164), although the active biological components they contain have not yet been identified. Table 4 lists the detailed effects of these extracts of MFH plants.

In conclusion, there is considerable biological activity and minimal toxicity in the extracts and secondary metabolites of MFH plants against periodontal tissue inflammation. Although there has been a substantial amount of *in vitro* and animal experimentation demonstrating the majority of the anti-inflammatory and anti-bone resorption benefits of MFH plants, clinical research is still in

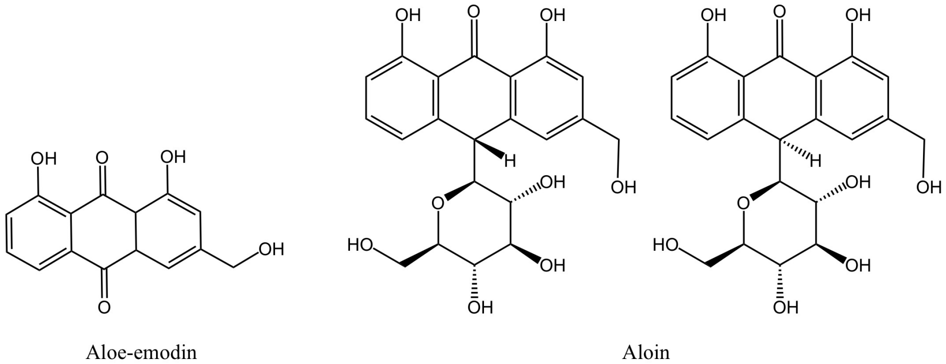


FIGURE 8
Anthraquinones derived from MFH plants with anti-inflammatory effects (created with KingDraw chemical structure editor).

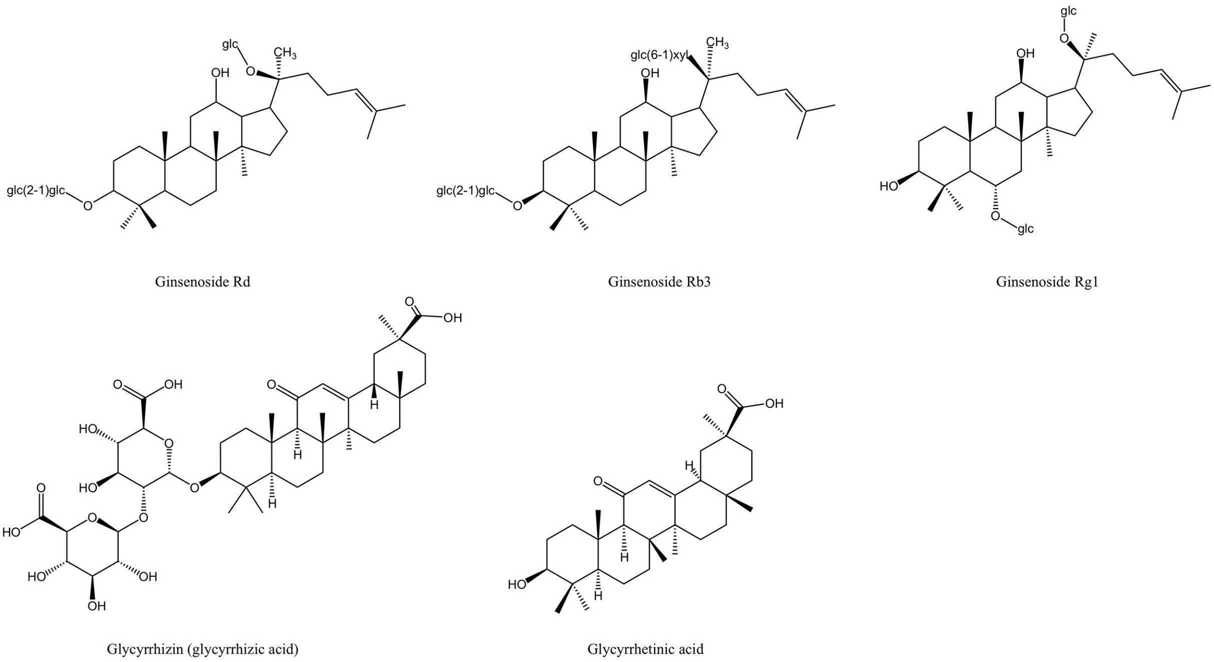


FIGURE 9
Saponin derived from MFH plants with anti-inflammatory effects (created with KingDraw chemical structure editor).

its infancy. Additionally, it is a difficult and time-consuming operation to identify and analyze the active components in some research that focus on extracts of MFH plants. There are still a lot of undiscovered linkages that need to be investigated, but some researches have established a causal link between the chemical makeup of some active chemicals and their anti-inflammatory and bone resorption action. However, the number of such studies is too limited. Furthermore, some researches indicate that the dosage or concentration of MFH plants is strongly related to their biological action, and high or low doses may significantly decrease or boost the biological activity of the active ingredient, such as large quantities of phenolic compounds that can cause oxidation (138). And different active component dosages may have various modes of action. For instance, various dosages of curcumin can influence various signal pathways and prevent the creation of certain pro-inflammatory substances (114). Therefore, dose control still requires special care from us.

6. Evidence from clinical studies of MFH plants

The number of clinical investigations is still extremely small, although some MFH plants have demonstrated considerable anti-periodontitis benefits *in vitro* and animal tests. The ability of MFH plants to enhance periodontal health in individuals with periodontitis has been validated by certain researchers, however, the majority of the studies have been modest in scope and substance. The present research

TABLE 4 Inhibitory effects of MFH plant extract on inflammation and bone resorption.

MFH plants	Related mechanism	Ref.
Angelica dahurica (Fisch. ex Hoffm.) Benth. & Hook.f. ex Franch. & Sav.	By blocking the expression of NF-κβ and the phosphorylation of Iκβ in LPS-stimulated Raw264.7 cells, *Angelica dahurica* extracts can down-regulate the expression levels of IL-1β, IFN-γ, IL-6 and IL-8. The expression of COX-2 and iNOS was also reduced after treatment with *Angelica dahurica* extract. Furthermore, *in-vivo* studies showed that *Angelica dahurica* extracts significantly improved inflammation and epithelial hyperplasia in rat models of experimental periodontitis.	(160)
Ginkgo biloba	The extract of its dried leaves can inhibit the activation of the MAPK pathway in RAW264.7 cells induced by *P.gingivalis* LPS, block the nuclear translocation of NF-κβ and activator protein-1. The expression levels of the pro-inflammatory cytokines TNF-α, IL-1β and IL-6 are expressed at lower levels in response to the extract of its dried leaves. In addition, the extract of *Ginkgo biloba* also induced the expression of HO-1 by improving the binding activity between Nrf2 and the ARE sequence of the HO-1 promoter region.	(161)
Houttuynia cordata	Its extract down-regulates the expression levels of pro-inflammatory cytokines IL-8, ICAM-1 and MMP-3 and their related genes by inhibiting the phosphorylation of ERK in HGECs induced by *A. actinomycetemcomitans.*	(162)
Chrysanthemum	By reducing the expression of osteoclast differentiation marker genes as well as the phosphorylation of MAPK p38 and JNK, chrysanthemum water extract can have an impact on osteoclast formation in RANKL-stimulated BMMs. Additionally, chrysanthemum water extract can reduce the expression of c-Fos and NFATc1, important transcription factors in osteoclast development, as well as the activation of phospholipase C gamma 2 and cAMP response element-binding proteins linked to osteoclast differentiation.	(163)
Evodia rutaecarpa	By inhibiting IL-1β-induced MAPK/ signal transducer and activator of transcription 3 activation in HGFs, the extract of the fruits of *Evodia rutaecarpa* significantly inhibited the expression of MMP-1 and MMP-3. In addition, the expression levels of the pro-inflammatory stimulators TNF-α, IL-8 and IL-6 were also downregulated.	(164)

and development philosophy for MFH plant products is centered on clinical adjuvant therapies, medicines and functional foods.

6.1. Medicine food homology plants related periodontal adjuvant therapy

Plant-based MFH products are frequently used in conjunction with periodontal therapy to help keep the therapeutic impact going strong. Babaei et al. (165) assigned 40 patients with chronic periodontitis to intervention and control groups and administered 1 g of *Cichorium intybus* L. (chicory) leaf methanol extract capsules and placebo capsules, respectively, twice daily for consecutive 8 weeks. Before the study, all subjects underwent non-surgical periodontal therapy. According to the findings, chicory leaf extract was able to significantly improve the depth of the periodontal pocket, increase total antioxidant capacity, uric acid and high-density lipoprotein cholesterol and decrease malondialdehyde, triglycerides, low-density lipoprotein cholesterol and total cholesterol levels in the intervention group compared to the control group and baseline ($p < 0.05$).

6.2. Medicine food homology plants related functional foods and oral care products

Twenty young adults with healthy periodontal conditions were recruited by Gao et al. (166) and divided into an intervention group and a control group before being given either *Phyllanthus emblica* L. gum or a placebo gum. It turns out that in the group of *P. emblica* gum, the generation of volatile sulfide was inhibited, and the overall bacterial count, *S. mutans*, and *P. gingivalis* counts were significantly reduced ($p<0.05$). Assiry et al. (167)recruited 50 subjects with moderate gingival scores and fair plaque scores without systemic diseases and randomly assigned them to the intervention and control groups. The intervention group received *Illicium verum* (star anise) mouthwash, whereas the control group received colored placebos, twice daily. Results indicate that subjects in the *I. verum* intervention group significantly improved in mean gingival index, papillary bleeding index and microbial count (P 0.05) when compared to the control group and baseline ($p<0.05$).

In summary, MFH plant-based functional foods and care items such as chewing gum, chewing tablets, mouthwash, toothpaste, and so on need to be enhanced in terms of flavor and taste while ensuring effectiveness, as adding MFH plant-based ingredients may result in an unpleasant odor and taste. How to strike the right balance between the degree of delicacy and the optimal clinical effect is one of the issues that need to be resolved. Future research should also take into account the low solubility issue with some active compounds generated from MFH plants. This issue can be resolved by developing a scientifically sound drug delivery system that will prolong the action duration inside the periodontal tissue and decrease drug loss.

7. Conclusion

The following might be used to summarize how MFH plants work to treat and prevent periodontitis: First, bacteria are the primary causes of inflammation. Bacterial cell membranes are susceptible to the effects of MFH plants and their secondary metabolites, which can cause bacterial cell disruption and expulsion of cell contents. They may also hinder the synthesis of biological macromolecules vital to bacterial survival at the same time, impairing bacterial growth and reproduction; Second, by preventing the action of bacterial virulence factors and the expression of associated genes, MFH plants and their secondary metabolites can also affect bacterial invasion, colonization, copolymerization, biofilm formation, and periodontal tissue damage; Additionally, MFH plants can lessen bone absorption by limiting the development of osteoclasts and can lower the level of inflammatory cytokines in periodontal tissue by controlling the synthesis of a range of signal pathways and regulatory variables; Last but not least, the modulation of antioxidant macromolecules, the downregulation of the oxidative stress response in periodontal tissue, and the lessening of damage to periodontal tissue are all possible functions of MFH plants. Significant progress has been made in the study of the use of MFH plants in treating periodontitis, which is encouraging for the creation of new MFH plant-related functional meals, oral care products, or additional methods of treating periodontitis.

Periodontitis, as a worldwide public health problem, mainly manifests as gingival bleeding and retraction, alveolar bone loss, bad breath, and so on. In extreme circumstances, it can lead to tooth loss and affect the patient's quality of life. Periodontitis is currently mostly treated with clinically necessary care and antibacterial adjuvant therapy. However, the development of multidrug-resistant bacteria brought on by antibiotics has long been a challenge that many academics are working to overcome. Therefore, one of the major research hotspots is the hunt for plant-based medicines that can replace antibiotics. The fact that variables other than oral ones can promote inflammation in periodontal tissue adds to the complexity of the etiology of periodontitis. It is undeniable that some systemic conditions, including diabetes and obesity, have strong associations with periodontitis. Dietary intervention is one of the most crucial treatment modalities for chronic disorders. The response to the question of whether a balanced diet may help with the prevention and treatment of periodontitis brought on by diabetes or obesity has been raised by a number of academics, and it is clear that it can. Consuming wholesome, anti-inflammatory foods and changing one's dietary habits have been demonstrated to help treat periodontitis in numerous clinical investigations. In keeping with the new idea of contemporary illness prevention, MFH plants have emerged as the ideal option for disease prevention and a balanced diet due to their dual usage as food and medicine. In conclusion, MFH plants are rich resources that should be further explored to support the clinical conversion of MFH plant-related products. For the future prevention and treatment of periodontitis, they are extremely promising natural products.

Author contributions

SQ: conceptualization, visualization, and writing–original draft preparation. SY: conceptualization and writing–review and editing. XM: writing–original draft preparation. RW: supervision, validation, and writing–review and editing. All authors have read and agreed to the published version of the manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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The efficacy of a whole foods, plant-based dietary lifestyle intervention for the treatment of peripheral neuropathic pain in leprosy: a randomized control trial protocol

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Introduction: Despite effective treatment of leprosy via WHO-approved multi-drug therapy (MDT), patients still suffer from debilitating neuropathic sequelae, including peripheral neuropathic pain (PNP), and continue to develop intercurrent etiologies (such as diabetes), and progressive existing neuropathy over time. Strategies seeking to improve physiological and metabolic wellness, including those that reduce systemic inflammation and enhance immune responsiveness to neurotoxic factors may influence underlying neuropathic etiologies. A whole food plant-based diet (WFPBD) has been shown to be effective in the management of neuropathic pain due to diabetes, limiting severity and relevant symptomology. Diabetes remains a significant sequela of leprosy, as up to 50% of patients in reaction requiring corticosteroids, may develop a biochemical diabetes. As nutritional interventions may modulate both leprosy and diabetes, a specific exploration of these relationships remains relevant.

Objectives: (1) To demonstrate the effect of a WFPBD lifestyle intervention, on neuropathic pain variables in leprosy; and (2) To contextualize the significance of diet in the treatment of chronic sequelae in leprosy by evaluating tolerability and side effect profile.

Methods: A prospective, randomized, controlled, single-blind, multicentre interventional trial is described. Weekly one-hour dietary counseling sessions promoting a WFPBD emphasizing vegetables, fruits, whole-grains, nuts, and legumes, omitting animal products, and limiting fat intake over a six-month duration will be implemented. Participants will be 70 age and sex-matched individuals experiencing active or treated "cured" leprosy and PNP, randomized to either intervention or control groups. Primary outcome measures include efficacy via visual analog scale, subjective questionnaire and objective quantitative sensory testing, as well as safety, tolerability, and harms of a WFPBD on PNP in leprosy. This study will be initiated after Research Ethics Board (REB) approval at all participating sites, and in advance of study initiation, the trial will be registered at ClinicalTrials.gov.

Expected impact: It is hypothesized that WFPBDs will mitigate progression and severity of PNP and potentially reduce the adverse events related to standard corticosteroid treatment of leprosy reactions, thereby reducing disease severity. By examining the effects of WFPBDs on PNP in leprosy, we hope to illuminate data that will lead to the enhanced therapeutic management of this neglected tropical disease.

KEYWORDS

leprosy, neglected tropical disease, peripheral neuropathic pain, nutrition, whole foods plant-based diet, portfolio diet, randomized control trial protocol

1. Introduction

Leprosy continues to affect nearly 200,000 individuals globally, despite being eliminated as a public health concern by the World Health Organization in 2000 (1). Causative agents, *Mycobacterium leprae* and *Mycobacterium lepromatosis*, prevail in low-middle income countries where many barriers to treatment adherence and effective prevention of neuropathic sequelae continue to challenge the clinical management of leprosy (1, 2). Patients experience hypopigmented and inflammatory cutaneous lesions, disabling sensory and motor neuropathies, and debilitating neuropathic pain, often leading to stigma and social ostracization (2–6). Despite the development of effective therapeutics via multidrug therapy (MDT), nerve release surgery, and other immunosuppressives decades ago, treatment of the associated neuropathic pain continues to remain largely ineffective. Standard pharmacological treatment of PNP using antidepressants, anticonvulsants, and opioids, results in a less than 30% reduction of pain (1, 7). Additionally, a significant side effect profile including anticholinergic effects, dizziness, confusion, hypertension, and weight fluctuation, contribute to poor adherence to PNP treatment overall (8). Given these extensive barriers, patients with leprosy sequelae, including PNP, continue to experience a reduced quality of life even with adequate access to gold standard therapeutics (6, 9, 10). In the absence of effective pharmaceuticals, alternative interventions must be explored to bolster patients' control of leprosy sequelae and the associated morbidity.

Lifestyle interventions have recently emerged as accessible and cost-effective strategies to reduce the burden and severity of neuropathic pain in diabetes. Strategies seeking to improve physiological and metabolic wellness, including those that reduce inflammation and enhance immune responsiveness to neurotoxic factors may influence underlying neuropathic etiologies. Nutrient supplementation has been instrumental in reducing host oxidative stress, strengthening the immune system, and mitigating potential adverse events in both leprosy and diabetes (11–15). Specifically, oral vitamin E and zinc supplementation may confer antioxidant effects, reducing daily analgesic requirements, and decreasing the incidence of leprosy symptoms overall (14, 16, 17). Likewise, studies assessing the use of oral vitamin D3 and omega-3 supplementation in diabetes have shown statistically significant improvements on subjective tests of neuropathy and pain, as well as objective tests of nerve health (11–15). Dietary interventions have also been specifically shown to reduce overall symptomology and improve the quality of life of individuals suffering from PNP due to diabetes (18–22). Many leprosy patients will develop impaired glucose tolerance due to genetic and lifestyle factors alone, and also due to the reliance on corticosteroids for control of inflammatory leprosy reactions (which can occur before, during, and after effective MDT). As patients experiencing leprosy often endure a biochemically induced diabetes, similar rationale may be applied. Prior to a final diagnosis of leprosy, patients are statistically significantly more likely to have diabetes (up to 14.2%) or pre-diabetes (up to 50%), when compared to healthy controls. Likewise, up to 65% of patients require corticosteroid treatment following reactions, resulting in steroid-induced hyperglycemia in up to 47% of individuals who were previously glucose tolerant (23–28). Additionally, given the high population prevalence of diabetes, lifestyle and genetic factors may predispose those with leprosy to diabetic neuropathy independent of corticosteroid use.

A WFPBD emphasizing vegetables, fruits, grains, and legumes, while omitting animal products, and limiting saturated fat intake has recently been shown to reduce diabetes related PNP severity and symptomology (19, 21, 22, 29, 30). In a cohort study assessing a WFPBD in 21 participants with type 2 diabetes, a statistically significant reduction of both serum triglycerides and total cholesterol, alongside a noticeable decrease in pain, weight, and insulin requirements was reported (22). Likewise, data from over 110 observational and clinical trials suggest that dietary patterns similar to a WFPBD are associated with a decreased presence of diabetes and significant improvements in biochemical profiles, including total LDL, and therapeutic requirements, for insulin in particular (21). Finally, a comprehensive randomized control trial seeking to address neuropathic pain management in 34 participants with neuropathy due to diabetes corroborates previous findings. Using both subjective questionnaire and objective quantitative sensory testing (QST), and electrophysiology, a significant decline in weight, body mass index (BMI), and glycemia was observed alongside a statistically significant improvement in neuropathic pain (19). Overall, WFPBDs have proven to be effective in the management of neuropathy due to diabetes, limiting endoneural ischemia, and providing sufficient glycemic control and lipid management, which when uncontrolled seem to exacerbate neuropathic pain. As a result, this phenomenon may translate to the management of PNP in leprosy, where diabetes comorbidity is common, and research has shown that diet and lifestyle interventions may be sufficient to control such steroid-induced hyperglycemia (23–28, 30–32). A WFPBD may also provide enhanced nutritional and antioxidant intake, conferring neuro-protective effects against leprosy alone while patients are actively undergoing antimicrobial MDT.

Major dietician groups suggest that a WFPBD is efficacious and superior in most, if not all populations. Dieticians of Canada, the British Dietetic Association, and the American Academy of Nutrition and Dietetics promote WFPBDs, suggesting improvements in weight, cholesterol, and risk of cardiovascular disease and type 2 diabetes (33–35). These groups also endorse that a WFPBD meets or exceeds recommended lipid, vitamin, mineral, fiber, protein, and amino acid requirements, when sufficient caloric intake is achieved (33–35). The wholegrains, nuts, seeds, beans, and fruits and vegetables readily supplied by a WFPBD can maximize intake of thiamine, pyridoxine, cobalamin, omega-3, zinc, and vitamins A, C, and E which are crucial to neurotransmitter and myelin synthesis, action potential propagation, and neuroprotection via capturing free radicals, and reducing oxidative stress (36–39).

We hypothesize that a WFPBD will have a multipronged beneficial effect, providing sufficient nutrient intake, neuro-protective benefits, and glycemic control to enhance host control of leprosy sequelae. A comprehensive prospective, randomized, controlled, single-blind, multicentre trial examining the efficacy, safety, and tolerability of a whole food plant-based diet on PNP in leprosy will inform any association between nutritional interventions and disease severity at the population level. Through reliable and validated techniques, such as comprehensive questionnaires and objective QST, a robust data set and analysis is expected to be generated. Overall, it is hypothesized that WFPBDs will mitigate progression of PNP as well as adverse events related to standard corticosteroid treatment of reactions, resulting in decreased neuropathic pain severity. By evaluating our current knowledge regarding the effects of WFPBDs on neuropathic pain in leprosy, we hope to illuminate data that will lead to enhanced therapeutic management and control of the impact of this neglected tropical disease.

2. Methods and analysis

2.1. Study design

This is a prospective, randomized, controlled, single-blind, multicentre trial examining the efficacy, safety, and tolerability of a WFPBD versus standard diet within a population living with PNP due to leprosy. An analytic framework capturing the target population, intervention, comparator, intermediate and ultimate outcomes to be assessed, as well as the impacts and considerations underpinning such a trial is presented in Figure 1.

2.2. Study objectives and hypothesis

The overall objective of this study is to demonstrate the effect of a dietary lifestyle intervention, specifically a WFPBD, on neuropathic pain variables in leprosy. It is hypothesized that patients may demonstrate a statistically significant improvement in sensory and motor neuropathy, as well as pain, on comprehensive questionnaires and objective QST and muscle testing both within and between groups at study end. Secondary objectives include contextualizing the significance of diet in the treatment of chronic leprosy sequelae by demonstrating high tolerability and a limited side effect profile alongside aforementioned improvements in neuropathic pain. It is hypothesized that a WFPBD has the potential to serve as a low-risk, low-cost, low-tech intervention for chronic neuropathic pain, improving function and reducing overall morbidity of leprosy.

2.3. Inclusion and exclusion criteria

Participants will be enrolled at the Tropical Disease Unit (TDU) in Toronto, Ontario, Canada, and one or more partner tropical

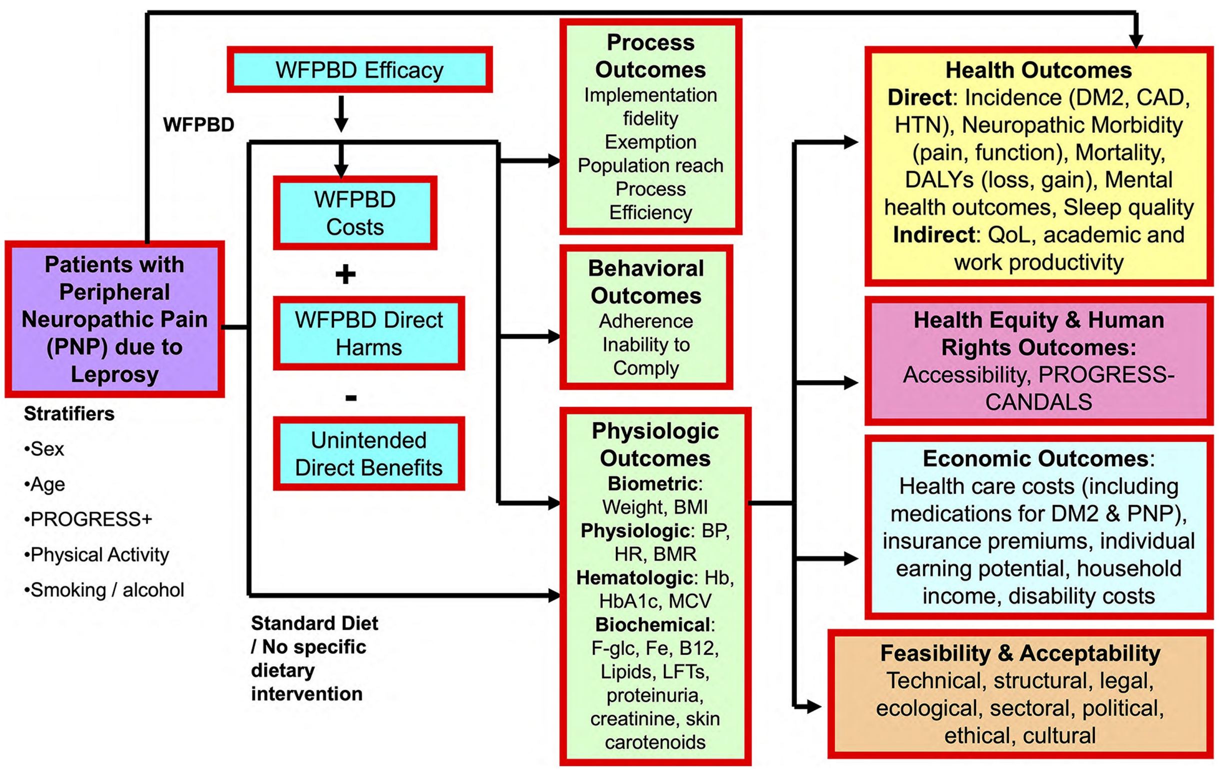

FIGURE 1
Analytic framework. BMI, body mass index; BMR, basal metabolic rate; BP, blood pressure; CAD, coronary artery disease; DALY, disability-adjusted life year; DM2, Type 2 diabetes mellitus; HR, heart rate; HTN, hypertension; LFTs, liver function tests; MCV, mean corpuscular volume; WFPBD, whole foods plant-based diet.

TABLE 1 Inclusion and exclusion criteria.

Inclusion	Exclusion
Presence of leprosy	Pregnancy
Clinical compatibility:	<18 years old
Thickened peripheral nerve	Already following a whole food plant-based diet
Presence of skin lesions	
Laboratory confirmation:	Experiencing neuropathy due to other significant underlying causes†
Positive slit skin smears	
Acid-fast bacilli on histopathology	No restriction on language as translation services will be provided
Presence of neuropathy	
Clinical compatibility on physical exam*:	
Glove and stocking paresthesia	
Abnormal touch perception sensations	
Subjective presence of pain	

*Including but not limited to; †Excluding biochemically induced diabetes.

medicine institutes, and will include patients experiencing active, or treated "cured" leprosy, as well as any degree of PNP. Inclusion into the trial requires: (1) clinically compatible leprosy based on the presence of thickened peripheral nerves (on physical exam, as well as ultrasound), and hypo- or anesthetic skin lesions; and/or (2) laboratory confirmed leprosy via positive slit skin smears and/or consistent histopathology and/or the presence of acid-fast bacilli on histopathology; and/or (3) a clinically compatible presence of neuropathy on physical exam including but not limited to glove and stocking paresthesia, abnormal touch perception sensations, and subjective pain (40–42) (Table 1). Sensory perception will be evaluated using 0.2–0.6 g Semmes-Weinstein monofilament, and the presence of 2/3 insensate sites will be considered "abnormal" (43). The use of objective QST as a standalone test for inclusion will be dependent on enrolment frequency to better preserve trial specificity. In the event of inadequate enrolment, a negative QST will not exclude patients from the trial to ensure adequate sensitivity, and vice versa. QST unreliably detects small fiber neuropathy, potentially representing a large portion of the target population (44, 45). Therefore, it is unlikely that it will remain a standalone inclusion criterion, however, will still be collected for downstream analysis. Finally, prospective participants who are pregnant, <18 years of age, already following a WFPBD (including vegetarian and vegan diets), and those experiencing neuropathy due to other significant causes alone, will be excluded (Table 1). Leprosy patients who fulfill inclusion criteria experiencing a biochemical diabetes due to corticosteroid therapy will remain eligible for inclusion and will be considered in downstream analysis (23–28). No restriction on language will be implemented as translation services will be made available across study centres.

2.4. Dietary intervention

2.4.1. Protocol diet and supporting evidence

The David Jenkins Portfolio Diet was originally designed to lower blood lipid levels in patients with hypercholesterolemia by emphasizing vegetables, fruits, grains, and legumes, while omitting animal products, and limiting saturated fat intake (46, 47). Specifically, the diet focuses on plant sterols (1 g/1000 kcals) as enriched margarine, soy and vegetable proteins (23 g/1000 kcals) as soy milk, meat alternatives, nuts, beans, chickpeas, and lentils, viscous fibers (9 g/1000 kcal) in the form of oats, barley, and psyllium, and low-calorie fruits and vegetables (46, 47) (Table 2). Following a comprehensive interventional trial in which 13 participants received the portfolio diet, a statistically significant reduction of LDL cholesterol, and coronary artery disease was observed ($p < 0.001$) alongside high compliance (93%) and acceptability ($p = 0.042$) (47). Similarly, in recent literature interventional trials have emerged assessing the efficacy of a WFPBD, like that of the portfolio diet, for neuropathic pain in individuals with diabetes. Specifically, in a trial assessing a low-fat plant-based diet, omitting animal products, and limiting fat intake to 20–30 g/day in 34 patients, a statistically significant reduction of pain on subjective neuropathy questionnaires and neuropathy on objective electrophysiology was observed ($p < 0.05$) (19). WFPBDs have been shown to provide sufficient glycemic control and lipid management which, when left unchecked, can exacerbate diabetes-related neuropathy. Given the absence of literature concerning the intersection of dietary lifestyle interventions and neuropathic pain of leprosy, it is hypothesized that a WFPBD will have similar physiological and neuro-protective benefits in a cohort of patients with leprosy and its neuropathic sequelae, in whom diabetes comorbidity is frequent.

2.4.2. Lifestyle counseling

Participants in the intervention group will be instructed to follow a WFPBD for 24 weeks. The study duration was chosen as a conservative estimate of comparable lifestyle-based interventional trials that demonstrated statistically significant improvements in diabetes-related neuropathy outcomes (18, 19). The diet will emphasize vegetables, fruits, whole-grains, nuts, and legumes, while omitting animal products, and limiting fat intake (Table 2). Selection of specific plant-based components may differ across study sites in concordance with local culinary preferences and cultural practices related to food. By tailoring the diet to the unique cultural diaspora affected by leprosy, many of which already endorse plant-based components, we seek to enhance adherence and acceptability to the diet overall. Likewise, current economic projections suggest that diets seeking to reduce animal products are more affordable than current standard diets across all socioeconomic levels – particularly due to inclusion of global staples such as tubers, beans, legumes, and rice – further enhancing accessibility (48–50). Participants will receive weekly support and guidance via 1 h counseling sessions with registered dieticians or the equivalent at each participating site. Sessions will be designed to disseminate comprehensive guidelines for following the WFPBD including culturally acceptable recipes and addressing concerns or knowledge gaps regarding the intervention. Participants in both the intervention group, and control group will be instructed to continue their respective leprosy therapeutics as prescribed throughout the duration of the study. Finally, dietary adherence will be measured via monthly random 24 h dietary recalls, and participants are free to withdraw at any point during the trial if they no longer wish to participate.

TABLE 2 Example portfolio diet for one day.

Breakfast		Lunch		Dinner		Snacks	
35 g	Oatbran	65 g	Vegetable chili	295 g	Vegetable curry	14 g	Almond × 2
150 g	Orange	67 g	High fiber bread	85 g	Soy burger	250 g	Soymilk × 2
7 g	Metamucil	17 g	Margarine	80 g	Beans	7 g	Metamucil × 2
33 g	High fiber bread	62 g	Soy deli slices	35 g	Barleys	175 g	Soy yogurt
8 g	Margarine	80 g	Tomato	100 g	Okra	10 g	Jam
18 g	Jam	150 g	Orange	200 g	Eggplant		
250 g	Soy milk			200 g	Cauliflower		
				80 g	Onions		
				60 g	Red pepper		

Adapted from "A dietary portfolio approach to cholesterol reduction: combined effects of plant sterols, vegetable proteins, and viscous fibers in hypercholesterolemia." by Jenkins et al. (47).

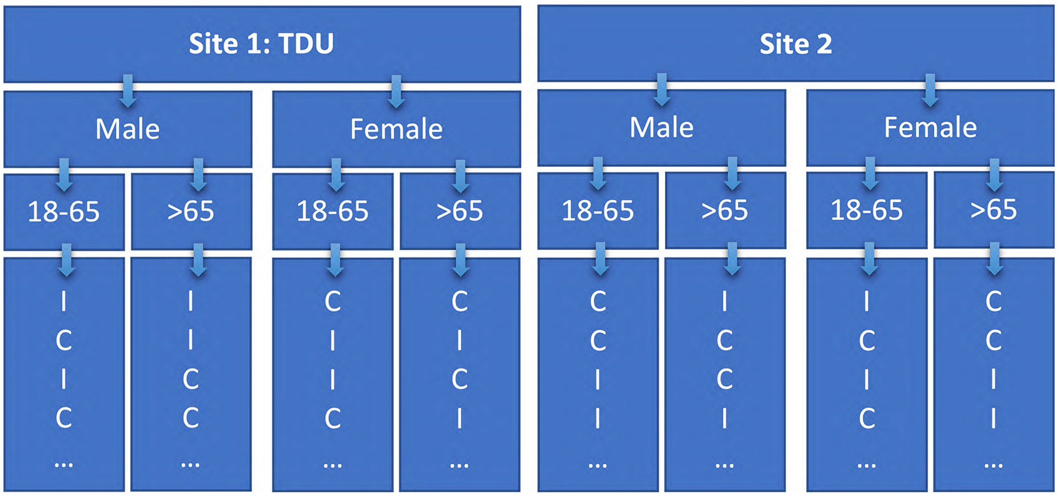

FIGURE 2
Stratified, block, randomization protocol. Adapted from: "Randomization in clinical studies." by Lim and In (52). TDU, Tropical Disease Unit.

2.5. Methodology

2.5.1. Collaboration

Clinical manifestations of leprosy are highly variable, hinging on several geographic, cultural, and genetic underpinnings (2). As such, to maximize the impact of trial outputs, we seek to address the global experience of leprosy through collaboration between the TDU in Toronto, Ontario, Canada, and one or more partner centres for excellence in the care of Hansen's disease patients abroad. Given migration patterns, selected study centres will account for endemic source countries and regions including the Philippines, the Indian sub-Continent, Southeast Asia, and South America, providing for a more representative data set (2, 51). Trial documents including patient informed consent will be prepared in multiple languages to harmonize procedures across study sites. Likewise, site leads at each respective centre will be responsible for coordinating recruitment, as well as data collection. Oversight will be maintained by a centralized lead at the TDU, who will be responsible for disseminating the randomization protocol, and ensuring overall procedural adherence across sites.

2.5.2. Consent, randomization, and blinding

Patients with a history of leprosy will be pre-screened for inclusion via clinical records prior to routine follow up. Study personnel will approach eligible patients experiencing active or treated ("cured") leprosy, as well as subjective neuropathic pain at participating tropical disease institutions. Eligible participants will receive a comprehensive in-person review of the trial protocol, including data collection requirements, and will be given the patient consent form. Patients will voluntarily confirm willingness to participate and will be free to withdraw at any point. Upon consent to enrolment, participants will be randomized to either the WFPBD intervention group, or standard of care control group. To ensure equal distribution and matching between study groups, randomization will be carried out using a stratified block method (52). Participants will be assigned to strata primarily by study site, followed by sex (male/female), and lastly age-band (18–65, >65) (Figure 2). Random sequence generation will be carried out using a computer-generated allocation sequence. Study investigators, physicians, and participants will not be blinded to group allocation due to the transparent nature of the dietary intervention and counseling. However, primary end points will be collected by independent study personnel, blinded to group allocation, allowing for a single-blinded protocol.

2.6. Statistical analysis

2.6.1. Sample size calculation

This is a novel RCT addressing the implications of a WFPBD on neuropathic outcomes in individuals with leprosy. This relationship has not been directly assessed in the current body of literature, however similar research questions have been assessed in individuals with diabetes mellitus. As such, the sample size calculation herein will utilize this literature as a proxy. The efficacy of a WFPBD diet on neuropathy in a diabetes cohort has been reported via the Michigan Neuropathy Screening Instrument (MNSI), including both subjective (questionnaire) and objective (physical assessment) measures. The sample size calculation was based on the MNSI questionnaire measurement as explicit details pertaining to the MNSI physical assessment were not provided. Specifically, both the type of QST utilized (vibration, perception, both, etc.) and the location the test was carried out (lesion, glove, stocking, etc.) were not mentioned. Therefore, the MNSI questionnaire was preferentially chosen as a proxy. Participants receiving the intervention reported a final mean MNSI questionnaire of 5.3 ± 2.5 compared to 7.1 ± 2.8 in the control group at study end (19). Using an opensource sample size calculator with two independent study groups, continuous endpoints, an alpha of 0.5 and 80% power, a final sample size of approximately 60 participants was ascertained (53, 54). This is a conservative estimate as source literature demonstrated a statistically significant effect on outcomes with a relatively low population of 34 individuals (19). Assuming high acceptability and a 14% withdrawal and/or loss to follow-up rate based on previous literature, a final sample size of ~70 individuals, 35 per group, will be needed to adequately power this trial (19, 47, 55, 56).

2.6.2. Continuous and categorical variables

Descriptive statistics including reported means ± standard deviation for continuous variables [questionnaires including MNSI-physical assessment, Neuropathy Total Symptom Score (NTSS), modified Medical Research Council Scale (mMRCS), Neuropathic Pain Symptom Inventory (NPSI), McGill Pain Questionnaire (MPQ), Pittsburgh Sleep Quality Index (PSQI), and International Physical Activity Questionnaire (IPAQ) summative scores, visual analog scale (VAS), anthropometrics, diabetes duration, hemoglobin A1c, and serum micronutrient levels] and proportions for categorical variables [number of adverse events, dietary adherence, insulin use, leprosy clinical status (according to the WHO and Ridley Jopling classification systems), frequency and prevalence of inflammatory leprosy reactions, corticosteroid use] will be reported by each study group (57). Between- and within-group comparisons will also be made for continuous variables using the Student's *t*-test with reported *p*-values, and for categorical variables using the chi square or Fisher's exact tests, reporting *p*-values with odds ratios and 95% confidence intervals. Statistics will also be reported for all time points including baseline, and end of study. Multivariate logistic regression adjusting for covariates [such as age, sex, PROGRESS+ factors (58, 59), level of physical activity, smoking status, alcohol consumption, comorbidities, diabetes status] and potential effect modifiers (such as change in weight over time, medication de-escalation over time) will be carried out to ascertain the impact of a WFPBD on PNP in leprosy patient sub-populations and under various conditions. All statistical analysis will be carried out using GraphPad Prism 8 (GraphPad, United States).

3. Projected outcomes

3.1. Data collection

Outcomes will be collected at both baseline and at study end by dedicated personnel blinded to group allocation. Data will be housed on a password-protected and encrypted database generated on a secure drive which will be locked in the respective study centres. Prior to database entry, all patient and study data will be anonymized, and a master list linking patient identification and consecutive study numbers will be generated, secured, and housed separately to said database and to which only the study investigators will have access. Data collected for this study cannot be linked to a specific patient, and the principal investigator and study researchers will be the only individuals who have access to this information. Following final data collection, data will be pooled across study centres and analysis will be conducted within the research lab of the principal investigator.

3.2. Primary outcomes

3.2.1. Michigan neuropathy screening instrument

The MNSI is a robust assessment of neuropathy identifiers that includes both a subjective questionnaire and objective measurements of perception via QST. Specifically, Semmes-Weinstein monofilaments will be used to measure sensation at the ulnar nerve-innervated dorsum of the hand bilaterally, given this site's predilection for leprosy associated nerve damage, while a 128 Hz tuning fork will be utilized to test for vibration perception thresholds at the great toe (43, 60). This screening instrument has been widely used and validated in both diabetes and leprosy related neuropathy cohorts (19, 60). Scoring is based on a binomial yes/no response to specific questions where yes = 1 point and no = 0 points. Additionally, any abnormal QST result = 1 point, and a score of 4 or greater indicates the presence of neuropathy (60). The MNSI will be conducted at both baseline and at study end and will be utilized as one of the measurements for sensory neuropathy (Figure 3).

3.2.2. Neuropathy total symptom score

The Neuropathy Total Symptom Score will also be used to formulate a more robust assessment of sensory neuropathy. Unlike the MNSI, the NTSS includes considerations for both neuropathy intensity and frequency. Based on a summative questionnaire, participants can be assigned a maximum of 21.96 points, indicating greater morbidity, and depicted as a matrix comparing neuropathy intensity (mild, moderate, severe) versus frequency (occasional, often, continuous) (61). This questionnaire has been widely used and validated in cohorts of individuals with diabetes, a common comorbidity of leprosy, and will strengthen the assessment of sensory neuropathy within this trial (23, 61). The NTSS will be carried out at both baseline and study end (Figure 3).

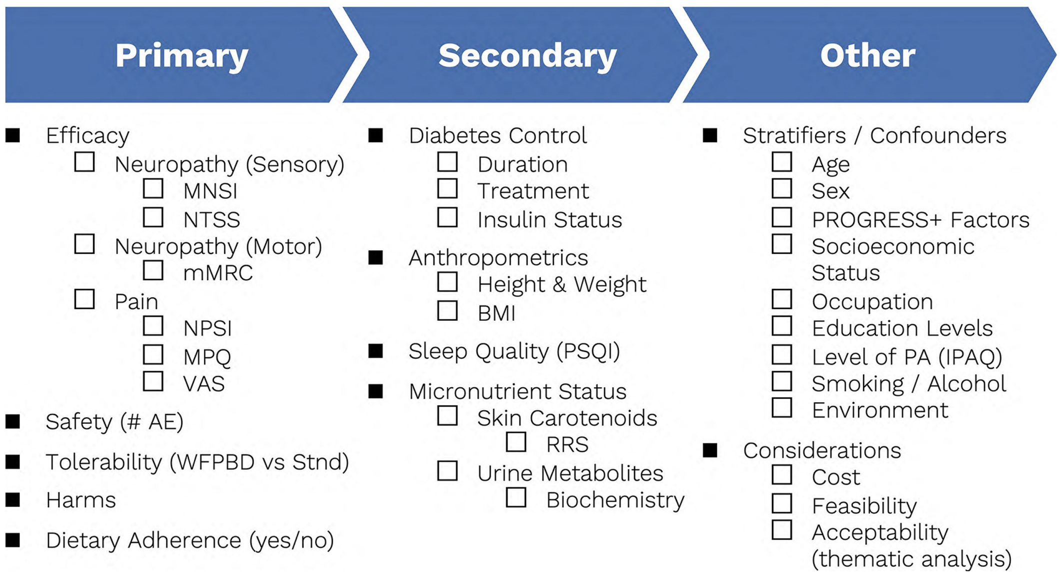

FIGURE 3
Outcomes, stratifiers, and additional considerations to be collected. AE, adverse events; BMI, body mass index; IPAQ, international physical activity questionnaire; mMRC, modified medical research council scale; MNSI, Michigan neuropathy screening instrument; MPQ, McGill pain questionnaire; NPSI, neuropathic pain symptoms inventory; NTSS, neuropathy total symptom score; PA, physical activity; PSQI, Pittsburgh sleep quality index; RRS, resonance Raman spectroscopy; Stnd, standard of care; VAS, visual analog scale; WFPBD, whole foods plant-based diet.

3.2.3. Modified medical research council scale

The modified Medical Research Council Scale is a reliable tool that has been commonly used to measure motor neuropathy in patients with leprosy (43). The mMRCS utilizes voluntary muscle testing (VMT) in the assessment of motor nerve function including the facial, ulnar, median, radial, and later popliteal nerves. Patients can be assigned a maximum of 5 points, which may be downgraded by any significant reduction of VMT. A score of less than 5 is indicative of decreased motor nerve function (43). The mMRCS will be utilized at baseline and at the end of study to provide a robust assessment of motor neuropathy in this trial (Figure 3).

3.2.4. Neuropathic pain symptom inventory

The Neuropathic Pain Symptom Inventory incorporates both measures of pain intensity and frequency including common patient pain descriptors such as burning, squeezing, pressure, and stabbing relative to the past 24 h (62). It has most commonly been used in the assessment of neuropathic pain in leprosy cohorts, wherein the higher the score the greater the pain, out of a possible 100 points (62–64). Participants will complete the NPSI questionnaire as part of a comprehensive neuropathic pain assessment at both baseline and at the end of the study (Figure 3).

3.2.5. McGill pain questionnaire

The McGill Pain Questionnaire will also be used to assess neuropathic pain throughout the trial, given a more robust set of patient pain descriptors. The MPQ classifies over 75 words into 4 descriptive pain categories including sensory, affective, evaluative, and miscellaneous, each with subcategories utilizing a scaled point system to indicate relative severity within each group, as well as over time. A maximum score of 78 points is possible, indicating most chronic and severe pain (65). This questionnaire has been utilized and validated within both diabetes and leprosy cohorts (19, 66). Alongside the NPSI, the MPQ will also be completed at both baseline and at the end of the study to provide the most comprehensive assessment of neuropathic pain possible (Figure 3).

3.2.6. Visual analog scale

Participants will also subjectively assess pain level on a 10-cm Visual Analog Scale between absolute poles of "No pain" and "Worse possible pain," both at baseline and at the end of the study. The VAS is a tool commonly used to assess pain given any underlying etiology, including both diabetes and leprosy, and is often utilized as the gold-standard when validating novel questionnaires assessing pain (19, 62, 63).

3.2.7. Safety, tolerability, harms, adherence

Additional considerations concerning the longstanding implementation of a WFPBD within this population will also be assessed at each counseling session. Data on safety via the number of adverse events, tolerability via drop-out rate, and emerging harms, against gold standard PNP therapeutics (or non-interventions, such as watchful waiting) will be collected and summarized. Dietary adherence reported as a proportionate yes/no will also be collected to ensure interventional feasibility. Based on the current landscape of the literature a WFPBD is expected to perform as well, if not better, than the current standard of care when considering implementation (19, 47, 55) (Figure 3).

3.3. Secondary outcomes

3.3.1. Anthropometrics, sleep quality, physical activity, and diabetes control

As a dietary lifestyle intervention can have a drastic effect on anthropometrics, height and weight will be measured at both baseline and at the end of the study and will be used to calculate body mass index (BMI) (Figure 3). Likewise, sleep quality has been associated with neuropathy severity, and must be monitored throughout the trial. The Pittsburgh Sleep Quality index is a validated questionnaire, widely used to assess sleep perturbation due to various etiologies. Participants can be assigned a maximum of 21 points indicating severe difficulties in all areas of sleep quality (67). The PSQI will be collected at baseline and at the end of the study. Self-reported physical activity will also be collected at such intervals using the International Physical Activity Questionnaire. The IPAQ includes 27-items designed to gauge the frequency and intensity of physical activity carried out in a 7-day period, encompassing occupational, transportation, housework, and leisure activities. It has been extensively tested and validated throughout 12 countries and has previously been utilized in assessing self-reported physical activity in both diabetes and leprosy cohorts (68–70). To avoid the potentially confounding effects of additional lifestyle levers, such as sleep quality and exercise, these assessments are paramount during downstream analysis. Lastly, in individuals experiencing a biochemical diabetes due to leprosy related corticosteroids, an assessment of diabetes control including duration of illness, therapeutics used, and insulin status will also be carried out to monitor any changes throughout the trial (Figure 3). Standard biochemistry, including serum cholesterol, triglycerides, hemoglobin-A1c, serum glucose, hepatic transaminases, creatinine, and basic micronutrient panel (e.g., serum ferritin, B12) will be taken to measure diabetes parameters and general physiological status. To better ascertain the relationship between the dietary lifestyle intervention and leprosy itself, neuropathy and neuropathic pain outcomes will be stratified by secondary outputs, with specific emphasis on diabetes status, and steroid use.

3.3.2. Micronutrient status

In order to avoid additional invasive blood draws in at-risk equity-deserving patient populations, alternative yet validated measures of individuals' micronutrient status will be implemented. Both skin carotenoids and urine metabolites can be utilized to define the baseline dietary habits of all participants. Resonance Raman Spectroscopy (RRS) has emerged as an inexpensive and non-invasive tool commonly used to measure skin carotenoid levels including alpha-carotene, beta-carotene, beta-cryptoxanthin, lycopene, lutein, and zeaxanthin (71, 72). Due to the high concentrations of carotenoids in fruits and vegetables, RRS has been used to reliably estimate dietary intake of such foods (71, 72). Its performance has been assessed across multiple geographies and in patients with varied skin tones, and a statistically significant correlation was not identified (71, 72). Similarly, urine metabolites can be assessed using standard laboratory biochemistry commonly available to study centres and can be utilized to estimate the remaining components of diet (73, 74). Consumption habits of fruits, vegetables, low fiber grains, fish protein, nuts, red meat, shellfish, dietary supplements, caffeine, alcohol, and fats and oils can be estimated and corroborated using relative levels of urine metabolites including methyl glutamate, mannitol, cytosine, suberate, omega 3, tryptophan, xylitol, lysine, creatine, vitamin B2, and vitamin E (73, 74). Micronutrient status assessment will be carried out at baseline and at study end to ensure significant micronutrient derangements have not occurred (Figure 3).

3.4. Potential stratifiers/confounders

Beyond primary and secondary endpoints, potentially confounding variables will be collected and utilized for downstream data analysis including: (1) demographic data: age, sex, socioeconomic status [relative within country and absolute according to World Bank definitions (75)], occupation (considering level of manual work, repetitive tasks, and prolonged standing/walking/climbing), household membership (living alone vs. with family members), and education level; and (2) lifestyle-related information: level of physical activity (via the international physical activity questionnaire), tobacco and cannabis smoking and alcohol consumption habits (amount consumed/day), and environment (urban vs. rural; meters a.s.l.). Effect modifiers including weight loss over time and de-escalation of medication over time will also be considered. Considerations of intervention cost, feasibility, cultural acceptability, and adherence will also be collected and summarized in a thematic analysis (Figure 3).

4. Ethics, dissemination, and access

In advance of study initiation and following Research Ethics Board (REB) approval at all participating centers, this trial will be registered with ClinicalTrials.gov clinical trial database (76) according to the Interventional Trial Protocol Registration Template.[1] Current literature suggests high acceptability, and a limited risk profile associated with a WFPBD (19, 21, 22, 47, 55, 56). As a result, a safety board will not be established, however, data on relevant safety, tolerability, and harms will still be collected for downstream analysis. Iterative updates to the trial protocol will be made available to the REB and trial updates will be populated within the ClinicalTrials.gov website as soon as they become available. Data, protocol updates, and study progress will be made available to relevant stakeholders including the site principal investigators, study personnel, and participants, and will be disseminated in the form of peer-reviewed journal publications, submitted conference abstracts/posters, presentations, and lay-language infographics.

5. Expected impact

This trial aims to investigate the potential neuro-protective impact of a WFPBD on sensory and motor neuropathy in leprosy, thereby strengthening the literature underpinning dietary lifestyle interventions for chronic diseases. Through comprehensive validated questionnaires and QST, a robust profile of neuropathy progression and the relative impact of a WFPBD will be ascertained. Given this assessment, this trial has the potential to inform on the development of novel guidelines to better manage the sequelae of leprosy, an infectious disease of significant global relevance. Patients experiencing a leprosy infection continue to suffer from debilitating therapeutic side effects and social ostracization, contributing to ever rising disability-adjusted life years (DALYs) lost (6, 77–79). Therefore, a WFPBD in the management of leprosy-related

1 https://prsinfo.clinicaltrials.gov/Interventional_Study_Protocol_Registration_Template_Jan_2018.pdf

neuropathy may mitigate the significant impact of the disease at both the patient and economic level. A WFPBD has the potential to serve as a low-risk, low-cost, low-tech intervention for chronic neuropathic pain, improving function and reducing the overall morbidity of leprosy. More broadly, this trial will also contribute to the growing literature regarding the importance of dietary lifestyle interventions in disease management and may lead to the continued investigation of this relationship in other diseases of relevance.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

MK contributed to protocol design and was primarily responsible for drafting the manuscript. AB conceived the protocol and contributed to design and writing of the manuscript. All authors provided input and comments on successive drafts of the manuscript, read, and approved the final draft.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Glossary

BMI	Body Mass Index
DALYs	Disability-Adjusted Life Years
IPAQ	International Physical Activity Questionnaire
MDT	Multidrug Therapy
mMRCS	modified Medical Research Council Scale
MNSI	Michigan Neuropathy Screening Instrument
MPQ	McGill Pain Questionnaire
NPSI	Neuropathic Pain Symptom Inventory
NTSS	Neuropathy Total Symptom Score
PSQI	Pittsburgh Sleep Quality Index
QST	Quantitative Sensory Testing
REB	Research Ethics Board
RRS	Resonance Raman Spectroscopy
TDU	Tropical Disease Unit
VAS	Visual Analog Scale
VMT	Voluntary Muscle Testing
WFPBD	Whole Foods Plant Based Diet

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A whole-food, plant-based program in an African American faith-based population

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Background: The African American (AA) population is disproportionately impacted by chronic disease as well as many of the leading causes of preventable death, including hypertension, obesity, heart disease, stroke, and type 2 diabetes. In the AA community of Kane County, Illinois, the incidence of chronic disease is particularly high. A standardized Zoom-based group program that gives participants the knowledge, skills, and support to adopt a whole-food plant-based diet has been shown to rapidly improve health. The results of a cohort analysis were analyzed to assess the effectiveness of this program within an AA community characterized by a high burden of chronic illnesses.

Methods: Participants were recruited from a network of 12 AA churches in Illinois to participate in Rochester Lifestyle Medicine Institute's "15-Day Whole-Food Plant-Based (WFPB) Jumpstart" program. The medically-facilitated 15-Day Jumpstart program provided WFPB nutrition education, coaching, and cooking demonstrations during seven 1 and 2-h Zoom sessions. Participants underwent pre- and post- metabolic screenings to assess for changes in their weight, vital signs, blood sugar, and cholesterol measurements. Changes in diet, biometrics, and patient-centered outcomes from baseline to the end of the program were assessed via paired *t*-tests for the normally distributed measures, and a Wilcoxon signed rank test for measures that were not normally distributed.

Results: Twenty-one AA adults participated. Ten of 16 who provided results had hypertension, 5 had diabetes, 5 had pre-diabetes, and 5 had hyperlipidemia. Participants ate more vegetables (median 2 servings at baseline vs. 3 during the program), greens (1 vs. 3), fruit (2 vs. 3), whole grains (1 vs. 2), and legumes (1 vs. 2). They decreased their consumption of meat, eggs and dairy, added fat, processed foods, and high-fat plant foods ($p<0.05$ for each comparison). Participants reported significantly better energy (median 5 at baseline vs. 9 during the program, on a 10-point scale), sleep (7 vs. 8.5), and mood (8 vs. 9). Average weight loss was 5.8 pounds (199.9 to 194.1, $p<0.001$), systolic blood pressure dropped from 129.7 to 119.9 ($p=0.02$), and total cholesterol dropped from 185.1 to 147.9 ($p<0.001$). All participants who provided data reported an intent to continue eating at least a partially WFPB diet following the program.

Conclusion: The 15-Day WFPB Jumpstart program led to significant changes in diet, resulting in improvement in several chronic disease measures in this AA community. This rapid improvement can reinforce behavior change. Further large-scale implementation is needed to confirm these preliminary results and to understand whether behaviors and outcomes are sustained.

KEYWORDS

African American, black-, whole food plant-based, faith-based, jumpstart, nutrition, lifestyle

Introduction

Chronic disease, exacerbated by obesity, impacts African Americans (AAs) disproportionately (1). The National Health and Nutrition Examination Survey conducted from 2015 to 2016 highlighted that, in comparison to Caucasians, AAs nationwide report a lower intake of fruits, vegetables, dietary fiber, and whole grains, and conversely a higher intake of sugary beverages and processed meats (2). In Kane County, Illinois, 67.8% of adults are overweight or obese (3). In Aurora, the largest city in the county, an AA church community health screening revealed that in 2018, 79% of the women and 86% of the men screened were overweight or obese (4). Additionally, when compared to Caucasians, AAs in Kane County were 3.7 times more likely to be hospitalized for diabetes, were 8.5 times more likely to be hospitalized for hypertension, and were more likely to die from stroke and heart disease than any other race (3). Given that hypertension, diabetes, and heart disease increase the lethality of COVID-19, the pandemic has highlighted the need for a health intervention (5). Poor nutrition plays a significant role in the development of chronic disease, and therefore provides an opportunity to reduce these health disparities (6, 7). Therefore, a health intervention to decrease AA chronic disease and obesity can significantly impact this minority community's overall health.

African Americans have a distinct cuisine which encompasses a diverse array of food choices and flavors. The African American Heritage Diet maintains that traditional AA cuisine is primarily plant-based, grown from gardens, with substantial quantities of fruits, vegetables, and whole foods (8). However, due to westernized influence and issues of access, current eating patterns are high in salt, oil, high-fat foods, and processed starches, resulting in an overall diet high in sodium, fat, and refined carbohydrates but deficient in fruits, vegetables, and other plant foods (8, 9). African Americans can benefit from adopting a whole-food plant-based (WFPB) diet (10, 11), which has been shown to decrease obesity, diabetes, and heart disease, and to help manage chronic diseases (12). The Rochester Lifestyle Medicine Institute (RLMI) 15-Day WFPB Jumpstart offers individuals the education, structure, and support to understand how to incorporate fruits, vegetables, whole grains, and legumes into their daily eating regimen (11). In this program, participants are instructed to eat only whole-food plant-based options, to limit salt and added sweeteners, and to exclude added oil.

Previous reports of outcomes in a primarily Caucasian population have demonstrated that the Jumpstart program rapidly gives people the knowledge, skills, and experience of a WFPB diet. By doing so, participants realize significant improvements in weight, blood pressure, cholesterol, and blood sugar in 15 days (13). This pilot program was initiated to identify an AA population with a high burden of chronic disease and an interest in following a WFPB diet. The program aimed to evaluate whether they would make significant dietary changes and experience positive health outcomes from moving to such a diet.

The AA participants were recruited from 12 AA churches in Kane County, Illinois. The clergy from the 12 churches were invited to participate in an informational webinar prior to the start of the program. At the webinar, they learned about the prevalence of chronic disease in Kane County AAs and received an overview of the 15-Day WFPB Jumpstart program and its potential benefits for their at-risk parishioners. Afterward, they were asked to distribute program recruitment flyers at their churches.

Overweight and obese parishioners were recruited to participate in the program. Most had at least one other chronic disease indicator. They underwent metabolic testing pre- and post- the 15-Day WFPB Jumpstart program to observe its effects on weight, blood pressure, cholesterol, blood sugar, and mood. The metabolic testing was done at an Ascension community health clinic. The medically-facilitated 15-Day WFPB Jumpstart programming was administered virtually.

Detail

The 15-Day program components consisted of an informational Zoom session that explained the program structure and the WFPB eating regimen. It also encouraged participants to forward the program information to their medical providers, as incorporating these healthy eating changes could reduce the need for prescription medications. Before beginning the program, the participants had completed a pre-Jumpstart questionnaire regarding their nutrition, the state of their health, and the results of their metabolic testing blood work. During the program, the participants had access to 7 medically-facilitated Zoom-based nutrition education and support sessions.

The program equipped participants with a comprehensive nutrition guide that included shopping lists and recipes for a WFPB diet. Additional nutrition resources were available in a Google Classroom. Between-session communication occurred in the Google Classroom where participants could ask RLMI staff questions about their health, the program, and the WFPB eating pattern. The 15-Day Jumpstart WFPB diet focuses on fruits, vegetables, whole grains and legumes. As has been previously described, "animal products are excluded. High-fat plant foods (e.g., nuts, nut and seed butters, olives, avocado, and coconut) are excluded, as are processed foods and foods with added oil or sugar. Foods that provide a concentrated source of natural sugars, such as dried fruits and maple syrup, are limited to 1 tablespoon per day. Patients are advised to eat 1 tablespoon per day of ground flax seeds to provide omega-3 fatty acids. Patients are not advised to count calories or control portions. In fact, they are encouraged to eat whenever they are hungry—as long as the food is compliant with the program" (13, pp. 375–376).

Participants had access to a cooking and meal preparation demonstration over Zoom. Mid-week check-ins were also held over Zoom. During these check-ins, the participants reported their progress in breakout rooms and asked questions. A virtual potluck allowed participants to share recipes they enjoyed and incorporated into their diets. These recipes were assembled into a cookbook for each participant. At the end of the program, participants completed a post-Jumpstart questionnaire to assess changes to their diet, health, and blood work.

Permission was obtained from the Ascension (formerly AMITA Health) Institutional Review Board to use the data collected from the program participants as part of the QI program. The program was deemed exempt.

One hundred and eight AA adults were invited to participate in the program via email outreach; out of 108 invitees, 21 (19.4%) agreed to participate. The program took place in May and August of 2022. Descriptive statistics were used to characterize the participants at baseline and at the end of the program. Since this was a small pilot study (<20 participants who provided pre-post data), a Shapiro–Wilk test was completed for all the variables, to test for normality. All the biometric measures were normally distributed except for the baseline waist measure. A paired *t*-test was used to evaluate outcomes for the normally distributed measures, and a Wilcoxon signed rank test was used to evaluate the change in waist measure. Several of the dietary components and the self-reported outcomes did not meet the cutoff ($p < 0.05$) for normality. Differences in diet and self-reported outcomes were therefore assessed using the non-parametric Wilcoxon signed rank test. Analysis was completed using IBM SPSS Statistics for Windows, version 29.0 (IBM Corp., Armonk, NY, United States).

Participants ranged in age from 21 to 74, with an average age of 58 (Table 1). 4.8% reported that they were Hispanic, and 4.8% preferred not to say. All but one of the participants were female. Ten of the 16 who provided results about their chronic conditions reported that they had hypertension, 5 had diabetes, 5 had pre-diabetes, and 5 had hyperlipidemia.

Participants increased their intake of vegetables, greens, fruits, whole grains, and legumes during the Jumpstart program (Table 2). They decreased their intake of meat, eggs and dairy, added fat, processed foods, and high-fat plant foods (Table 2). Average weight loss was 5.8 pounds, systolic blood pressure dropped 9.7 mm Hg, and total cholesterol dropped 37.1 points (Table 3). Participants reported significantly better energy, sleep, and mood (Table 4). All participants who provided data reported an intent to continue eating at least a partially WFPB diet following the program. Five of the 16 who responded said they would eat more WFPB foods; 4 said they would stay on a WFPB diet for the foreseeable future, adding back some high-fat plant foods, and 7 said they would do their best to stay on a WFPB diet but at times might eat some foods that were not part of this eating pattern. Ninety-three percent of the respondents agreed that they had confidence that a very low fat whole-food plant-based diet was the best for their health; 100% stated that they learned important information about the role of nutrition in their health; 100% felt they gained the skills they needed to make positive changes in their health (Table 5).

Discussion

The participants decreased their intake of high fat and sugary foods by focusing on increasing vegetables, leafy greens, fruits, whole grains, and legumes. The session with two cooking demonstrations was pivotal in helping participants understand the "how" of incorporating more plant foods into their diet. During the 2-h virtual session, they were educated on the technique of sautéing vegetables without oil, batch cooking, and meal prep. The session four virtual potluck was instrumental in helping participants understand that eating a whole-food, plant-based diet was not only doable but a delicious way to eat. The virtual potluck required all participants to share their favorite WFPB recipe and a meal photograph, which was incorporated into a participant cookbook. During this session the participants did virtual presentations of their dish, shared preparation tips and answered questions. The virtual, weekly check-in sessions allowed participants to address their barriers to implementing the WFPB diet and assess if they were correctly adhering to the outlined eating regimen. Participants realized that they had preconceived notions on the meaning of eating healthy and that their perceptions did not always correlate with the 15-Day Jumpstart's literal meaning of fruits, vegetables, whole grains, and legumes. In the 15-Day WFPB Jumpstart, they learned practical and easy-to-implement tips on how to make sustainable lifestyle changes. Because of this education, the participants addressed potential nutritional deficiencies—such as a lack of fiber, and high calorie foods with low nutrient density– that often lead to chronic diseases. In addition, the Rochester staff, due to their willingness to tailor the dietary recommendations to the participants' cultural preferences, were able to overcome perceived cultural barriers and successfully implement the principles of the 15-Day WFPB Jumpstart in this AA study population.

In addition to improvements in energy, sleep and mood, participants lost weight, had a reduction in abdominal girth, and decreased systolic blood pressure, total cholesterol, LDL and HDL. Except for HDL, all of these changes have been shown to be beneficial to heart health and reducing cardiac risk. Long-term adoption of a very low fat whole-food, plant-based diet has been shown to be effective in reversing heart disease (14). The changes in cholesterol profile seen in this pilot program are consistent with adopting this dietary pattern (13, 15–17). One study of this change in cholesterol profile questioned the predictive value of HDL in populations who do not consume a typical Western dietary pattern, and suggested that, since HDL is part of the assessment for metabolic syndrome, this approach may not be useful in evaluating lifestyle programs that utilize a WFPB dietary pattern (17).

Since some of the 15-Day Jumpstart participants missed multiple sessions, this may have led to less than a full experience of the program. Seventeen of the 21 participants (81%) attended 4 or more sessions, which is the organization's definition of participation in the program, as it represents at least 5 h of program content, and significant time to interact with program staff. In this population, there are various stressors that may have impacted the participants. Several of the participants were seniors who were primary caregivers to their elementary school-aged grandchildren. Session attendance could have been made more convenient for busy participants by recording sessions for later viewing. It should be noted that sessions should not conflict with church meetings, like mid-week Bible Study or Sunday services, as occurred during this study. For some, in-person meetings tied to these activities might help to boost participation.

Future efforts should focus on motivating the participants to attend all of the sessions and to complete post-Jumpstart questionnaires. Increasing attendance will also give participants more opportunity to develop the skills and obtain the resources needed to

TABLE 1 Participant characteristics.

Characteristic (*N*=21)	
Age—mean (range)	58 (21–74)
Race—African American	100%
Ethnicity	
Hispanic	4.8%
Non-Hispanic	90.5%
Prefer not to say	4.8%
Gender	
Female	95.2%
Male	4.8%

TABLE 2 Changes in dietary components during the Jumpstart program.

	n	Beginning of program [median (range)]	End of program [median (range)]	Z score	*p*-value**
Measure (servings)					
Vegetables	16	2 (0–3)	3 (1–15)	−3.20	0.001
Leafy greens	16	1 (0–3)	3 (1–6)	−3.46	<0.001
Fruit	16	2 (0–3)	3 (1–6)	−3.11	0.002
Whole grains	16	1 (0–3)	2 (1–6)	−3.10	0.002
Legumes	15	1 (0–3)	2 (1–6)	−3.22	0.001
High fat plant food	16	2 (0–5)	0 (0–2)	−3.08	0.002
Meat	15	3 (0–5)	0 (0–2)	−2.85	0.004
Eggs and dairy	16	1.5 (0–3)	0 (0–1)	−3.02	0.003
Added fat	16	3 (0–10)	0 (0–1)	−3.41	<0.001
Processed food	16	3.5 (0–10)	0 (0–2)	−3.31	<0.001
Rating of adherence*	15	4 (1–9)	9 (6–10)	−3.43	<0.001

*Rated adherence to a very low fat whole-food plant-based diet on a scale from 0 to 10.
***p*-value calculated using the Wilcoxon signed rank test.
Results presented only for participants who reported pre-and post-data; total group $N = 21$.

TABLE 3 Jumpstart program biometric measure outcomes.*

	n	Beginning of program [mean (SD)]	End of program [mean (SD)]	Difference [mean (SD)]	95% confidence interval		*P*-value
					Lower	Upper	
Weight (pounds)	17	199.9 (26.3)	194.1 (24.7)	−5.8 (4.1)	−7.9	−3.7	<0.001
Waist circumference (inches)**	15	40.8 (4.3)	38.9 (3.8)	–	–	–	–
Systolic blood pressure (mm Hg)	15	129.7 (9.2)	119.9 (11.4)	−9.7 (13.5)	−17.2	−2.2	0.02
Diastolic blood pressure (mm Hg)	15	77.9 (6.6)	74.5 (6.8)	−3.3 (8.0)	−7.8	1.1	0.13
Cholesterol (mg/dL)	14	185.1 (32.0)	147.9 (28.0)	−37.1 (22.7)	−50.2	−24.0	<0.001
LDL (mg/dL)	15	99.9 (38.3)	79.5 (25.2)	−20.5 (32.0)	−38.2	−2.8	0.03
HDL (mg/dL)	15	57.4 (17.0)	45.7 (15.2)	−11.7 (8.5)	−16.4	−7.0	<0.001
TG (mg/dL)	15	99.1 (47.7)	115.4 (60.5)	16.3 (38.2)	−4.8	37.5	0.12
Glucose (mg/dL)	15	101.8 (16.4)	98.8 (16.4)	−3.0 (10.2)	−8.6	2.6	0.27

*Changes, confidence intervals and *p*-values calculated via paired *t*-test, except for waist circumference.
**Waist circumference was not normally distributed at baseline according to the Shapiro Wilks test; median waist circumference decreased from 39 to 38 inches (Wilcoxon signed rank test, $Z = -3.31$; $p < 0.001$).
Results presented only for participants who reported pre-and post-data; total group $N = 21$.

make sustainable changes. Faith leaders spend a considerable amount of time attending to the health needs of their parishioners by praying for the sick, visiting patients in the hospital, and planning and conducting funerals. Launching such interventions in faith-based organizations necessitates forming collaborations with clergy and establishing the shared goal of health promotion in their congregations. Clergy can play a vital role by incorporating spirituality into this health intervention (e.g., prayer, scripture reading, devotions, etc.) and can highlight the biblical imperative of pursuing a healthy lifestyle. As a trusted source of information, clergy can encourage participants to regularly attend the sessions. This would lead to a greater likelihood of following the recommendations, which in turn could increase success.

A WFPB diet can be used as a conduit to help AAs lower their chronic disease risk and reduce obesity (18). According to the 2015 National Harris Poll, 8% of AAs adopted a vegan or vegetarian diet as compared to 3% of all other Americans (19). This statistic suggests that the AA community is receptive to eating a WFPB diet. The 15-Day Jumpstart succeeded in providing a framework for how to transition to this dietary pattern, and participants incorporated

TABLE 4 Jumpstart program self-reported outcomes.*

	n	Beginning of program [median (range)]	End of program [median (range)]	Z score	*P*-value**
Energy	16	5 (2–10)	9 (7–10)	−3.09	0.002
Sleep	16	7 (2–9)	8.5 (7–10)	−3.21	0.001
Mood	16	8 (2–10)	9 (6–10)	−2.73	0.006
Pain	16	4 (1–8)	4 (1–9)	−1.20	0.23

*Rated on a scale from 0 to 10.
***P*-value calculated using the Wilcoxon signed rank test.
Results presented only for participants who reported pre-and post-data; total group $N = 21$.

TABLE 5 Self-report of knowledge, confidence and skills resulting from program (n=15).

	Strongly agree (%)	Agree (%)
"I am confident that I know about the type of eating pattern that is best for my health."	53.3	40.0
"I learned important information about the role of nutrition in health."	53.3	46.7
"I gained the skills I need to make changes to my health."	60.0	40.0

more fruits, vegetables, and nutrient rich foods into their eating regimen.

Participant recruitment was challenging because many individuals who could have benefitted from this nutritional program did not feel they could implement it. Individuals voiced concerns about eliminating meat and dairy from their diets. They perceived that a WFPB diet would not be satisfying or palatable. A recruitment event that showcased the medical benefits of a WFPB diet coupled with a live cooking demonstration that allowed participants to taste the food can be utilized to increase interest and participation and assuage participants' concerns.

Limitations

One of the biggest limitations of the study was its small sample size: 21 participants. However, this was designed as a pilot program to serve as "proof of concept." Participants made significant changes in eating patterns, and as a result, both experienced improvements in health and expressed an intention to continue at least a partially WFPB diet. A larger, randomized prospective trial would provide more precise estimates of the impact of this program on an African American community. The results seen in this study suggest that a larger study is warranted. Approximately 19% of the individuals who were invited participated in the program, and it is feasible that with increased awareness of the outcomes, the enthusiasm of the participants, and ongoing collaboration with the clergy, the interest in the program could increase.

Not all of the people who signed up participated fully. Some of the program's sessions had a scheduling conflict with Sunday church services, which created a barrier to regular attendance. Many participants did not thoroughly understand the 15-Day Jumpstart principles which resulted in mistakes in their choices of meal ingredients. This constraint can be addressed by including a component that would evaluate the participants' understanding of the program's dietary instructions. For example, including a simple quiz or a hypothetical scenario could confirm that the participants understand the Jumpstart guidelines. This could be done early in the program, to correct any misunderstanding, and enable full participation.

Self-reported outcomes, such as mood, energy, and sleep, were assessed as part of a QI program. As a result, the team used single-question queries rather than more extensive validated tools, in order to maximize response rate. A prospective study using validated tools would help to confirm these preliminary findings. Self-reported measures are subject to reporting bias. Participants are aware of the desired responses, namely, improvement in these measures. However, participants also experienced improvements in objective measures, such as weight, vital signs, and lipids.

Conclusion

This pilot program was initiated to evaluate whether an AA population with a high burden of chronic disease could be identified, who would be interested in participating in a program to educate them about the benefits of a WFPB diet. Furthermore, it was important to know whether they would make the dietary changes recommended by the program, and whether they would experience positive health outcomes from moving to a WFPB diet.

A nutrition intervention can be utilized to mitigate the disproportionate chronic disease health disparities that plague AAs. This medically-facilitated, 15-Day WFPB Jumpstart program provides the support, education and the practical tools to incorporate increased fruit, vegetable, whole grain and legume intake while eliminating meat, dairy and foods that are processed, contain increased sugar, or are high in fat. This study also highlighted the need to include AA clergy in community health partnerships as they are highly vested in health promotion that benefits their congregants. Their influence as respected faith leaders can be utilized to encourage participation in the 15-Day WFPB Jumpstart program, thereby realizing the shared goal of improving health and decreasing chronic disease.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material. Further inquiries can be directed to the corresponding author.

Author contributions

FN assumed multiple responsibilities, including participant recruitment, supervising pre- and post-metabolic screenings, maintaining communication with Frontier journal throughout the submission, peer review, and publication process, ensuring compliance with all specified journal submission guidelines, addressing post-publication correspondence, and serving as the principal investigator. TB was the lead educator for all of the virtual training sessions. BG and MD served as research managers and assisted in conceptualizing and coordinating the health and nutrition intervention in an African American faith-based setting. BP assumed the role of the data coordinator and prepped all data for the statistician. SF was the co-investigator and performed statistical analyses; analyzed and summarized all data; and assisted FN in writing and revising the manuscript. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Scoping review of the association of plant-based diet quality with health outcomes

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Introduction: The association of plant-based dietary patterns with health outcomes has traditionally been assessed without considering nutritional value. The plant-based dietary index (PDI), first published in 2016, overcomes this limitation with both a healthful PDI (hPDI) and an unhealthful PDI (uPDI), based on the quality of plant foods consumed plus the frequency of animal foods. We sought to summarize the breadth of research using the hPDI and uPDI to gain insight into how the quality of plant-based dietary patterns might be associated with health outcomes.

Methods: Scoping review of studies that used the PDI, hPDI, or uPDI to report associations with health outcomes. Multiple databases were searched from 2010 through April 2023 with 2 authors independently assessing eligibility and extracting data. In addition to assessing the association of the indices to health outcomes, we determined the frequency of concordant or discordant findings for hPDI versus PDI and for hPDI versus uPDI.

Results: We included 95 articles (54% longitudinal, 37% cross-sectional, and 9% case–control) with a median sample size of 3,646. Higher hPDI levels were associated with favorable health outcomes in 36% of comparisons (most often for obesity, mortality, diabetes, cardiovascular disease, and psychiatric disorders), compared to 25% for the PDI and only 2% for the uPDI. Conversely, higher levels of the uPDI were associated with unfavorable health outcomes in 33% of comparisons, in contrast to under 1% for the hPDI and 2% for the PDI. When the hPDI association to an outcome was discordant with the uPDI or PDI, the significance and directionality always favored the hPDI over the uPDI, and nearly always favored the hPDI over the PDI.

Discussion: Dietary indices that account for the quality of plant foods can show health benefits that might be missed by a generic plant-based index. A greater focus on the quality of plant foods could improve nutrition guidelines, raise awareness about the benefits of adding unrefined plant foods to the diet, and empower consumers to make incremental additions of such foods to displace unhealthy foods. We anticipate increasing use of indices that address food quality in future research.

KEYWORDS

vegan, vegetarian, plant-based diet, food frequency questionnaire, plant-based dietary index, diet quality, health outcomes, food as medicine

Introduction

Researchers often use food frequency questionnaires to assess how dietary patterns are associated with disease prevalence, incidence, and mortality. Resulting publications have traditionally used this information to create a simple dichotomy into diets with plant versus animal foods (e.g., vegetarian vs. omnivore), without considering the nutritional value of the plant foods consumed. This could potentially reduce, or obscure, any association of whole, fiber-rich healthy plant-foods with reduced disease incidence and mortality, compared to vegetarian diets with less healthy plant-foods, such as refined grains, processed foods, and sugar-sweetened snacks and beverages.

An example of the imprecision resulting from not addressing the overall quality of plant-based diets is the association of higher carbohydrate intake with increased mortality in a global health study (1). The investigators did not distinguish between whole-grain versus refined carbohydrates, making the results about carbohydrates overall difficult to interpret or generalize. Conversely, when carbohydrate quality is explicitly considered, a dose–response relationship is observed for whole-grain carbohydrates high in fiber and a reduced risk of mortality, type 2 diabetes, cardiovascular diseases, and colorectal and breast cancer (2). Similarly, consuming unrefined plant foods (e.g., nuts, fruits, vegetables and whole grains) can reduce the risk of stroke, heart failure, and coronary heart disease, whereas the opposite is seen for refined plant foods (e.g., refined grains and sugar-sweetened beverages) (3).

One solution to the impact of plant-based diet quality on health outcomes has been to calculate an overall *plant-based dietary index (PDI)* based on a food frequency questionnaire and to then stratify the PDI as a *healthful PDI* or an *unhealthful PDI* (Table 1) based on the type of plant foods consumed and the amount of animal foods (4). Plant foods considered healthy include nuts, fruits, legumes, vegetables and whole grains, whereas those considered less healthy include sweets, potatoes, refined grains, fruit juices, and sugar-sweetened beverages. Using this general approach to assessing diet quality, pooled analyses of cohort studies have shown the benefits of a healthful PDI for cardiovascular disease (5, 6), type 2 diabetes (4, 7), and weight reduction (8, 9). Others have used the term provegetarian dietary pattern (PVD), instead of PDI, for a similar classification into healthful versus unhealthful. Showing, for example, how the healthful PVD may reduce breast cancer risk (10).

The advantage of considering plant-based diet quality when assessing health outcomes warrants a scoping review to map the available research evidence and to identify knowledge gaps (11). Although less common than systematic reviews, scoping reviews are increasing in popularity with established methodology and reporting standards (12–14). In contrast to systematic reviews, which synthesize quantitative evidence on the efficacy of an intervention for a specific condition, a scoping review offers primarily qualitative insight into a field of study through a broad, birds-eye view of a topic or subject area (13). Given the relatively recent distinction in the nutrition literature of healthy versus less healthy plant-based diets, we considered a scoping review ideal for exploring how this concept has influenced subsequent publications on the association of plant-based diets with health outcomes. Therefore, the goal of this scoping review is to highlight the importance of assessing plant-based diet quality so others can incorporate plant food quality into reviews, guidelines, and policies that associate diet with health outcomes.

Methods

Protocol

Our scoping review protocol was based on standards developed by JBI, the Joanna Briggs Institute, specifically for conducting a scoping review (13). The manuscript was structured in adherence to the Preferred Reporting Standards for Systematic Reviews and Meta-Analysis (PRISMA) extension for scoping reviews (14). The premise for this review is defined using the PICO criteria below for population, intervention, comparisons, and outcomes:

- Population: adults and children enrolled in studies comparing plant-based diet quality to health outcomes
- Intervention: dietary assessment using a food frequency questionnaire with categorization into an overall PDI or PVD, a healthful PDI or a healthful PVD (hPDI or hPVD), and an unhealthful PDI or an unhealthful PVD (uPDI or uPVD)
- Comparisons: when more than one index is reported, association with outcomes for the overall index versus the healthful index and for the healthful index versus the unhealthful index
- Outcomes: disease incidence, prevalence, or mortality as reported by the investigators, with hazard ratios for the highest dietary index level versus the lowest level (e.g., by quartiles, quintiles, deciles).

Eligibility and search criteria

To be included in this review, the source article had to report original research assessing the association of a plant-based diet with a

TABLE 1 Composition of plant-based dietary indices.*

Plant-based index emphasis	Healthy plant foods	Less healthy plant foods	Animal foods
Overall PDI: higher intake of all plant foods and lower intake of all animal foods Healthful PDI: higher intake of healthy plant foods and lower intakes of unhealthy plant foods and all animal foods Unhealthful PDI: higher intake of unhealthy plant foods and lower intakes of healthy plant foods and all animal foods	Whole grains Fruits Vegetables Nuts Legumes Vegetable oils Tea/Coffee	Refined grains Fruit juices Potatoes Sweets/deserts Sugar-sweetened beverages	Meat Fish/seafood Animal fats Dairy Eggs Miscellaneous animal-based foods

PDI, plant-based dietary index.
*Food categories as defined by Satija et al. (4).

clinically relevant health outcome. The study design could be observational (e.g., cohort, case–control, or cross-sectional), experimental (e.g., clinical trial, randomized controlled trial), or population-based (e.g., national survey data) but must have included a healthful plant-based dietary index (hPDI or hPVD), an unhealthful index (uPDI or uPVD), or both. We excluded reviews, systematic reviews, meta-analyses, commentaries, case series, and correspondence (e.g., consensus reports).

Peer-reviewed articles meeting the above criteria, and addressing the PICO question above, were included if published between the period of January 2010 through April 2023, without language restrictions. Searches were performed with the assistance of an experienced information specialist in databases that included MEDLINE/PubMed, CINAHL, EMBASE, and Web of Science. The initial search strategy, drafted by an information specialist and refined through team discussion, was implemented in MEDLINE/Med, CINAHL, and EMBASE and used the terms "((healthy AND unhealthy) OR (healthful AND unhealthful)) AND (vegetarian OR vegan OR plant-based OR provegetarian OR pro-vegetarian OR plant-predominant)." Upon reviewing the initial search results we noted that some of the relevant articles cited publications that might also be relevant to our review, but instead of" unhealthy or unhealthful" used the terms "less healthy or less healthful." We therefore updated the search with the expanded terms: ""((healthy AND unhealthy) OR (healthful AND unhealthful) OR (healthy AND "less healthy") OR (healthful AND "less healthful") OR (healthy AND overall) OR (healthful AND overall)) AND (vegetarian OR vegan OR plant-based OR provegetarian OR pro-vegetarian OR plant-predominant)."

Selection of sources of evidence

To increase consistency, dual reviewers (HJM, MAW) screened articles for relevance, with disagreements on study selection and data extraction resolved by consensus and discussion, if needed. To reduce the possibility that articles were missed in the MEDLINE/Med, CINAHL, and EMBASE searches, a final search was performed in Web of Science for publications citing any of three key articles considered representative of source articles for the review (see Results for specific articles used).

A data-charting form for Excel was developed to extract all information from each source article, including information on authorship, article characteristics (publication year, country of origin, study aims or purpose), study sample (origin, size, demographics), sampling method (convenience, random, population cohort), sampling time frame (recruitment years), methodology (study design, food frequency questionnaire details), dietary classification (e.g., healthful unhealthful), follow-up information, outcomes assessed (including comparisons, such as by extreme quartiles, quintiles, or deciles), results (usually adjusted hazard ratios), and conclusions. We did not perform a risk of bias assessment for the included source articles because this is unnecessary in a scoping review (11) and is not part of the recommended reporting standards (14).

Summary measures and results synthesis

We performed a descriptive and qualitative analysis, seeking to map the existing evidence and to highlight how considerations of plant-diet quality might impact associations with clinically important outcomes. We did not include quantitative data. Such as effect size, nor did we perform any data pooling using meta-analytic techniques, but we do include quantitative results for individual studies in the online Supplementary Appendix. Findings are reported using the PDI, which was used in 95% of studies, recognizing that this also includes a few studies that used the PVD. As consistent with scoping review methodology, we did formally test hypotheses using measures of statistical significance (12–14).

The primary outcome data from each source article was the association of the PDI, hPDI, and uPDI to each of the reported outcomes, as reflected by comparing the highest level (quartile, quintile, or decile) of each index to the lowest level. An association was termed "favorable" if both statistically significant and a higher index level correlated with a better health outcome (e.g., less disease, lower mortality, better cardiometabolic marker). Conversely, an association was termed "unfavorable" if both statistically significant and a higher index level correlated with a worse health outcome (e.g., more disease, higher mortality, adverse cardiometabolic marker). We did not judge any statistically non-significant associations as favorable versus unfavorable, nor did we seek to make direct statistical comparisons between different indices.

We further assessed secondary outcomes on the concordance, or discordance, of the associations for the 3 indices (PDI, hPDI, uPDI) by comparing the statistical significance and directionality of the relationship to outcome in a specific study. This was used to classify comparisons between hPDI versus PDI and between hPDI versus uPDI as "favors hPDI," "both same," or "favors" comparator (PDI or uPDI):

- Favors hPDI: when comparing the hPDI to the PDI (or uPDI) the comparison "favors hPDI" if the hPDI had a significantly favorable HR and the PDI (or uPDI) had a non-significant HR, or if the hPDI had a non-significant HR but the PDI (or uPDI) had significantly unfavorable HR. In both cases the HRs were discordant and the hPDI did "better" than the comparator, leading a result that "favors hPDI."
- Both same: when comparing the hPDI to the PDI the comparisons was deemed "both same" if the HRs for each index were concordant: both significantly favorable, both non-significant, or both significantly non-favorable. The same criteria applied to comparing the hPDI to the uPDI.
- Favors PDI: when comparing the hPDI to the PDI the comparison "favors PDI" if the PDI had a significantly favorable HR and the hPDI was non-significant, or if the PDI had a non-significant HR but the hPDI had significantly unfavorable HR. In both cases the HRs were discordant and the PDI did "better" than the PDI, leading a result that "favors PDI."
- Favors uPDI: when comparing the hPDI to the uPDI the comparison "favors uPDI" if the uPDI had a significantly favorable HR and the hPDI was non-significant, or if the uPDI had a non-significant HR but the hPDI had significantly unfavorable HR. In both cases the HRs were discordant and the uPDI did "better" than the uPDI, leading a result that "favors uPDI."

The above comparisons are reported for studies contributing to specific outcome (e.g., all-cause mortality, hypertension, metabolic syndrome) and were also combined for all comparisons and outcomes

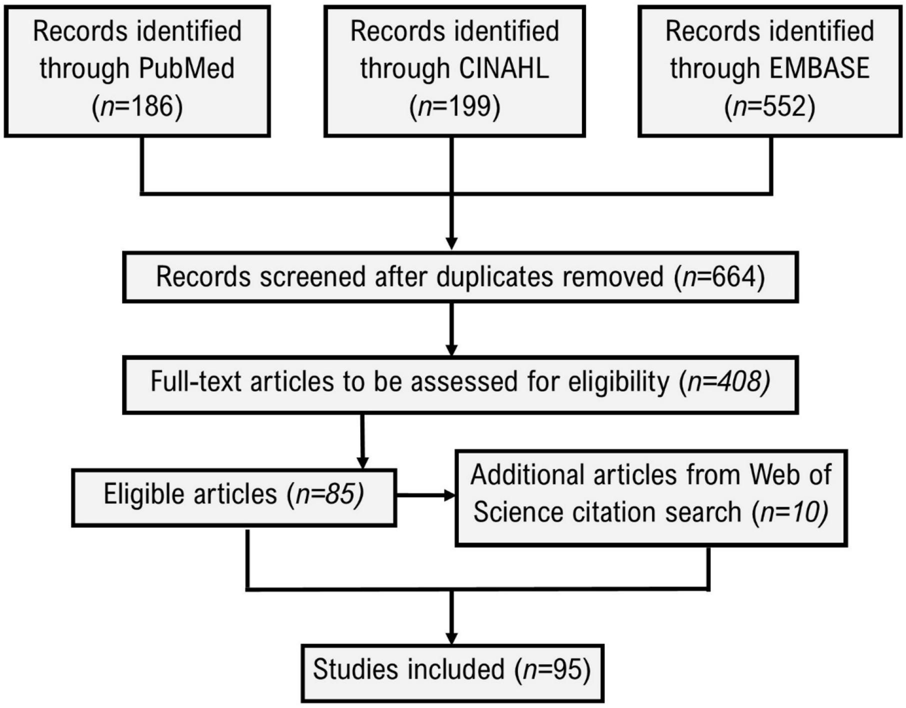

FIGURE 1
Selection of evidence sources for scoping review.

to give a global perspective of how stratifying a plant-based diet based on food quality might impact associations.

Results

The literature search (Figure 1) identified 95 source articles (10, 15–108), for which full details of data extraction can be found in the online Supplementary Appendix. The Web of Science search was based on citations of three articles (23, 46, 87), published between 2017 and 2019, identified in the prior searches and considered representative of those sought for the review. Articles were published between 2017 and 2023 with a median sample size of 3,646, ranging from 22 to 592,571, and with upper and lower quartiles of 456 and 14,568, respectively. The countries of origin for the source articles were United States ($n = 30$ publications), Iran ($n = 20$), Korea ($n = 9$), China ($n = 8$), Spain ($n = 8$), United States/United Kingdom ($n = 3$), Australia ($n = 3$), Germany ($n = 3$), Singapore ($n = 3$), Saudi Arabia ($n = 2$), Greece ($n = 2$), France ($n = 2$), Japan ($n = 1$), and Belgium ($n = 1$).

All studies were observational, with a longitudinal (cohort) design for 54%, cross-sectional for 37%, case–control format for 9%. The PDI was used in 95% of studies, with only 5 studies reporting PVG as the primary outcome (10, 21, 38, 78, 79). The index combinations were PDI/hPDI/uPDI in 69 studies, PDI/hPDI in 9, hPDI/uPDI in 7, PVG/hPVG/uPVG in 5, PDI/hPDI/uPDI/PVG in 3, and hPDI only in 2. The primary outcomes were obesity in 21 studies, cardiometabolic risk factors in 20, mortality in 10, diabetes in 9, psychiatric disorders in 9, men's health in 8, cardiovascular disease in 7, breast cancer in 5, inflammation in 5, chronic kidney disease in 3, sleep quality in 3, quality of life in 2, bone biomarkers in 2, and 1 each for asthma, glioma, fecundability, COVID-19, micronutrients, and infant growth.

TABLE 2 Association of plant-based indices with health outcomes, showing the frequency of association type (favorable, unfavorable, or nonsignificant) for each index (hPDI, PDI, or uPDI).

Association*	hPDI, $n = 268^{\dagger}$ (%)	PDI, $n = 260^{\dagger}$ (%)	uPDI, $n = 249^{\dagger}$ (%)
Significant favorable association	97 (36.2)	64 (24.6)	5 (2.0)
Significant unfavorable association	1 (0.4)	1 (0.4)	81 (32.5)
Nonsignificant association	170 (63.4)	195 (75.0)	163 (65.5)

PDI, overall plant-based dietary index; hPDI, healthful PDI; uPDI, unhealthful PDI.
*Association with outcome was significant if $p < 0.05$, favorable if the highest level of the index (e.g., quartile, quintile, decile) was associated with a more favorable outcome than the lowest level, unfavorable if associated with a more unfavorable outcome.
†Number of comparisons for the specific index, which exceeds the number of studies (95) because of multiple comparisons in most studies.

The hPDI demonstrated the most frequent association with favorable health outcomes (Table 2), with 36.2% having significantly more favorable results ($p < 0.05$, as reported by the investigators) when comparing the highest hPDI level to the lowest. Conversely, higher uPDI levels were associated with unfavorable health outcomes for 32.5% of comparisons. The hPDI was almost never (0.4%) associated with unfavorable outcomes and the uPDI was rarely associated (2.0%) with favorable outcomes. Although 24.6% of higher PDI levels were associated with favorable health outcomes, the hPDI was about 50% more likely to demonstrate this type of relationship (36.2% vs. 24.6%).

When discordant associations (Table 3) were observed for the hPDI versus a comparator (PDI or uPDI), the results most often favored the hPDI (23.0%) over the PDI and always favored the hPDI (52.3%) over the uPDI. Concordant associations were most often observed for the hPDI versus PDI (70.4%) with a minority of hPDI versus uPDI associations showing concordance (47.7%). For all comparisons combined, 59.6% had concordant results, 36.9% were discordant favoring the hPDI, and only 3.5% were discordant favoring the comparator (PDI or uPDI).

For the outcomes in Table 4 with at least 10 comparisons of the highest versus lowest index levels, the most frequent significantly favorable associations with the hPDI were found for psychiatric disorders (94% of comparisons), diabetes (64%), cardiovascular disease (45%), mortality (43%), and obesity (42%). The most frequent significantly unfavorable associations with the uPDI were found for psychiatric disorders (50%), mortality (39%), obesity (36%), and cardiometabolic risk factors (31%). The hPDI level was more frequently associated with favorable outcomes than the uPDI was associated with unfavorable outcomes for psychiatric disorders (94% vs. 50%), diabetes (64% vs. 9%), and cardiovascular disease (45% vs. 9%).

Tables 5–13 show the frequency of concordant versus discordant plant-based index comparisons by specific outcome studied. In

TABLE 3 Concordant versus discordant comparisons, showing the frequency of comparison outcome (discordant favoring hPDI, concordant, or discordant favoring comparator) for hPDI versus comparators (PDI or uPDI).

Comparison	Discordant, favoring hPDI (%)	Concordant* (%)	Discordant, favoring comparator (%)
hPDI versus PDI, $N = 213$	49 (23.0)	150 (70.4)	14 (6.6)
hPDI versus uPDI, $N = 193$	101 (52.3)	92 (47.7)	0 (0)
Combined, $N = 406$	150 (36.9)	24 (59.6)	14 (3.5)

PDI, plant-based dietary index; hPDI, healthful PDI; uPDI, unhealthful PDI.
*Concordant: hPDI and comparator have same statistical significance (e.g., significant vs. non-significant) and directionality (positive vs. negative association with outcome).

TABLE 4 Favorable versus unfavorable plant-based index associations with specific outcomes.

N†	Outcome		Statistically significant associations of plant-based indices to outcome*						Studies (references)
			Favorable			Unfavorable			
		Tests#	hPDI (%)	PDI	uPDI	hPDI	PDI	uPDI (%)	
21	Obesity	36	15(42)	9	0	0	0	13 (36)	(24, 29, 34, 38, 42, 47, 48, 55, 60, 65–67, 69, 72, 78, 83, 88, 91, 98, 99, 105)
20	Cardiometabolic risk factors	77	12(16)	11	3	1	0	24 (31)	(16, 19, 26, 34, 40, 47–49, 51, 57, 58, 65, 66, 76, 88, 90, 91, 99, 100)
10	Mortality	23	10(43)	10	0	0	0	9 (39)	(20, 23, 35, 44, 46, 50, 59, 82, 95, 101)
9	Diabetes	11	7(64)	4	0	0	0	1 (9)	(24, 29, 30, 36, 53, 57, 89, 96, 106)
9	Psychiatric disorders	16	15 (94)	8	0	0	0	8 (50)	(18, 32, 39, 61, 63, 73, 103, 105, 107)
8	Men's health	23	3(13)	1	0	0	1	2 (9)	(28, 56, 64, 66, 67, 75, 77, 104)
7	Cardiovascular disease	11	5(45)	2	0	0	0	1 (9)	(25, 41, 44, 54, 76, 87, 101)
5	Breast cancer	13	3 (23)	5	0	0	0	2 (15)	(10, 79, 84–86)
5	Inflammation	9	3 (33)	1	0	0	0	0 (0)	(17, 24, 27, 81, 89)
4	Gastrointestinal cancer	7	6(86)	5	1	0	0	3 (43)	(52, 79, 97, 102)
4	Quality of life	5	5(100)	3	0	0	0	5 (100)	(23, 68, 93, 108)
3	Chronic kidney disease	9	1 (11)	2	0	0	0	3 (33)	(45, 70, 94)
3	Sleep quality	3	2 (66)	0	0	0	0	3 (100)	(32, 43, 81)
2	Bone biomarkers	6	2(33)	1	0	0	0	2 (33)	(37, 89)
1	Glioma	1	1 (100)	1	0	0	0	1 (100)	(74)
1	Fecundability	1	1 (100)	0	0	0	0	1 (100)	(62)
1	COVID-19	3	3 (100)	N/A	N/A	0	N/A	N/A	(71)
1	Infant growth	9	0 (0)	0	0	0	0	1 (11)	(33)
1	Micronutrients	2	1(50)	2	0	0	0	2 (100)	(21)
1	Asthma	3	1(33)	1	1	0	0	0 (0)	(15)

PDI, plant-based dietary index; hPDI healthful PDI; uPDI unhealthful.
†Number of source articles reporting the outcome.
#Total number of statistical tests comparing highest versus lowest index level; percentages shown for favorable hPDI and unfavorable uPDI associations are based on this number as the denominator.
*Comparison of highest level (quartile, quintile, or decile) to lowest level.

TABLE 5 Mortality and cardiovascular diseases, concordant versus discordant plant-based index comparisons.

Outcome	*N*	hPDI versus PDI statistical significance with outcome			hPDI versus uPDI statistical significance with outcome			Studies (references)
		Favors hPDI*	Both same†	Favors PDI‡	Favors hPDI*	Both same†	Favors uPDI‡	
All-cause mortality	10	1	6	2	5	5	0	(20, 23, 35, 44, 46, 50, 59, 82, 95, 101)
Cardiovascular disease mortality	7	0	6	0	5	2	0	(25, 35, 41, 44, 54, 87, 101)
Cancer mortality	4	0	2	2	1	3	0	(23, 50, 59, 95)
Breast cancer mortality	1	0	1	0	0	1	0	(20)
Non-breast cancer mortality	1	1	0	0	1	0	0	(20)
Coronary heart disease	2	1	1	0	1	1	0	(87, 101)
Cardiovascular disease	4	1	2	1	2	2	0	(44, 54, 76, 101)
Stroke	2	1	1	0	1	1	0	(25, 101)

PDI, plant-based dietary index; hPDI, healthful PDI; uPDI, unhealthful PDI.
*Favors hPDI if hPDI hazard ratio statistical significance for the outcome is more favorable than the comparator (PDI or uPDI): e.g., hPDI significantly favorable and comparator non-significant or unfavorable, or hPDI non-significant and comparator unfavorable.
†Both same if hPDI hazard ratio has same relationship to outcome as comparator (both significantly favorable, both non-significant, or both significantly unfavorable).
‡Favors comparator (PDI or uPDI) if hazard ratio statistical significance for the outcome is more favorable than the hPDI: e.g., comparator significantly favorable and hPDI non-significant or unfavorable, or comparator non-significant and hPDI unfavorable.

Table 5, mortality, comparisons of the hPDI versus PDI are largely concordant, but some of the outcomes for hPDI versus uPDI are often discordant, as seen for all-cause mortality and cardiovascular disease mortality. A similar pattern is seen in Table 7 for psychiatric disorders (anxiety, cognitive impairment, and depression) and in Table 11 for obesity (fatty liver disease, visceral adiposity, central obesity, general obesity, and overweight or obese). Specific outcomes in other tables also show discordance that favors the hPDI over the uPDI, including Table 6 (hypertension, metabolic syndrome, and HDL cholesterol), Table 8 (breast cancer and colorectal cancer), Table 9 (serum insulin and type 2 diabetes), and Table 13 (sleep quality index).

Discussion

The aim of our scoping review was to highlight the importance of assessing plant-based diet quality, beyond using "plant-based" as an umbrella term (e.g., vegan, vegetarian), when assessing the association of diet type with health outcomes. We found a robust, and rapidly growing, body of literature that investigates how the quality and nutritional value of a plant-based diet is positively associated with health outcomes. The 95 studies we identified, most published in 2021 or later, represent diverse population cohorts from investigators in the United States, Western Europe, Middle East, Asia, and Australia. The diverse outcomes (Table 4) are most often related to the broad topics of obesity, cardiometabolic risk factors, overall- and disease-specific mortality, diabetes, cardiovascular disease, psychiatric disorders, men's health, and cardiovascular disease.

For 33 to 36% of comparisons (Table 2), the highest levels of the hPDI and uPDI are associated with favorable and unfavorable health outcomes, respectively, whereas the highest PDI levels have favorable associations in only 25% of comparisons. Moreover, when the index associations are discordant (Table 3), the hPDI is more favorably associated with outcomes than the uPDI in 52% of comparisons and the hPDI is more favorably associated with outcomes than the PDI in 23% of comparisons. In aggregate, these findings show that stratifying the PDI into healthful versus unhealthful indices is superior to the PDI alone in assessing how plant-based diets are associated with health outcomes.

Our findings also identify some gaps in the existing knowledge base. For example, we did not identify any studies from investigators in Africa, South America, Central America, Scandinavia, or Eastern Europe, which raises concerns about generalizability, potentially to resource-challenged countries and regions. There is also limited information on how plant-based diet quality is associated with many clinical outcomes, based on conditions not listed in Table 4 and on those with only a few source articles (e.g., COVID-19, quality of life, sleep quality, fecundability, infant growth, glioma, bone biomarkers, and some cancers). Even when there are many source articles in an outcome category, more comparable outcomes may only be covered in 1 or 2 studies (Tables 5–13) and the measures used are heterogeneous.

The gaps and heterogeneity noted help to explain why relatively few meta-analyses have been performed using not just PDI, but also hPDI and uPDI. In all published reviews, however, where this distinction has been made, 4–6,9 the investigators find significant quantitative benefits related to diet quality, consistent with our qualitative and descriptive findings. This work builds upon a precursor concept of assessing mortality with a provegetarian food pattern, emphasizing plant-derived foods of any quality, in contrast to broad dietary classifications as vegan, vegetarian, or omnivore. Satija et al. (4) in 2016 ushered in the current focus on healthful versus unhealthful plant-based indices, when they showed substantially lower risk of developing type 2 diabetes with a diet rich in high-quality plant foods (Table 1), and a lower intake of animal foods and less healthy plant foods.

A benefit of defining a dietary pattern based on the frequency of healthy plant-foods consumed is the ability to study large populations using continuous indices (PDI, hPDI, uPDI), based on dietary assessment data to evaluate the relative quality of individuals' dietary

TABLE 6 Cardiometabolic risk factors, concordant versus discordant plant-based index comparisons.

Outcome	*N*	hPDI versus PDI statistical significance with outcome			hPDI versus uPDI statistical significance with outcome			Studies (references)
		Favors hPDI*	Both same†	Favors PDI‡	Favors hPDI*	Both same†	Favors uPDI‡	
Hypertension	5	1	4	0	4	1	0	(48, 49, 51, 57, 88)
HDL cholesterol	8	0	8	0	8	6	0	(26, 34, 48, 65, 78, 90, 91, 99)
LDL cholesterol	5	0	5	0	0	4	1	(26, 34, 65, 90, 99)
Lip accumulation product	1	0	1	0	0	1	0	(88)
Metabolic syndrome	5	1	4	0	4	1	0	(19, 47, 48, 66, 76)
Non-HDL	1	0	1	0	0	1	0	(90)
Systolic blood pressure	4	1	3	0	1	3	0	(15, 34, 65, 78)
Diastolic blood pressure	4	2	2	0	1	3	0	(16, 34, 65, 78)
Trimethylamine oxide	1	0	0	1	0	0	1	(40)
Total cholesterol	5	1	4	0	1	4	0	(34, 65, 90, 91, 99)
Total cholesterol/HDL	1	1	1	0	1	1	0	(65, 99)
Triglycerides, high	7	0	7	0	2	5	0	(26, 34, 48, 65, 88, 90, 91)
Triglyceride-glucose index	1	0	1	0	0	1	0	(88)
Triglyceride/HDL	1							(65)
Weight	1	0	0	1	0	1	0	(26)
Waist circumference	4	0	4	0	1	3	0	(34, 78, 91, 99)
Waist, hyper-triglycemic	1	0	1	0	0	1	0	(91)
Glucose, high	5	0	3	1	1	4	0	(26, 34, 48, 65, 78, 88)

HDL, high-density lipoprotein; LDL, low-density lipoprotein; PDI, plant-based dietary index; hPDI, healthful PDI; uPDI, unhealthful PDI.
*Favors hPDI if hPDI hazard ratio statistical significance for the outcome is more favorable than the comparator (PDI or uPDI): e.g., hPDI significantly favorable and comparator non-significant or unfavorable, or hPDI non-significant and comparator unfavorable. †Both same if hPDI hazard ratio has same relationship to outcome as comparator (both significantly favorable, both non-significant, or both significantly unfavorable).
‡Favors comparator (PDI or uPDI) if hazard ratio statistical significance for the outcome is more favorable than the hPDI: e.g., comparator significantly favorable and hPDI non-significant or unfavorable, or comparator non-significant and hPDI unfavorable.

TABLE 7 Psychiatric disorders, concordant versus discordant plant-based index comparisons.

Outcome	*N*	hPDI versus PDI statistical significance with outcome			hPDI versus uPDI statistical significance with outcome			Studies (references)
		Favors hPDI*	Both same†	Favors PDI‡	Favors hPDI*	Both same†	Favors uPDI‡	
Anxiety	3	1	2	0	3	0	0	(32, 73, 105)
Cognitive impairment	4	2	3	0	0	1	3	(61, 63, 103, 107)
Depression	3	1	2	0	3	0	0	(32, 73, 105)
Stress	4	3	1	0	4	0	0	(18, 32, 73, 105)
Impulsivity	1	1	0	0	1	0	0	(39)

PDI, plant-based dietary index; hPDI, healthful PDI; uPDI, unhealthful PDI.
*Favors hPDI if hPDI hazard ratio statistical significance for the outcome is more favorable than the comparator (PDI or uPDI): e.g., hPDI significantly favorable and comparator non-significant or unfavorable, or hPDI non-significant and comparator unfavorable.
†Both same if hPDI hazard ratio has same relationship to outcome as comparator (both significantly favorable, both non-significant, or both significantly unfavorable).
‡Favors comparator (PDI or uPDI) if hazard ratio statistical significance for the outcome is more favorable than the hPDI: e.g., comparator significantly favorable and hPDI non-significant or unfavorable, or comparator non-significant and hPDI unfavorable.

intakes (9). Moreover, these indices often identify benefits of healthy plant foods that might be missed when using a single overall measure of plant foods in the diet (Tables 2–4). Plant-based diet indices overcome limitations of discrete dietary categories because they align with the continuum of plant-forward, flexitarian, diets that exist in real-world settings. Further, the goal of increasing healthy plant foods in a diet, as opposed to restricting animal foods, is not only appealing but aligns with research showing that mortality may be driven more by the paucity of healthy plant foods (e.g., whole grains, fruits, nuts/seeds, legumes) than by the excess of meat (red and processed) and unhealthy plant foods (e.g., sugar-sweetened beverages) (109).

Differentiating between healthy versus less healthy aspects of plant-based diets has significant implications for researchers, policy makers (e.g., clinical practice guideline developers), and for consumers

TABLE 8 Cancer incidence, concordant versus discordant plant-based index comparisons.

Outcome	*N*	hPDI versus PDI statistical significance with outcome			hPDI versus uPDI statistical significance with outcome			Studies (references)
		Favors hPDI*	Both same†	Favors PDI‡	Favors hPDI*	Both same†	Favors uPDI‡	
Prostate cancer, total	1	0	1	0	NS	NS	NS	(64)
Breast cancer	5	1	4	0	2	3	0	(80, 84–86)
Breast cancer, recurrence	1	0	1	0	0	1	0	(20)
Colorectal cancer	3	0	3	0	3	1	0	(52, 97, 102)
Esophageal cancer	1	0	1	0	1	0	0	(79)
Stomach cancer	1	0	1	0	1	0	0	(79)
Pancreatic cancer	1	0	1	0	1	0	0	(79)

PDI, plant-based dietary index; hPDI, healthful PDI; uPDI, unhealthful PDI.
*Favors hPDI if hPDI hazard ratio statistical significance for the outcome is more favorable than the comparator (PDI or uPDI): e.g., hPDI significantly favorable and comparator non-significant or unfavorable, or hPDI non-significant and comparator unfavorable.
†Both same if hPDI hazard ratio has same relationship to outcome as comparator (both significantly favorable, both non-significant, or both significantly unfavorable).
‡Favors comparator (PDI or uPDI) if hazard ratio statistical significance for the outcome is more favorable than the hPDI: e.g., comparator significantly favorable and hPDI non-significant or unfavorable, or comparator non-significant and hPDI unfavorable.

TABLE 9 Diabetes, concordant versus discordant plant-based index comparisons.

Outcome	*N*	hPDI versus PDI statistical significance with outcome			hPDI versus uPDI statistical significance with outcome			Studies (references)
		Favors hPDI*	Both same†	Favors PDI‡	Favors hPDI*	Both same†	Favors uPDI‡	
Gestational diabetes	2	0	1	1	0	2	0	(31, 106)
HOMA-IR	1	1	0	0	1	0	0	(89)
QUICKI	1	0	1	0	0	1	0	(89)
Serum insulin	2	1	0	1	2	0	0	(24, 89)
Type 2 diabetes	5	2	3	0	4	0	0	(30, 36, 53, 57, 96)
Hemoglobin A1c	1	0	1	0	0	1	0	(26)

HOMA-IR, homeostatic model assessment of insulin resistance; PDI, plant-based dietary index; hPDI, healthful PDI; uPDI, unhealthful PDI; QUICKI, quantitative insulin sensitivity check index.
*Favors hPDI if hPDI hazard ratio statistical significance for the outcome is more favorable than the comparator (PDI or uPDI): e.g., hPDI significantly favorable and comparator non-significant or unfavorable, or hPDI non-significant and comparator unfavorable.
†Both same if hPDI hazard ratio has same relationship to outcome as comparator (both significantly favorable, both non-significant, or both significantly unfavorable).
‡Favors comparator (PDI or uPDI) if hazard ratio statistical significance for the outcome is more favorable than the hPDI: e.g., comparator significantly favorable and hPDI non-significant or unfavorable, or comparator non-significant and hPDI unfavorable.

TABLE 10 Inflammation and inflammatory markers, concordant versus discordant plant-based index comparisons.

Outcome	*N*	hPDI versus PDI statistical significance with outcome			hPDI versus uPDI statistical significance with outcome			Studies (references)
		Favors hPDI*	Both same†	Favors PDI‡	Favors hPDI*	Both same†	Favors uPDI‡	
High-sensitivity C-reactive protein	5	1	3	1	1	4	0	(17, 24, 27, 81, 89)
Interleukin 1 beta	1	0	1	0	0	1	0	(81)
Interleukin 6	1	0	1	0	0	1	0	(24)
Transforming growth factor beta	2	0	1	1	0	1	0	(27, 81)
osteocalcin	1	0	1	0	1	0	0	(89)
Human C-telopeptide of type 1 collagen	1	1	0	0	1	0	0	(89)
25-hydroxy vitamin D	1	0	1	0	0	1	0	(89)
Parathyroid hormone	1	0	0	1	0	1	0	(89)

PDI, plant-based dietary index; hPDI, healthful PDI; uPDI, unhealthful PDI.
*Favors hPDI if hPDI hazard ratio statistical significance for the outcome is more favorable than the comparator (PDI or uPDI): e.g., hPDI significantly favorable and comparator non-significant or unfavorable, or hPDI non-significant and comparator unfavorable.
†Both same if hPDI hazard ratio has same relationship to outcome as comparator (both significantly favorable, both non-significant, or both significantly unfavorable).
‡Favors comparator (PDI or uPDI) if hazard ratio statistical significance for the outcome is more favorable than the hPDI: e.g., comparator significantly favorable and hPDI non-significant or unfavorable, or comparator non-significant and hPDI unfavorable.

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TABLE 11 Obesity, concordant versus discordant plant-based index comparisons.

Outcome	*N*	hPDI versus PDI statistical significance with outcome			hPDI versus uPDI statistical significance with outcome			Studies (references)
		Favors hPDI*	Both same†	Favors PDI‡	Favors hPDI*	Both same†	Favors uPDI‡	
Adiponectin	1	1	0	0	1	0	0	(24)
Adiposity, subcutaneous	1	0	1	0	0	1	0	(83)
Adiposity, visceral	2	1	1	0	2	0	0	(83, 88)
Alanine transaminase	1	0	1	0	1	0	0	(69)
Alkaline phosphatase	1	0	1	0	0	1	0	(69)
Aspartate transaminase	1	0	1	0	1	0	0	(69)
Body mass index	6	0	5	1	0	4	0	(65–67, 78, 91, 99)
Body mass index ≥30	1	0	1	0	0	1	0	(34)
Leptin	1	1	0	0	1	0	0	(24)
Leptin, free index	1	1	0	0	1	0	0	(24)
Leptin, soluble receptor	1	1	0	0	1	0	0	(24)
Liver disease, fatty	4	1	2	1	1	3	0	(55, 60, 69, 83)
Liver signal intensity	1	0	1	0	0	1	0	(83)
Liver, fatty index	1	0	1	0	1	0	0	(68)
MUO by IDF criteria	1	1	0	0	1	0	0	(72)
MUO by HOMA-IR criteria	1	1	0	0	1	0	0	(72)
Obesity, central	5	0	5	0	2	2	1	(29, 42, 47, 88, 105)
Obesity, general	2	1	1	0	2	0	0	(88, 98)
Overweight or obese	2	0	2	0	2	0	0	(38, 105)
Retinol binding protein 4	1	0	1	0	0	1	0	(24)

HOMA-IR, Homeostatic model assessment of insulin resistance; IDF, International Diabetes Federation; MUO, metabolically unhealthy obestity phenotype; PDI, plant-based dietary index; hPDI, healthful PDI; uPDI, unhealthful PDI.
*Favors hPDI if hPDI hazard ratio statistical significance for the outcome is more favorable than the comparator (PDI or uPDI): e.g., hPDI significantly favorable and comparator non-significant or unfavorable, or hPDI non-significant and comparator unfavorable.
†Both same if hPDI hazard ratio has same relationship to outcome as comparator (both significantly favorable, both non-significant, or both significantly unfavorable).
‡Favors comparator (PDI or uPDI) if hazard ratio statistical significance for the outcome is more favorable than the hPDI: e.g., comparator significantly favorable and hPDI non-significant or unfavorable, or comparator non-significant and hPDI unfavorable.

TABLE 12 Infant growth, concordant versus discordant plant-based index comparisons.

Outcome	*N*	hPDI versus PDI statistical significance with outcome			hPDI versus uPDI statistical significance with outcome			Studies (references)
		Favors hPDI*	Both same†	Favors PDI‡	Favors hPDI*	Both same†	Favors uPDI‡	
Overweight at 2 m	1	0	1	0	0	1	0	(33)
Overweight at 4 m	1	0	1	0	0	1	0	(33)
Underweight at 2 m	1	0	1	0	0	1	0	(33)
Stunted at 2 m	1	0	1	0	0	1	0	(33)
Stunted at 4 m	1	0	1	0	1	0	0	(33)
Microcephaly at 2 m	1	0	1	0	0	1	0	(33)
Microcephaly at 4 m	1	0	1	0	0	1	0	(33)
Macrocephaly at 2 m	1	0	1	0	0	1	0	(33)
Macrocephaly at 4 m	1	0	1	0	0	1	0	(33)

PDI, plant-based dietary index; hPDI, healthful PDI; uPDI, unhealthful PDI.
*Favors hPDI if hPDI hazard ratio statistical significance for the outcome is more favorable than the comparator (PDI or uPDI): e.g., hPDI significantly favorable and comparator non-significant or unfavorable, or hPDI non-significant and comparator unfavorable.
†Both same if hPDI hazard ratio has same relationship to outcome as comparator (both significantly favorable, both non-significant, or both significantly unfavorable).
‡Favors comparator (PDI or uPDI) if hazard ratio statistical significance for the outcome is more favorable than the hPDI: e.g., comparator significantly favorable and hPDI non-significant or unfavorable, or comparator non-significant and hPDI unfavorable.

TABLE 13 Miscellaneous outcomes, concordant versus discordant plant-based index comparisons.

Outcome	N	hPDI versus PDI statistical significance with outcome			hPDI versus uPDI statistical significance with outcome			Studies (references)
		Favors hPDI*	Both same†	Favors PDI‡	Favors hPDI*	Both same†	Favors uPDI‡	
Chronic kidney disease	1	1	0	0	1	0	0	(45)
Glioma	1	0	1	0	1	0	0	(74)
Endothelial dysfunction	2	0	4	0	NS	NS	NS	(65, 67)
Erectile dysfunction	3	1	2	0	NS	NS	NS	(28, 65, 67)
Fecundability	1	1	0	0	1	0	0	(62)
PSA, elevated	1	1	0	0	NS	NS	NS	(75)
Severe COVID	1	1	NS	NS	0	NS	NS	(71)
Sleep, later chronotype	1	NS	NS	NS	1	0	0	(43)
Sleep, quality index	2	1	1	0	2	0	0	(32, 81)
Testosterone, total	3	0	3	0	NS	NS	NS	(55, 65, 67)
Quality of life, healthy aging	1	0	1	0	NS	NS	NS	(108)
Quality of life, physical score	1	0	1	0	1	0	0	(22)
Quality of life, mental score	1	0	1	0	1	0	0	(22)

PDI, plant-based dietary index; hPDI, healthful PDI; uPDI, unhealthful PDI.
*Favors hPDI if hPDI hazard ratio statistical significance for the outcome is more favorable than the comparator (PDI or uPDI): e.g., hPDI significantly favorable and comparator non-significant or unfavorable, or hPDI non-significant and comparator unfavorable.
†Both same if hPDI hazard ratio has same relationship to outcome as comparator (both significantly favorable, both non-significant, or both significantly unfavorable).
‡Favors comparator (PDI or uPDI) if hazard ratio statistical significance for the outcome is more favorable than the hPDI: e.g., comparator significantly favorable and hPDI non-significant or unfavorable, or comparator non-significant and hPDI unfavorable.

and the public (Table 14). Beyond focusing on overall diet quality, the healthfulness of individual foods has also received increased attention with nutrient profiling systems such as the Food Compass, which assigns a score from 1 (least healthful) to 100 (most healthful) based on 54 attributes across 9 domains: nutrient ratios, vitamins, minerals, food ingredients, additives, processing, specific lipids, fiber and protein, and phytochemicals (110). The healthy plant foods in Table 1 receive high scores on the Food Compass (110), which is associated with optimal cardiometabolic health and lower all-cause mortality (111). In contrast, the less healthy plant-based foods and the animal foods in Table 1 receive much lower scores.

The inclusion of potatoes as a less healthy food in Table 1 is based on Satija and colleagues (4), who pioneered the concept of hPDI versus uPDI. We did not, however, assess the specific food components of the dietary indices in our included studies, so we do not know how specific investigators categorized potatoes. The association of potato consumption with health outcomes is controversial, with some pooled analyses of prospective studies finding a higher risk of hypertension or type 2 diabetes (112–114), but others showing no association with obesity, mortality, type 2 diabetes, or cardiovascular disease (115, 116). One study found a higher risk of type 2 diabetes with French fries, which was reduced by replacing potatoes with whole grains (112).

The animal foods in Table 1 do not distinguish by their potential health impact (healthy vs. less healthy) even though their inclusion in the diet adversely affects the plant-based dietary indices. Systematic reviews, however, have often shown adverse associations of omnivore diets with many of the health outcomes in our source articles, including obesity (117), type 2 diabetes (118), breast cancer (119), all-cause mortality (120), coronary artery disease (5, 121), inflammatory biomarkers (122), and cardiometabolic risk factors (123, 124). Similarly, the Global Burden of Disease Study found positive associations of high dietary trans fats, red meat, processed meat, and sugar-sweetened beverages with mortality from non-communicable diseases, but larger associations were found when the diet was low in healthy plant foods (whole grains, fruits, nuts, seeds, legumes, or vegetables) (109). Consuming fish and seafood have less consistent health associations compared with meat or plant foods (119, 120, 124), which is also the case for eggs and dairy products (125–127).

Strengths of our research include using *a priori* protocols for conducting and reporting the scoping review (13, 14), which is the first to systematically assess the contributions of hPDI and uPDI as correlates of health status. As recommended as a best practice when conducting a scoping review (14), we used dual, independent investigators to assess study eligibility and extract data, thereby reducing bias and improving accuracy. We contribute to understanding of how the quality of a plant-based diet can impact associations with health outcomes overall (Tables 2, 3), focusing on the novel concept of concordance versus discordance (Tables 3, 5–13), which has not been previously reported. We identified gaps in the existing knowledge base and provided perspective on the implications of our review findings for investigators, policy makers, and consumers (Table 14).

Limitations of our research, as for any systematic review, relate primarily to the breadth of available source articles. We used rigorous techniques, with dual investigators, to identify source articles in PubMed/MEDLINE, CINAHL, and EMBASE, but recognize that the subsequent Web of Science citation search was done post-hoc, which may have introduced bias, but is similar to checking source article bibliographies for additional relevant articles in a traditional systematic review. A scoping review does not include assessing study

TABLE 14 Benefits of using the healthful and unhealthful plant-based dietary index in nutrition research.

Benefit of classifying PDI in terms of hPDI and uPDI	Implications for researchers	Implication for policy makers	Implication for public/ consumers
Can calculate healthful and unhealthful indices from preexisting dietary intake data	Facilitates research because no new data required to calculate PDI, hPDI, and uPDI	Using existing studies is efficient and is cost-effective by limiting need for new data	No need to complete new food surveys beyond those already included
Does not require *a priori* or self-reported dietary groupings (vegan, vegetarian, omnivore)	Reduces concerns over degree of adherence to a specific diet or dietary category	Obviates need to deal with vague and heterogeneous diet categories	Avoids categorizing diet patterns and related value judgments (e.g., ethical vegan)
Provides a continuous dietary index, not just a binary measure of adherence to a specific diet type	Allows comparisons by index extremes (quartiles, quintiles, deciles) and dose–response analysis	Guidance is facilitated by low versus high index level comparisons and by dose–response information	Comparisons of high versus low index outcomes are easy to grasp for healthy versus unhealthy plant-based foods
Shows benefits of healthy plant foods that might be missed by a PDI or diet category that does not consider plant-food quality	hPDI may better detect positive associations with outcomes than an overall PDI in a given sample (Tables 2–13)	Emphasizes healthy foods, not just foods in a specific diet or food group, allowing more nuanced dietary recommendations	Raises awareness about the benefits of eating healthy foods and why being "plant-based" does not ensure a high diet quality
Shows detriments of unhealthy plant foods that might be missed by a PDI or diet category that does not consider plant-food quality	uPDI may better detect negative associations with outcomes than an overall PDI in a given sample (Tables 2–13)	Highlights unhealthy refined and highly processed plant foods and beverages to avoid in nutrition guidelines	Raises awareness about the detriments of refined grains, fruit juices, sweets, sugar-sweetened beverages, and processed foods
Conceptualizes healthy eating as a continuum of food choices, not as strict adherence to a specific diet type, or as plant- versus animal-foods	Generalizability of findings is increased by seeing impact of quality changes and by aligning better with real-world diets	Guidance may promote better adherence if promoting healthy plant foods, rather than shunning animal or unhealthy foods	Empowers consumers to make incremental additions of healthy plant foods that may ultimately displace unhealthy foods

PDI, plant-based dietary index; hPDI, healthful PDI; uPDI, unhealthful PDI.

quality or pooling data with meta-analytic techniques (13), so we do not know the overall risk of bias or the level of heterogeneity in study protocols, outcome assessment, or results reporting. Our goal, however, was to help inform decisions and raise awareness about the importance of plant-based diet quality when interpreting evidence, in contrast to a systematic review for which risk of bias assessment is an inherent aspect of evidence synthesis.

Although all studies used the hPDI, uPDI, or both (or in a few cases the hPVD, uPVD, or both), there were some differences in how the indices were defined and calculated, even if based on the broad principles in Table 1. The general concept, however, of distinguishing healthy versus less healthy plant-based foods, is incorporated in most current scoring methods for assessing plant-based diet quality (128). Further, the extreme comparisons of index levels were based on varying thresholds, which included quartiles, quintiles, and deciles. We did not provide quantitative estimates of effect size (individual studies or pooled analyses), although this is more a limitation of scoping reviews, in general, than our specific research. Last, we do not know the generalizability of our findings to specific populations (e.g., pregnant or lactating women), but the included articles were often based on large population cohorts (see online Supplementary Appendix) that would support relevance to diverse subject groups.

Another limitation relates to assessing concordance (Table 3) using statistical significance as the primary determinant, and directionality of the association (positive vs. negative) as a secondary determinant for statistically significant associations. This could explain the relatively high levels of concordance between the hPDI and PDI (70.4%), and, to a lesser extent, between the hPDI and uPDI (47.7%), because the magnitude of effect size is not part of this determination. Although we purposefully did not report effect sizes, we did observe that they nearly always favored the hPDI in magnitude, even if not statistically significant (see individual study outcome data in the online Supplementary Appendix).

Conclusion

Our findings, based on 95 included studies, demonstrate that distinguishing healthy versus less healthy plant foods in dietary indices can better detect significant associations with health outcomes than a single, overall plant-based dietary index. A high level of healthy plant food consumption was most often associated with favorable outcomes for obesity, mortality, diabetes, cardiovascular disease, and psychiatric disorders, whereas a high level of less healthy plant food consumption was most often associated with unfavorable outcomes for obesity, mortality, psychiatric disorders, and cardiometabolic risk factors. When there were discordant associations for the hPDI compared to the uPDI or PDI, the findings always favored the hPDI over the uPDI, and nearly always favored the hPDI over the PDI.

These results, combined with the implications of healthy plant food consumption for researchers, policy makers, and consumers (Table 14), suggest that the current global trend of rapid growth in related research and publications is likely to continue. Future research should incorporate measures of diet quality when assessing the association of plant-based diets with health outcomes. With increasing reporting and standardization of plant-based indices that adjust for diet quality, we anticipate a blossoming number of systematic reviews and meta-analyses that will assist guideline developers and policy makers in making informed, evidence-based recommendations.

Author contributions

RR conception and design of the work, data analysis and interpretation, drafting of the work, approval for publication of the content, accountability for all aspects of the work. HJ and MW design of the work, data acquisition, critical revision of content, approval for publication of the content, accountability for all aspects of the work. All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

The handling editor AB declared a shared committee American College of Lifestyle Medicine with the authors RR at the time of review.

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Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fnut.2023.1211535/full#supplementary-material

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The role of a starch-based diet in solving existential challenges for the 21st century

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Diet plays a fundamental role in our major chronic diseases, in climate change, and in our resistance to infectious diseases. The eating patterns that best support the health of people and our planet are based on traditional starchy staples. Historically, a wide variety of starches have provided the bulk of the food for most of the people who have walked our Earth. For example, rice has been food for Asians, corn for Central Americans, potatoes for people of the Andes, and for the Middle East, "the bread basket of the world," food has meant wheat and barley. Focusing on our ethnicities can expose altruistic natures, and before it is too late, allow us to *make the change* from destructive animal-food based-diets to plant-food based-diets; ones that are *health-supporting* for people and our planet.

KEYWORDS
diet, chronic disease, climate change, heart disease, COVID-19, greenhouse gas, animal agriculture, vegan

Introduction

Diet is the common denominator for mitigating the negative impacts of chronic diseases, climate changes, and now the COVID-19 pandemic. Each in its own right is threatening the lives of every human being on the planet. Progress in solving problems created by the first two challenges, chronic diseases and climate change, has been negligible; we seem content with eventual doom, barely noticing our demise, like the proverbial frog in the pot of water brought to a slow boil. However, truly radical behavior would be to let destructive dietary behaviors to continue, as they currently are, unchecked.

Fortunately, the novel coronavirus pandemic has acted as a high decibel alarm for these impending catastrophes; and as a "time machine" moving us a decade ahead in terms of focusing our attention on solving all three of these broad cultural calamities. Because of this viral pandemic, in fewer than 12 months, we have traded business- and pleasure-related travel for work- and leisure-experiences centered around the home, fossil fuels are being rapidly replaced by renewable energy sources, and our minds are now opening to once unthinkable possibilities for solving the world's existential challenges. Although only a small step towards planetary recovery, a 10% reduction in greenhouse gas (GHG) has occurred within the first year of the first appearance of the first novel coronavirus, SARS-CoV2 (1).

Chronic disease: it's the food!

Worldwide and historically, chronic diseases, including obesity, diabetes, CHD (atherosclerosis), arthritis, kidney disease, and GI disorders are found exclusively in financially affluent social castes. Over 80% of people in developed countries worldwide now suffer from one or more of these medical conditions (2).

The cause is diet: classical paintings and writings portray the obese king with his gout inflicted foot propped on a stool, sitting with his sickly-looking royal court, before an opulent spread of animal foods (cows, pigs, chickens, and fishes); followed by pastries for the final culinary festivity.

Healing with diet-therapy for these chronic diseases has its roots in history also; and diet-therapy should be fundamental to the practice of medicine today, in the 21st century. Diet-therapy is the treatment of diseases by causing improvements in people's short- and long-term food patterns. One of the earliest descriptions of this "low-tech medicine" is provided by a controlled trial carried out nearly 2,600 years ago, and reported in the first chapter of Daniel of the Bible (1:12–15): *Daniel's men, who ate only vegetables (pulses) and drank water for a study period of 10 days were found to be stronger, healthier, younger-looking, more-handsome, and/or without-blemish, when compared to men eating at the king's table.*

Historically, the wealthy class was limited to only a few members; the king and his personal court. At the other end of the spectrum were the masses, the working populations, who obtained the bulk of their calories from beans, corn, potatoes, rice, and/or wheat with a few fruits and vegetables. These people were strong, fit, and healthy (as long as they had enough food). With the Industrial Revolution and the harnessing of fossil fuels in the mid-1800s, wealth came to common folks; followed by a shift to very rich meals (the kind once reserved for the privileged few); and as expected, diseases of affluency quickly became epidemics, and now they are pandemic (worldwide) (3).

Climate change: it's the food!

I, along with most of you, was first made aware of the existential perils of climate change by Al Gore's documentary, *An Inconvenient Truth,* in 2006. He clearly laid out the disastrous future ahead with his solutions being largely limited to curtailing the fossil fuel industries. No mention was made of the livestock industries' contributions to global warming. Nor did his 2017 *Sequel* provide enlightenment on the potential role of curtailing our addiction to meat-eating for saving our home. In 2006, the Food and Agriculture Organization of the United Nations (FAO) published highly-influential research, *Livestock's Long Shadow;* a nearly 400-page report finding livestock's contribution to GHG production to be nearly 18% of the total; while all transportation (buses, trains, cars, planes, etc.) accounts to less than 14% (4). When accounting for several additional factors, those underestimated by the FAO report, livestock actually accounts for 51% of the GHG produced annually (5).

The *EAT-Lancet* Commission, considered to be the authoritative word on the subject of climate crises and diet, published their conclusions in 2019: The livestock industry is a major detriment to planetary survival; and that we have fewer than 12 years to take action before tipping points are reached where life as we once knew it will no longer be possible. In March of 2020, the *EAT-Lancet* Commission reported that replacing beef, pork, and poultry with a plant-food based-diet reduced the GHG associated with people's diets by up to 50%, depending on the type and degree of substitution (vegan being most effective) (6). Further encouragement about the power of food comes from scientific findings that changing from a standard Western diet to a vegan diet can reduce GHG production by as much as 80% (7).

COVID-19: it's the food!

While people waited in line for an effective and safe vaccine to become available for them, they forfeited another powerful, cost-free, side-effect-free, self-administered intervention: the resolution of co-existing conditions, such as obesity, diabetes, hypertension, heart disease, and kidney disease. People, professionals, and politicians have largely ignored the fact that all of these conditions are due to the foods we eat—the rich Western diet—and these illnesses are easily cured by eating a starch-based diet (8, 9).

Anthony Fauci, MD from the NIH, told members of Congress in a June 2020 meeting that, "…whether or not you have serious consequences, hospitalizations, intubations, and death, relate very strongly to the prevalence and incidence of underlying comorbid conditions…" (10). In other words, healthier people do not become mortally ill as often. This same optimistic prognosis was also made by the Centers for Disease Control and Prevention (CDC) on June 15, 2020 when the Morbidity and Mortality Weekly Report (MMWR) announced the risk of hospitalization is increased 6-fold and risk of death by 12-fold in people with co-existing diseases (11). Overseas, the editor of the *British Medical Journal*, July 20, 2020, reminded readers that in order to deal effectively with this pandemic, "we need diets richer in whole grains, fruit, vegetables, and legumes, with less red meat, refined carbohydrates, and highly processed foods" (12).

Vaccinations have brought hope to people—an expectation that someday this nightmare will be over. Unfortunately, variants are emerging worldwide. The problem being with the genetic drift common to viruses, fueled by a warming planet, a plethora of novel contagious microbes will become our future. Does this mean a new vaccine every 3 months? Possibly. Let us not forget that we have highly effective public health measures (masks, social distancing, hand-washing), and the widespread adoption of traditional diets that eliminate comorbid- or premorbid- conditions, almost overnight.

Back to the future with traditional diets

A simple U-turn, back to traditional diets followed by the more than 107 billion human inhabitants who have walked planet Earth, is the change in eating patterns I am proposing. All large populations of trim, healthy, athletic-competing, war-fighting people throughout verifiable human history have obtained the bulk of their calories from starches. Examples of thriving populations include the Japanese, Chinese, and other Asians, who ate sweet potatoes, buckwheat, and/or rice; Incas in South America who ate potatoes; Mayans and Aztecs in Central America were known "as the people of the corn;" and the Middle East, formally known as "the breadbasket of the world," fed hundreds of millions on a diet of wheat and barley. I say "ate," rather than "eat," because, since the early 1980s Western eating patterns have prevailed over traditional eating patterns based on staples, like corn, potatoes, rice, and wheat. This is, by no coincidence, the period of time that the greatest damage to Earth from climate change has occurred.

The vast majority want a viable future for their children; they just do not know how to attain this elusive, but precious, goal. People are poised for big changes in their lives, especially after realizing that there is no going back to "normal," and that in fewer than 30 years, nearly one-third of all plants and animals are predicted to become extinct (13, 14). Some may believe that, "More research and more discussion need to be done before we act." We do not have the luxury of time to make our conclusions acceptable to everyone. Present circumstances dictate that observations, deductive reasoning, incomplete science, and a bit of faith must prevail in our decision to act now.

Looking back, to only 50 years ago, the majority of people on Earth followed a starch-based diet; and many of us are old enough to remember these times. How ironic to realize how knowledge commonly held within one lifetime—the traditional starch-based diet—would also be a necessary part of the solution to mitigating climate change for the next half century, and beyond, for the lifetimes of many future generations. We have a world to save and every bite counts.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

JM: Conceptualization, Writing – original draft.

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Conflict of interest

JM is co-founder of the McDougall Program which teaches the importance of a whole food, starch-based diet to treat and reverse chronic disease.

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Carbohydrate confusion and dietary patterns: unintended public health consequences of "food swapping"

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The 2025–2030United States Dietary Guidelines process is currently underway, and the 2025 Dietary Guidelines Advisory Committee is examining and evaluating a list of prioritized scientific questions identified by the United States Department of Health and Human Services and the United States Department of Agriculture. One of the questions that will be evaluated is if changes should be made to USDA Dietary Patterns based on whether starchy vegetables and grains are, or can be, consumed interchangeably. These foods have historically been classified in distinct food groups. Menu modeling analyses evaluating the impact of replacing starchy vegetables with grains result in declines in key nutrients of concern. Given their unique nutrient contributions and the fact that many cultural foodways within the United States population include both starchy vegetables and grains, it is important for dietary recommendations to continue to categorize starchy vegetables and grains separately.

KEYWORDS

potatoes, nutrition, starchy vegetables, carbohydrate quality, diet quality, nutrients of concern, dietary guidelines

Introduction

Foods rich in carbohydrates, such as grains, fruits, legumes, nuts and seeds, and vegetables, including starchy vegetables, provide the bulk of dietary intake for most global cuisines and food patterns (1). Grain crops alone, namely maize, wheat, and rice, comprise 51% of the total kilocalories consumed globally, while roots and tuber crops comprise 5.3% (2).

As the work of the 2025–2030 U.S. Dietary Guidelines Advisory Committee (DGAC) continues, the U.S. Department of Health and Human Services (HHS) and U.S. Department of Agriculture (USDA) released a list of proposed scientific questions that will inform the work of the DGAC (3). Among key questions being evaluated include:

- Considering each life stage, should changes be made to the USDA Dietary Patterns (Healthy United States-Style, Healthy Mediterranean-Style, and/or Healthy Vegetarian), and should additional Dietary Patterns be developed/proposed based on:

o Findings from systematic reviews, data analysis, and/or food pattern modeling analyses.
o Population norms (e.g., are starchy vegetables often consumed interchangeably with grains?), preferences (e.g., emphasis on one staple grain vs. another), or needs (e.g., lactose intolerance) of the diverse individuals and cultural foodways within the United States population?

Notably, the DGAC is considering if starchy vegetables can be considered as interchangeable with grains. This perspective substantiates the need to consider the diversity of complex carbohydrate-containing foods, each with a unique role to contribute to overall nutrition and dietary health. Nutrient-dense dietary patterns include both grain foods and starchy vegetables. These food groups are currently considered separately, and they must remain separate to ensure people are encouraged to consume complementary nutrients from each of these food groups.

Further, this paper includes a menu modeling analysis which demonstrates the nutritional differences between starchy vegetables and grains in an overall dietary pattern. Using complex carbohydrate foods, specifically starchy vegetables (e.g., potatoes) and grains, interchangeably is at best, not a useful strategy, but at worst, may increase the risk of micronutrient inadequacy and/or dietary imbalances.

Carbohydrate foods: a spectrum of composition and consumer use

Complex carbohydrate foods have varied forms and structures

Carbohydrate foods are often lumped into one macronutrient category, despite their wide nutritional variations. Simple carbohydrates, such as mono-and disaccharides, can be intrinsically present in foods, as in fruit, or isolated and used as an ingredient, as for sucrose from cane sugar.

"Complex" carbohydrates can be even more varied. Starches and fibers can have different lengths and compositions. Even fiber, a subclass of complex carbohydrates, is far from homogenous, with its various soluble, insoluble, cellulose, hemicellulose, pectins, lignins, and variants (4). Dietary fiber is found only in foods already rich in carbohydrates, unless specifically added through processing.

Structurally, carbohydrates have a common glycerol backbone, but otherwise their chemical structures are broad, divided into various mono-, di-, and polysaccharides, resulting in differing degrees of digestibility, bioavailability, and function.

The term "starch" can also have multiple meanings. Most starch is easily broken down into its component simple carbohydrates, but "resistant starch" (RS) passes to the large intestine intact and undigested. Even RS is known to have five variants (5). Two such variants are relevant to this discussion:

- RS3: also known as retrograded starch, forms after cooking high-starch foods like potatoes or rice, then cooling and refrigerating them, causing their long amylose chains to recrystallize into double helices that amylase cannot break down.
- RS5: formed when starchy foods are fried, producing a starch-lipid matrix.

Resistant starch has been widely studied in recent years, with studies showing possible benefits to lipid metabolism, body weight, and as a prebiotic to improve gut health (5). Resistant starch has also been demonstrated to be particularly effective at promoting a healthy microbiome (6). This emerging evidence suggests that the role of "starch," refined or whole, may be more varied, and more valuable, than merely as a component of complex carbohydrates.

Culinary use of carbohydrate foods is widely varied

Some carbohydrate foods, such as fruits and vegetables, can be eaten alone, even raw, while others are more commonly used as ingredients, either in cooked meals or snacks, or as ingredients, such as grain flour in breads and baked goods. Carbohydrate-containing foods can be eaten in savory or sweet preparations, allowing them a versatile role in the diet.

Wheat, rice, and maize (corn) are the three most commonly consumed grains in the world (7). Even in refined and enriched form, that is, containing mostly the starchy endosperm, without the germ or outer bran layer, these staple grains often serve as "vehicle foods" for delivering vegetable and protein components of meals. Starchy grains have long been a culinary staple of many cultures, but also as indulgent foods for lower-nutrient savory or sweet snacks and desserts. Starchy vegetables, such as potatoes, are vegetables in their own right and also serve as "vehicles" or delivery mechanisms for additional nutrient-dense foods, such as other vegetables, healthy fats, and lean proteins.

In many cultures, starchy vegetables and grains have also provided an economical means of "stretching" modest amounts of proteins while still providing a satiating and nutrient-dense meal. Examples include combining potatoes with eggs in a Spanish frittata (Tortilla de Patatas) or a skillet meal that mixes lean ground beef with potatoes and vegetables. These two dishes have their variations in many cuisines and provide a way to extend more moderate amounts of proteins, while increasing overall vegetable consumption.

Starchy vegetables, in contrast to grains, are seldom consumed with added sugar, either as a staple vegetable in a meal, or as a snack, the exception being candied sweet potatoes or sweet potato pie, but overall consumption of these is low. The term "grain-based desserts," for instance, does not have a potato equivalent. Whether starchy vegetable or starchy grain, either can contain added fats and/or sugars. Dietary balance, which includes consideration for quantity and frequency of consumption, remains a cornerstone of dietary guidelines.

Starchy vegetables and grains have significantly different nutrition profiles

Grains and starchy vegetables share the commonality of being complex carbohydrates, and in the case of whole grains, fiber as well. However, that is where much of their similarities end.

Significant differences between grains and starchy vegetables exist in their micronutrient content. Starchy vegetables, such as potatoes, are more known for their starch content than for their potassium, iron, B_6, and vitamin C content. Potatoes are a good source of potassium, one of the "nutrients of public health concern" identified by the 2020–2025 United States Dietary Guidelines for Americans (8) (DGA, 2020–2025). A medium-sized potato with skin (5.3 oz) and two slices of whole wheat bread (two slices) have similar energy value, approximately 110 vs. 160 kcal, respectively. However, the following are among their differences in nutrient content (9, 10):

- Potassium:
  - o Medium-sized potato: 15% daily value (DV)
  - o Whole wheat bread: 3% DV

- Vitamin C:
  - o Medium-sized potato: 30% DV
  - o Whole wheat bread: 0%

- Vitamin B6:
  - o Medium-sized potato: 10% DV
  - o Whole wheat bread: 8% DV

- Iron:
  - o Medium-sized potato: 6% of the DV
    - Notably, the low phosphorous content of potatoes makes their iron more bioavailable than the iron in plant foods with higher phytate content (11). Their higher vitamin C content also aids iron absorption.
  - o Whole wheat bread: 9% DV

- Fiber:
  - o Medium-sized potato: 8% of the DV
  - o Whole wheat bread: 14% of the DV

Grains and starchy vegetables both lose fiber when processed by removal of the bran and germ from grains, and removal of the skin from potatoes. If potatoes are boiled, there can be additional loss of potassium through leeching. Mineral content is well retained whether potatoes are baked, fried, roasted, or microwaved (12). Frying and baking, because they decrease moisture content, actually increase the concentration of key nutrients, including potassium.

Compared with starchy vegetables, such as potatoes, grains tend to be lower in potassium and vitamin C, but intrinsically provide higher amounts of other nutrients, such as thiamine, zinc, and vitamin E. If grains are consumed in "whole" form, their bran and germ components can be sources of phytochemicals, mostly as polyphenols (13). The majority of grain foods purchased however, are in the form of refined grains, where the germ and bran layers, and the nutrients they contain, are removed (14). In the United States, refined grains are required to contain added iron, folic acid, riboflavin, niacin, and thiamin, given these nutrients are lost during the refinement process (15).

Among macronutrient differences between grains and potatoes, whole wheat bread contains 7.2 g of protein in two slices (64 g), compared with 3 g in a medium-sized potato (5.3 oz) of similar energy content (9, 10). While neither food is considered a major protein source, the protein quality in potatoes is superior, with a biological value (BV) of 90 (16), which is comparable to the BV of protein in egg and milk (11, 17) and higher than the BV of other excellent plant protein sources, including soybeans (16).

Classification of grains and starchy vegetables in scientific literature

Tools for collecting dietary intake data have varied over time, and have included various questionnaires, 24-h recalls, and interviews. The National Health and Nutrition Examination Survey (NHANES) uses trained interviews to conduct dietary recalls on two separate days (18). Other large-scale studies have used a semi-quantitative food frequency questionnaire (FFQ), often using one developed by the Harvard School of Public Health (19).

These data collection tools do not always consistently classify foods, especially starchy vegetables. The USDA and the DGAs consider all white potatoes as vegetables. Yet, the FFQ used in many large observational studies, groups white potatoes with breads, cereals, and starches, but other starchy vegetables, such as sweet potatoes, including sweet potato fries, and butternut and acorn squashes, with the vegetable group (19). The nutrient compositions of white and sweet potatoes are quite similar. Sweet potatoes do have more beta-carotene (20) but white potatoes have far more potassium (9).

Given these inconsistencies, a tool that addresses the quality of carbohydrate-containing foods would be a meaningful addition to inform the categorization of foods for development of food-based dietary guidelines.

Carbohydrate quality: an important consideration for dietary recommendations

At a time when most Americans do not eat enough vegetables, moving a group of vegetables to a different food group, could result in vegetable consumption in food assistance programs and other efforts affected by DGA. Given the diverse variety and nutrient composition of carbohydrate-containing foods, others have suggested the usefulness of an evidence-based metric for measuring carbohydrate food quality (21). It has been postulated that such a tool would be useful for informing not only nutrition researchers, but also food developers and those setting future public dietary guidance, including the DGAC. When multiple nutrient profiling methods were applied to high-carbohydrate foods, the authors concluded that the nutrient content of white potatoes warranted greater priority in dietary recommendations (22).

Among these justifications for a more holistic metric of carbohydrate quality was better alignment with current dietary guidance, including a focus on micronutrients to encourage, as well as ones to limit. Current global dietary guidelines encourage consumption of whole grains and many, including the 2020–2025 DGA, note fiber and potassium among the "nutrients of concern" because more than half the population consumes insufficient amounts. Additionally, the DGAs have consistently encouraged reduction of saturated fat, sodium, and added sugars, due to historical overconsumption by most consumers.

The result was the development of a metric known as the Carbohydrate Food Quality Score (CFQS), which builds onto the 10:1:1 model of carbohydrate:fiber:free sugar first developed by Liu et al., and considers sodium, potassium, added sugars, and whole grains, all of which were addressed in the 2020–2025 DGAs (23). More research using this score to address the health outcomes of consuming whole grains, and various dietary patterns is warranted. Thus far, the CFQS correlates strongly with two other measures: the Nutrient-Rich Food Index and the Nutri-Score, with a more robust assessment of carbohydrate quality.

Menu modeling analysis demonstrates nutrition consequences of swapping starchy vegetables and grains

The question regarding interchangeability of starches and grains suggests a need to evaluate their unique nutrient contributions. A comparison of the nutrients these foods provide through menu modeling is one way to understand the differences between starchy vegetables and grains and demonstrate how they are not nutritionally similar or interchangeable.

Table 1 shows a 2,000 kcal "foundation" menu that aligns with USDA's "Food Pattern Models" and the 2020–2025 DGA (24).

Table 1 also outlines a comparison menu, and is also aligned with 2020–2025 DGAs, but this menu replaces the starchy vegetables in Menu 1 with grains, with at least half the grains being whole grains. Both meal patterns provide approximately 2,000 cal. These findings (detailed in

TABLE 1 Menu modeling comparison.

	Menu #1—Foundational menu—healthy United States (2,092 kcal)	Menu #2—Replace 100% starchy vegetables with grains (2021 kcal)
Breakfast	Scrambled eggs: • Two eggs • Cooked in 0.5 TBSP olive oil	Scrambled eggs: • Two eggs • Cooked in 0.5 TBSP olive oil
	Hash browns: • 2 oz. hash browns	Toast: • 2 oz whole wheat bread
	Toast: • 1 oz. whole wheat bread	Orange: • 1/2 medium orange
	Orange: • 1/2 medium orange	Coffee: • 8 oz coffee
	Coffee: • 8 oz. coffee	
Morning snack	Yogurt with corn flakes, fruit: • 1/2 cup nonfat Greek yogurt • 1/2 cup corn flakes • 1/4 cup blueberries	Yogurt with corn flakes and fruit: • 1/2 cup nonfat Greek yogurt • 1/2 cup corn flakes • 1/4 cup blueberries
Lunch	Spinach/chicken salad and whole wheat pita with a side of blue corn chips: • One cup spinach • 1/2 cup whole cherry tomatoes • One TBSP Ranch dressing • 2 oz. roasted skinless chicken breast • 0.25 oz. sunflower seeds • One large whole wheat pita pocket • 1 oz. blue corn tortilla chips	Spinach/chicken salad and whole wheat pita with a side of blue corn chips: • One cup spinach • 1/2 cup whole cherry tomatoes • One TBSP Ranch dressing • 2 oz. roasted skinless chicken breast • 0.25 oz. sunflower seeds • One large whole wheat pita pocket • 1 oz. blue corn tortilla chips
	Milk: • 8 oz. nonfat milk fortified w/vitamins A & D	Milk: • 8 oz. nonfat milk fortified w/vitamins A & D
	Apple: • One medium apple	Apple: • One medium apple
Afternoon snack	Cheese and popcorn: • 0.75 oz. cheddar cheese, reduced fat • Three cups air popped popcorn	Cheese and popcorn: • 0.75 oz. cheddar cheese, reduced fat • Three cups air popped popcorn
Dinner	Steak, baked potato, and broccoli, and chocolate: • 3 oz. broiled lean top sirloin • 5 oz. baked russet potato, skin on (medium potato) • 1 tsp. sour cream • 1/2 cup boiled broccoli	Steak, rice, and broccoli: • 3 oz. broiled lean top sirloin • *½ cup white rice, cooked* • *One pat butter, unsalted* • 1/2 cup boiled broccoli
	Milk: • 8 oz. nonfat milk fortified w/ Vitamins A & D • 1 oz. dark chocolate	Milk: • 8 oz. nonfat milk fortified w/ Vitamins A & D • 1 oz. dark chocolate
[Menu footnote]	This menu item follows the Healthy United States dietary pattern and features a variety of whole grain and refined grains	Note on page 2 of the food pattern reports for Healthy United States-Style Eating Patterns that vitamins D and E is usually low (46 and 68%, respectively for adult males and females). The foundation menu meets or exceeds the % RDA reflected in this perspective

Table 2) highlight the nutritional differences between potatoes and grain foods and underscore the importance of maintaining potatoes in the vegetable group. While swapping grains for potatoes may increase intakes of some key nutrients, others will decrease significantly. Consuming grains instead of potatoes (the no starchy vegetable diet) may result in several nutritional risks including:

- Decreased intake of potassium (−21%).
- Shortfalls in dietary fiber intake (−10%).
- Reduced intake of choline (−2%) and vitamins B6 (−17%), C (−11%), and E (−5%).

Of particular concern are fiber and potassium, considered as "nutrients of public health concern" by the 2020–2025 DGA (page 49), because "low intakes are associated with health concerns." Replacing potatoes with grains resulted in a considerable decrease in potassium content (−21%). Many starchy vegetables are good sources of potassium (e.g., one medium potato provides 15% DV). Consuming grains in place of starchy vegetables may further widen the gap between recommended and actual intakes of potassium. A meaningful decrease in fiber intake (−10%) also occurred when grains replaced potatoes. This finding reinforces the need to include both starchy vegetables and grains in the diet to obtain adequate intake of fiber, especially given that currently 90% of women and 97% of men do not meet dietary fiber intake recommendations (25). It is important to emphasize that, while potatoes are a vegetable, they are not a replacement for, nor interchangeable with, non-starchy vegetables. Currently, only one in 10 adults meets recommendations for vegetables so consumption of all varieties of vegetables should be encouraged (26).

TABLE 2 Nutrient differences when starchy vegetables are replaced with grains.

Nutrient	% Change – 100% Starchy vegetable replaced with grains (i.e., 100% grains) menu
Potassium	**−21%**
Sodium	**−12%**
Calcium	+1%
Choline	−2%
Dietary Fiber	**−10%**
Vitamin D	0%
Vitamin B1	+7%
Vitamin B6	**−17%**
Vitamin B12	0%
Vitamin C	**−11%**
Vitamin E	−5%
Folate	+5%
Iron	+1%
Zinc	+1%

Bold values are nutrient variances of at least 10%.

Discussion

To minimize confusion about carbohydrate recommendations, it is critical to clarify the unique differences between starchy vegetables and grains given their significant nutrient contributions to the American diet. Nutrition analysis clearly demonstrates that starchy vegetables, including potatoes, are not nutritionally interchangeable with grains. Both are high in carbohydrates, but their micronutrient contributions are different and deserve dietary recommendations that respects this difference.

As with grains, a diverse intake of starchy vegetables should be encouraged. The limitation of these menu modeling results is that potatoes were the only starchy vegetable included. Additional modeling done with other culturally relevant starchy vegetables, and over 7 days or more, may show different results.

This perspective addresses white potatoes, in part because they are the most commonly consumed starchy vegetable and have the same nutritional strengths as other starchy vegetables, particularly with respect to their content of potassium, vitamin C, and dietary fiber. Those with color in the edible portion, such as butternut and acorn squash, also contain beta-carotene, as do sweet potatoes, but other starchy vegetables do not, such as beets and cassava (yuca). Yet all, except white potatoes, are grouped as vegetables in much of the scientific literature that uses the aforementioned FFQ.

Carbohydrate guidance should focus not only on the unique nutritional assets of each, but also their varied culinary uses and cultural relevance within diverse foodways. All starchy vegetables have nutrient profiles that are distinct from those of grain foods and should retain their categorizations as separate food groups in dietary guidance.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

KA: Writing – original draft, Writing – review & editing.

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Conflict of interest

This study received funding from Potatoes USA. The funder had the following involvement with the study: composition and data analysis of the menu modeling. KA was compensated by Potatoes USA for preparation and revision of the manuscript.

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Adoption and implementation of produce prescription programs for under-resourced populations: clinic staff perspectives

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Background: Produce prescription programs represent a promising intervention strategy in the healthcare setting to address disparities in diet quality and diet-related chronic disease. The objective of this study was to understand adoption and implementation factors related to these programs that are common across contexts and those that are context-specific.

Methods: In this qualitative case comparison study, we conducted qualitative interviews with eight clinic staff from five primary care “safety net” clinics, identified by a partnering non-profit organization that operated the programs, in April–July 2021.

Results: Across clinics, the ability to provide a tangible benefit to patients was a key factor in adoption. Flexibility in integrating into clinic workflows was a facilitator of implementation. Fit with usual operations varied across clinics. Common challenges were the need for changes to the workflow and extra staff time. Clinic staff were skeptical about the sustainability of both the benefits to patients and the ability to continue the program at their clinics.

Discussion: This study adds to a growing body of knowledge on the adoption and implementation of produce prescription programs. Future research will further this understanding, providing the evidence necessary to guide adopting clinics and to make informed policy decisions to best promote the growth and financial sustainability of these programs.

KEYWORDS

produce prescription programs, implementation, qualitative, clinic staff, food as medicine

1. Introduction

Most U.S. adults have suboptimal diet quality despite some recent improvements, and disparities in diet quality have persisted or worsened for most dietary components (1, 2). These disparities in diet quality, in turn, contribute to disparities in chronic diseases (3). Healthcare systems can help address poor nutrition, and in this context produce prescription programs represent a promising intervention strategy.

Typically in produce prescription programs, patients with a diet-related health condition or food insecurity are referred by healthcare providers and receive economic incentives,

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often in the form of electronic cards or paper vouchers, to redeem for fruits and vegetables at retail food outlets (4). Retail food outlets may include grocery stores, farmers markets, or mobile markets. Programs often include some form of nutrition education, such as one-on-one counseling or classes, although the amount of nutrition education can vary considerably among programs (4, 5). While the effectiveness of these programs is still being studied, there is a growing body of evidence that they can positively impact fruit and vegetable consumption and food insecurity, as well as health outcomes including BMI, blood pressure, and glycated hemoglobin (HbA1c, or "A1c") for patients in poor cardiometabolic health (6–8).

For these programs to achieve their potential in terms of public health impact, they will need to be widely and sustainably adopted within the healthcare system. It is therefore critical to understand factors that influence the decision to adopt these programs as well as barriers to and facilitators of their implementation and sustainability (9). It is also important to gauge provider perceptions of the impact of the program on patient outcomes. Qualitative methods are best suited to understand these implementation factors and perceived impacts because they allow for an in-depth examination of what is happening within clinics and why (10).

Few studies have examined factors related to the implementation of produce prescription programs. Most studies that examined implementation factors in-depth evaluated programs running at 3–4 clinics in a single state, and all partnered solely with farmers markets (11–13). These prior studies reveal several barriers, including staff time and turnover, different electronic health record (EHR) systems (11), and a lack of resources for sustainability (12); as well as facilitators: adapting clinic workflow (11), provider dedication (12, 13), and the ability to leverage existing relationships and programs (13). However, no consistent barriers or facilitators were revealed across these studies. To our knowledge, there is only one study in the peer-reviewed literature on implementation factors across multiple programs in different states. Stotz et al. (14) obtained perspectives from 16 health care providers from produce prescription programs that had been funded through the U.S. Department of Agriculture's Gus Schumacher Nutrition Incentive Program (GusNIP). Common barriers included limited staff time and difficulty with patient and provider engagement; in terms of facilitators, EHR-based screening systems and full-time paid staff members to manage the program facilitated implementation in the clinics that had them.

While prior research identifies a number of barriers and facilitators to implementation, it does not fully address factors that may be common across contexts and those that may be context-specific. Furthermore, only one other study examines factors that influence clinics to adopt a program (11). We used a qualitative comparative case study approach to obtain perspectives from administrative clinic staff on produce prescription programs implemented in five "safety-net" clinics serving low-income populations that otherwise varied by geography, some aspects of the program, and populations served by the programs. This research contributes to and extends prior research to understand the factors related to adoption and implementation of produce prescription programs. This understanding will support the successful growth of these programs, since it can inform implementation at multiple levels: individual clinics, healthcare systems, and policy.

2. Methods

2.1. Design, setting, and sample

Our academic team partnered with a non-profit organization to conduct an evaluation of their produce prescription programs, including this qualitative assessment of factors related to adoption and implementation. The non-profit partner is a leading national organization that has supported and developed nutrition incentive programs throughout the U.S. The non-profit partner operated the produce prescription programs by recruiting clinics and retailers as well as securing funding for the programs. Funding sources included a state department of public health, a food company, and healthcare organizations. All clinics served low-income populations. In all programs, enrolled participants received a financial incentive (paper voucher or electronic gift card), delivered once per month, to purchase produce at grocery stores. The programs otherwise varied by geography, monthly dollar amount, nutrition education component, size of the program, and the specific population served (Table 1). The programs also varied in length: the shortest programs in this study were 6 months and the longest were 10 months (Table 1). Program duration varied based on the resources the non-profit partner was able to secure and by the goals of the partnering clinics. The variability among programs allowed us to take a qualitative comparative case study approach (15).

We interviewed staff from a convenience sample of five clinics that had partnered with the non-profit partner to implement a produce prescription program within the past 2 years. Interviews were conducted in April–July 2021. Clinic staff to be interviewed were identified by our partnering non-profit organization as the primary implementer at the respective clinics.

The research team has expertise in qualitative methods and implementation science (SCF), economics (SBC), and nutritional epidemiology (FFZ). The team also included a project administrator (ZL) and a doctoral student whose dissertation research focused on food is medicine interventions (KH). The team was concurrently working on a quantitative analysis of the produce prescription programs.

2.2. Interview procedures

The interview guide was informed by Proctor's framework (9) and covered three areas: (1) factors related to the decision to adopt; (2) "implementation and logistics," covering items such as fit with usual practices; and (3) "impact and sustainability," including perceptions of the impact on patient outcomes and sustainability at the patient and clinic levels. A phenomenological approach was taken and the guide was semi-structured with open-ended questions. Table 2 contains the interview questions. Questions were developed by the team's qualitative expert (SCF) with input from the rest of the research team, the non-profit partner, and a clinic staff member who had implemented one of the programs.

Interviews were conducted online via the Zoom videoconferencing application either by SCF, ZL, KH, or by two graduate research assistants. SCF trained the other interviewers. All but one of the interviews were conducted one-on-one with the study team member and clinic staff. At Clinic 5, one of the interviews was conducted with both the medical administrative assistant and the business systems

TABLE 1 Clinic characteristics.

Program	Number and title of staff interviewed	Type of program	Type of clinic	Eligibility	Geographic region	Dollar value of monthly produce prescription incentive	Program duration (months)	Program size (# participants)	Delivery mode	Nutrition education component
Clinic 1	1, Wellness coordinator and coach	Pediatric	Community health center	Children ages 1–5 years	South	$60	8	Large (>300)	Card	Two videos, approx. 60 min each
Clinic 2	1, Chief executive officer	Pediatric	Community health center	Children age 2–18 with household food insecurity	Northwest	$60	6–7	Medium (100–300)	Card	None
Clinic 3	1, Ambulatory care pharmacist	Adult	Community health center	Adults with diabetes or pre-diabetes.	Midwest	Year 1: $30 per household member; Year 2: $90 for all households	10	Small (<100)	Voucher	Group-based administered by RD
Clinic 4	1, Program manager	Adult	Community health center	Adults with diabetes or pre-diabetes.	Midwest	$90	10	Medium (100–300)	Voucher	Year 1: one-on-one counseling with clinic staff Year 2, online groups with RD
Clinic 5	4, Nurse manager, head of clinics, medical administrative assistant, business systems associate	Adult	Hospital	HbA1c > 6.5%.	Northeast	$60	6	Large (>300)	Voucher	Minimal; opportunity to connect with programming by RD

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TABLE 2 Produce prescription program—interview guide for clinicians.

Questions about adoption
1. Think back to when you were deciding whether to do this program. What motivated you to participate in the program?
a.Tell me what you thought about the materials the clinic received from [non-profit partner].
b. What other information would you have wanted that you did not have when making the decision?
2. Describe how easy or hard it was for staff to understand the program.
a.Talk about any pushback there was from your administration about running the program at your clinic.
Questions about implementation and logistics
3. Describe how well this program fit within your clinic's usual practices.
a.What was required to run the program in terms of personnel?
i. Who did it fall to the most?
ii. Describe how easy or hard it was for staff to administer the program.
iii. Approximately how much "extra" time was spent by staff members with each program participant, compared to how much time they would spend during a visit when the program was not taking place? [Probes: nutrition education, registering patients, and follow-up with program patients].
iv. To what degree was the time spent by any staff explicitly compensated by [non-profit partner]? [If informant does not know:] Who else on staff could better answer this?
b. How involved were the doctors in the program?
i.In your opinion, how much should doctors be involved with the implementation of the program vs. other clinic staff?
c.How could the program be made more efficient for clinic operations?
d. What costs, if any, were incurred by the clinic to run the program that were not covered by [non-profit partner]?
i.[If informant does not know:] Who else on staff could better answer this?
e.If you were to do this program over again in your clinic, what would you do differently?
4. Describe how well this program fit within your own usual set of practices.
a.In what ways, if any, did it become part of your routine?
b. How adequate was the amount of time you had to manage the program?
c.How adequate was the time you had to talk with patients about healthy foods?
d. In what ways, if any, did the program affect the way you worked with patients?
i.In what ways, if any, have those changes remained since the program ended?
e.How did you recruit families for the program?
i.What was most successful in terms of recruitment?
ii. What did not work as well?
f.Describe how easy or hard it was patients to understand the program.
i.What questions did patients ask about the program?
5. What are your impressions of the adequacy of the produce incentive that the participants received from [non-profit partner]?
a.What would have been the right amount?
Questions about impact and sustainability
6. Talk about your impressions of the program overall.
a.As you reflect on the program overall, in what ways did it meet your expectations?
i.In what ways, if any, did it fail to meet your expectations?
b. What, if anything, surprised you about the program?
7. Tell me your thoughts about the program's ability to help your patients – please do not mention any names or specific identifying information about these patients.
a.In what ways, if any, was it a useful tool for them?
b. In what ways, if any, did the program improve the quality of care you felt you could provide?
c.What types of patients did it seem to work best with?
i.Describe an example of a patient who had a very positive experience with the program. What made it such a great experience for that family?
d. What types of patients did it seem to not work as well for?
i.Describe an example of a patient who the program did not work for.
e.Tell me your thoughts about whether your patients will sustain any changes in fruit and vegetable consumptions that they made during the program.
f.What could the program do to help patients sustain the benefits?
i.What could the clinic do?
8. What would clinics need to be able to sustain the program?

associate together. Interviews lasted 24–58 min. Participants received a $50 gift card for remuneration. The protocol was reviewed and deemed exempt by the Tufts University Health Sciences Institutional Review Board. Informed consent was obtained verbally from all participants.

2.3. Analysis

The interviews were recorded and transcribed, and then coded using NVivo software (version 12, QSR International, Doncaster, Australia). SCF and ZL were primarily responsible for the analysis.

We used a directed qualitative content analysis approach, which is fundamentally deductive (16). We drafted an initial codebook based on the interview guide. We then conducted a review of the transcripts and added codes for topics that arose in the data. Once the codebook was established, SCF and ZL independently coded one transcript. We determined inter-rater reliability, with kappa coefficient of 0.8 or greater at each code deemed as acceptable. Based on this testing, we discovered minor differences in interpretation of codes; the codebook was revised accordingly, mainly by clarifying code definitions, and all transcripts were subsequently coded by ZL. The codebook remained stable at this point, reflecting code saturation (17). We then examined the data for both common themes and differences across the sites (15).

3. Results

We interviewed eight clinic staff from the five clinics in our sample. For clinics 1 through 4, we interviewed one staff member, who was the primary implementer. In clinic 5, because we had a strong research collaboration with the clinic, we were able to interview four clinic staff to obtain perspectives from multiple types of stakeholders. At that clinic, in addition to the primary implementer, we also interviewed the head of clinics, a medical administrative assistant, and the business systems associate. The multiple perspectives at this one clinic offered a well-rounded view, which enhanced but did not fundamentally change the results. While six clinics had implemented a produce prescription program in partnership with the non-profit partnering organization in the timeframe, one primary implementer failed to complete an interview due to leaving her position shortly after being identified.

We present findings according to major topics covered in the interview guide: adoption, implementation, and impact on patients and sustainability.

3.1. Adoption

Clinic staff at all clinics described enthusiasm about the program and a willingness to adopt it at all levels of decision-making (*…it seems like hierarchy-wise it was a support at all levels…—Head of Clinics, Clinic 5*). For willingness to adopt, there were similarities across sites that converged into two main themes: simplicity of the program and potential benefits for patients.

Clinic staff described the produce prescription program, as presented to them by the non-profit partner, as easy to understand. They said that staff at the non-profit partner had provided adequate information about the produce prescription program and had been available to answer any questions. Clinic staff perceived the produce prescription program as reasonably flexible and relatively free of "red tape" in comparison to other programs their clinics had adopted to help their patients (which were not produce prescription programs, and often not focused on nutrition specifically).

Clinic personnel were motivated to adopt the program because of the potential benefit to the patients, especially given the need in the populations that they served.

> *So yeah, I'm dealing with an underserved population, whose—my mission is to support them, so that was a no-brainer. And many of our initiatives, again, like I said, come from partners from outside. So any partner outside willing to partner with us, with our patients, we tend to work on them with open arms, for the most part. (Head of Clinics, Clinic 5)*
>
> *That was something our dietitian was hearing left and right, was that just fruits and vegetables cost too much. And so she's trying to work with them on changing eating habits and they're saying I don't have the access to those things, so we thought it was a great way of removing that barrier and exposing people to some of the benefits of fruits and vegetables. (Ambulatory Care Pharmacist, Clinic 3)*

Only one site described any pushback to program adoption. At Clinic 1, the primary implementer was enthusiastic about the program, but was initially concerned that the clinic did not have the patient base to meet the recruitment expectations of the non-profit partner. This concern was alleviated by opening the program up to community members who were not patients at the clinic.

3.2. Implementation

Because of the flexibility allowed by the non-profit partner, there was variation in how the program was implemented at each site and in the clinics' experiences with the implementation.

> *But [the non-profit partner] tried to stay pretty hands off, from the perspective of letting us develop something that was, you know, better for our own clinic, right. So they gave some guidance and they gave some ideas, but it's not like they handed us kind of like a turnkey program and just said go. They let us really develop what was—what we felt like was most needed for our patients and what worked within our workflow much, much better. (Ambulatory Care Pharmacist, Clinic 3)*

Interviewees described five major tasks involved with program implementation: (1) recruiting/identifying patients and determining eligibility; (2) distributing and tracking the produce prescription incentives; (3) responding to patient inquiries related to the incentive; (4) obtaining and tracking outcome measurements (which included participant fruit and vegetable intake, food insecurity, HbA1c, blood pressure, and BMI/BMI z-score; in some cases it required scheduling extra appointments for these measurements); and (5) providing nutrition education. These tasks fell to different staff members at the different clinics and for some, shifted over time.

Physicians were minimally involved in implementation at all clinics. Their involvement ranged from attendance at several community recruitment events to initial identification of eligible program participants. The various tasks related to the program fell instead to front office staff, nurses, medical assistants, registered dietitians, the pharmacist, a health and wellness educator, and a volunteer.

There was variation and no major theme identified around perceived fit with regular clinic operations. At Clinic 1, implementation was described as essentially a seamless fit with normal operations. At this clinic, a full-time health and wellness education professional was primarily responsible for implementing this and other special projects. In contrast, interviewees at the remaining clinics described challenges to implementation since the program required changes in standard workflows and put demands on staff time.

The interviewee at Clinic 2 described putting in upfront effort to integrate the program into the EHR and other systems. At this clinic, physician involvement initially presented a challenge, and they shifted implementation to front office and nursing staff. With the upfront effort to create the protocols and the change in implementer, the program fit well within usual clinic practices thereafter.

> *And so, at first we were running those through the provider and some of the nursing team. But that became a little problematic, in that they would forget or, you know, [the patients are] there for diabetes and hypertension and some of these other things, and so the provider's thinking about prescriptions and those kinds of things and they're not thinking about the gift card as well, so we quickly removed it from the provider piece and put it on the front office and the nursing. And so between those two, the nurses would recommend based on what happened in the office, and then the front office could verify that they didn't have, you know, that they were kind of an underserved patient…So they implemented—once we moved to that piece it went pretty smoothly. (Chief Executive Officer, Clinic 2)*

At Clinics 3 and 4, the interviewees described major challenges in the first year of the program. Both sites included a substantial nutrition education component that required adaptations in the second year due to the COVID-19 pandemic. In both cases, they found that the modified model, which was remote, group-based nutrition education implemented by a registered dietitian, worked better.

> *It was interesting that the pandemic provided us the opportunity to do something that worked really well. I think that that support group type setting was something that provided a lot of efficiency. Working with registered dietitians as opposed to staff members who are involved in direct care and had a lot of patient appointments anyways, this seemed to more naturally fit into the registered dieticians' workflow. They were able to handle a lot of the follow-up that typically would have been—or in the previous year, was very burdensome to the staff that was involved. Obviously, there's always room for improvement, but that second year was really a good model of what worked well and would be something that we would probably mimic if we were going to be doing that for another year. (Program Manager, Clinic 4)*

Clinic 5 experienced the most serious challenges to implementation. Clinic staff perceived the program as time- and resource-intensive. Here, the four staff interviewed described the program as a "collective responsibility" that required thoughtfulness and effective communication among many members of the clinic staff. For part of the program, they had a volunteer for 20 h per week, and many responsibilities fell to this person.

> *…we also had a volunteer at the time from a program that we work with at the hospital that filled a lot of the data collection and updating spreadsheets and things like that, so we were very lucky to have someone that didn't have their daily tasks, that were being pulled from like their daily responsibilities, and so she kind of took on the little coordinator kind of role…. (Nurse Manager, Clinic 5)*

In this busy clinic, even with minimal nutrition education, implementation required multiple tasks and remained challenging.

> *…so the only thing was like because we have to do it like during—when the patient was here. And usually we do have a workflow, like when a patient arrives, do the vital signs so—and to incorporate the [outcome measures requested by the non-profit organization], so we have to change the workflow to see how that we can place the order for the hemoglobin A1c and then how we can communicate a provider to place the order, and then after that we have to do—do the whole information on the tablet with that ID number and things like that, so it was a lot of—(Business Systems Associate, Clinic 5)*
> *—Lots of, yeah, lots of hands on—a lot of manual tracking, and yeah. (Medical Administrative Assistant, Clinic 5)*

3.3. Impact on patients and sustainability

There was a high level of similarity across clinics in how interviewees described the impact on patients. A major theme was that they appreciated having something concrete to give to patients to help their social, nutritional, and economic struggles and improve their health.

> *…again it was another component in supporting the social determinants infrastructure by dealing with their basic needs of eating and eat—and hopefully eating better with the fresh fruits and vegetables. (Head of Clinics, Clinic 5)*
>
> *So we've always kind of tried to help in some of those social determinants and some of those areas where our patients really struggle, but we've never been able to do it in a focus on being healthy as well, so that's where this really was an amazing benefit, is because now it was truly something that was specifically for people who we knew needed to be healthier and couldn't afford to do that. (Chief Executive Officer, Clinic 2)*
>
> *I think anytime that we have something that we can actually give them, that's concrete ways to change their eating behaviors is really helpful. Rather than just telling people to eat better, we can give them something to help them eat better. (Program Manager, Clinic 4)*

Additional benefits that were mentioned by some of the interviewees, but not consistently across clinics, included patients feeling supported by the clinic, benefiting from the nutrition education, and increasing engagement with the clinic, especially during the pandemic.

> *I think the interaction too with the staff was nice for the patients because even during Covid it was like people were isolated and you still had the staff reaching out to say hey, don't forget your vouchers or hey, another mailing is coming in…there was still communication going back and forth, even during Covid when patients might have felt like isolated. So yeah, I think again the benefit outweighed the amount of work it took to implement it. (Nurse Manager, Clinic 5)*

Most clinic staff thought that patients were satisfied with the monthly produce prescription incentive amount, even though the dollar amount varied somewhat across clinics.

A second theme related to impact on patients was that clinicians were skeptical about patients sustaining any changes that they had made without an ongoing incentive for free fruits and vegetables. Staff at clinics that had not provided much nutrition education felt that providing more in combination with incentives might be helpful in sustaining long-term dietary changes. Overall, though, the level of poverty among patients participating in the program was the basis for clinic staff skepticism of long-term program benefits. Staff expressed concern that without the additional dollars provided by the program, patients would have less ability to purchase the same amount of fruits and vegetables. The program manager at Clinic 4 suggested that financial education could possibly help the patients learn to fit produce into their budgets, an approach that had been tried at Clinic 3 in a small way at one of the final classes.

> *I don't know if there is an amount of financial education or maybe working to get people other resources to show them how to do this. I think that maybe it's the potential of trying to find other ways to show patients or get them to acknowledge how improving their A1c made them feel, to the point where that would cause them to readjust some of their budget to include more fresh fruits and vegetables. Like I was saying before, just from some of the feedback, some people just have such deep poverty that that really is challenging. (Program Manager, Clinic 4)*

Only the wellness coordinator and coach at Clinic 1 was hopeful about the sustainability of changes. In this pediatric program, he felt that once parents saw that their children were willing to eat different types of produce, they would be more willing to purchase it after the conclusion of the program.

> *And in that way, I think a lot of parents and participants were able to benefit from it, because they were able to experiment. So I think it really played a huge role, because even though they got off the program [because the program ended] they were using that $60 for six months, and they were able to say, okay, these were some of the things that work. And now they could—when they're investing their own money they can feel more confident knowing if I buy these grapes, my daughter's gonna eat them. (Wellness Coordinator and Coach, Clinic 1)*

In terms of sustainability of the program at the clinic level, there was consistency across clinics and a major theme was that the clinics would run the program again if given the opportunity, but they could not do so without external funding.

> *And then funding, if you had a state that was willing to put some money into it to make it sustainable, or if you had a large, generous foundation or something like that that was willing to year over year really invest in to see, does this actually make a change over the course of, you know, 5 years of providing fresh fruits and vegetables to a family. And then see what the data would show, but without that kind of commitment, just like here, it was awesome while we had it. We'd definitely do it again in a heartbeat. But as soon as it went away, we look to the next kind of program to help our patients. (Chief Executive Officer, Clinic 2)*

> *And there might be push back [if I asked the healthcare corporation for money for the program] like I do not—I do not have enough leverage, I think, with my population to extol resources from the program from the corporation. However, for, let us say a department that brings in revenue to the system. Let us say, like the bariatric surgery program. They may exert leverage to say, "I need additional resources to administer this program." See my point, they—whereas mine I go into the CEO or I have poor patients who I do not get money for, can you give me resources to administer this program. As opposed to, "I'm bariatric surgery and bringing in X millions, and this would be a great adjunct to what we do." Right, they have greater leverage. (Head of Clinics, Clinic 5)*

4. Discussion

This study is one of the first to explore implementation factors related to produce prescription programs across multiple program types. In this qualitative study, clinic staff described simplicity, flexibility and the ability to provide something tangible to their patients as factors in the decision to adopt the program. There were challenges to implementation at most clinics, and the need for changes to the workflow and extra staff time were common ones. Physicians were minimally involved compared to other clinic staff. Clinic staff expressed skepticism about the sustainability of both the benefits to patients and the ability to continue to offer the program at their clinics.

4.1. Adoption

Participants described several key factors related to adoption. A major factor in program adoption was compatibility, or the degree to which the innovation fit within existing values, experiences, and systems (18). While there were otherwise several major differences across the sites, all were "safety net" clinics serving very low-income populations, and staff indicated that their clinics were serial adopters of programming to help meet the needs of their patients. The produce prescription program was compatible with this practice and the flexibility also made it seem compatible with existing workflows. Perhaps also because of their prior experience with adopting other programs, clinic staff perceived a low barrier to entry, since the non-profit partner addressed most of the program cost. Clinic staff also described the program as being easy to understand, a factor related to the communications and materials provided by the non-profit partner. A theme in our study and in Stotz et al.'s (14) interviews with providers participating in GusNIP-funded programs was that clinic staff appreciated having something tangible to offer patients, which provided a relative advantage over other clinic-based programming. In another study of produce prescription programs connected to Medicaid in one state, a theme among multiple types of stakeholders, including healthcare payers, administrators, and researchers, as well as clinicians was that produce prescription programs likely represented a relative advantage in terms of increased patient engagement and satisfaction with healthcare (19). These characteristics may be useful in promoting further growth of produce prescription programs.

4.2. Implementation

In addition to being a factor in the decision to adopt, across the sites in our study, flexibility was also described as a key facilitator of implementation. Other studies conducted have consistently described the need for flexibility and adaptability in the implementation of produce prescription programs (11, 12, 20). However, in interviews conducted for a report by the Center for Health Law and Policy Innovation, some interviewees also indicated the need for standardized solutions to facilitate implementation and promote sustainability (20). In their implementation study of a program for hypertensive patients, some elements were standardized by providing clinic staff with training on how to counsel patients, develop a referral process, and integrate the program into the EHR system (11). This suggests that while flexibility is critical, some training and standardization may help ease the start-up issues that several of the clinics in our study described. It may also help increase adoption of produce prescription programs (21). Standardization could facilitate future comparisons across clinics, with the potential for improving the effectiveness of programs as the evidence starts to accumulate regarding best practices. Additional systematic studies of implementation will help clarify which aspects of the programs might be standardized and which should be left to the clinics to adapt to best fit with their local workflows.

While we found that flexibility was a common facilitator of implementation, staff time was a common barrier across the clinics. A solution to staff time issues suggested by our results is assisting clinics with upfront changes that will alleviate workflow inefficiencies, such as adding fields to the EHR. Noting the differences among the clinics, our results also suggest that staff time issues might be alleviated if responsibilities for managing the program fall to staff whose job is well-aligned, such as health educators. Similarly, in Stotz et al.'s (14) interviews with providers participating in GusNIP-funded programs, hiring a full-time staff member to manage all aspects of the program emerged in a theme on solutions to challenges. While a volunteer effectively served this manager role for Clinic 5, relying on volunteers is not likely to be a desirable model for most clinics. At Clinic 5, the volunteer's time ended before the program did, causing further issues; also, Stotz et al. (14) address the inequitable nature of this unpaid labor.

Our results indicate that produce prescription programs can be implemented, potentially more effectively, by clinic staff other than physicians. The study with hypertensive patients had similar findings (11). Both that study and ours involved "safety net" clinics, in which physicians face greater time and other resource constraints in working with medically underserved populations (22). It will be important to continue to conduct implementation research to understand the best role for physicians and other clinic staff in different types of clinics.

4.3. Impact on patients and sustainability

While a major theme was that providing a tangible form of support had a positive impact on patients, all clinic staff expressed skepticism about sustainability at both the level of patients' individual habits and at the clinic level. In a field scan of produce prescription programs, self-supported programs (funded through the organizational budget) lasted the longest, an average of 4.5 years, but only 4% were self-supported (4). Because of this issue, there is growing interest in policy solutions, such as coverage options within Medicare and Medicaid and the expansion of GusNIP programs (4, 20). In September 2022, the Biden administration released the National Strategy on Hunger, Nutrition and Health, which listed as priorities expanded Medicare and Medicaid coverage of produce prescriptions, universal screening for food insecurity in federal health systems, and produce prescription pilots in Indian Health Services and Veterans Health Administration (23). These policy developments signal a move toward greater sustainability and an increased need for effective and efficient implementation of produce prescription programs across a range of settings in the U.S. Yet, concerns about long-term sustainability have been raised by some produce prescription providers, given recent guidance from the Centers for Medicare and Medicaid Services that coverage of produce prescription programs should be limited to a maximum of 6 months (24).

4.4. Strengths and limitations

This study had multiple strengths and limitations. It is one of the first studies to compare adoption and implementation factors across clinic sites. However, the programs were all associated with the non-profit organization that partnered with our research team and therefore this study only includes perceptions related to the specifics of produce prescription programs associated with that organization. Another limitation is the small number of clinics in the sample. While the overall sample was small, it allowed us to compare across clinics. We also achieved code saturation (17), suggesting the robustness of themes. However, we may not have fully achieved data saturation in this small sample (25). Future studies that include a larger number and greater diversity of clinics will more fully address the similarities and differences in factors related to adoption and implementation of produce prescription programs.

4.5. Implications for practice

Based on our findings, the following points may be helpful to clinics considering the adoption of a produce prescription program:

- Communicating how the program fits with the values and practices of the clinic will help ensure that staff will persist in resolving barriers to implementation. The ability to provide a tangible support to patients was also a motivator for clinic staff.
- Ensuring that program logistics are simple and flexible may facilitate adoption and implementation.
- It is likely that up-front effort to build the program into workflows, including integrating it into the EHR system and possibly other forms of patient tracking, will pay off in terms of smooth implementation.
- Clinics may consider the involvement of multiple clinic staff to implement programs. Reliance primarily on physicians may impede implementation in some clinics.

- More intensive and targeted nutrition education and counseling (e.g., group classes, ideally led by a registered dietitian) should be considered in future programming. Especially in areas of high poverty, some form of financial education could be considered as well.
- Clinics may be unable to bear the cost of sustaining the program. Other solutions should be explored to ensure the sustainability of the program.

4.6. Conclusion

This study contributes information on factors related to adoption of produce prescription programs and corroborates previous research about barriers to implementation, including staff time. It also provides further evidence of common facilitators, such as the flexibility and adaptability of the programs. Our findings suggest the importance of policy solutions to ensure sustainability of produce prescription programs. This study described implementation in “safety net” clinics of programs that received resources from the same non-profit partner. Additional research is needed to understand implementation of produce prescription programs more fully across a range of settings, to further determine which barriers and facilitators are common and which are unique in different contexts. These studies will provide the evidence necessary to guide adopting clinics and to make informed policy decisions to best promote the growth and sustainability of these programs.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving humans were approved by Tufts University Health Sciences Institution Review Board. The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent for participation was not required from the participants or the participants' legal guardians/next of kin because the protocol was deemed exempt. Verbal consent was obtained.

Author contributions

SF, SC, and FZ contributed to study conception. SF, ZL, and KH made substantial contributions to data acquisition. SF and ZL analyzed the data. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Dietary and lifestyle factors associated with troublesome gastroesophageal reflux symptoms in Vietnamese adults

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Background: Dietary and lifestyle habits related to troublesome gastroesophageal reflux symptoms (tGERS) differ significantly across populations. There have yet to be studies on the Vietnamese population.

Aims: To identify dietary and lifestyle habits associated with tGERS in Vietnamese adults.

Methods: A cross-sectional survey was conducted among Vietnamese adults aged 18 years and older from March 2023 to May 2023. Participants were recruited online through a widely read national newspaper and Facebook, one of Vietnam's most popular social media platforms. The survey questionnaire comprised 27 questions covering participants' basic demographic information, dietary and lifestyle habits, the presence and characteristics of tGERS, and inquiries about specific dietary and lifestyle patterns, foods, and beverages associated with tGERS.

Results: A total of 4,400 valid responses were collected, including 2050 participants without tGERS and 2,350 participants with tGERS. Multivariate analysis showed several factors associated with tGERS, including eating beyond fullness (OR 1.383, CI95% 1.127–1.698), tight clothing (OR 1.627, CI95% 1.256–2.107), stress (OR 1.566, CI95% 1.363–1.800), and insomnia (OR 1.321, CI95% 1.129–1.546). Among habits associated with tGERS, eating beyond fullness was the most frequently reported (64.6%). Interestingly, although a short meal-to-bed time and staying up late after midnight were not risk factors for tGERS, they were two common factors associated with tGERS in symptomatic participants, particularly those with nocturnal reflux symptoms. For food triggers, the three most common ones were greasy foods (71.9%), sour/spicy soups (64.7%), and citrus fruits (36.0%). In terms of beverages, carbonated soft drinks were at the top of triggering tGERS (40.3%), and beer and orange juice were the second and third most common triggers, accounting for 35.7 and 30.6%, respectively.

Conclusion: We reported the dietary and lifestyle habits associated with tGERS in Vietnamese adults for the first time. These findings will serve as a basis for future studies on the primary prevention and nondrug management of tGERS in Vietnam.

KEYWORDS

gastroesophageal reflux disease, Vietnamese, diet, lifestyles, risk factors

Introduction

Gastroesophageal reflux disease (GERD) is a prevalent upper gastrointestinal disorder worldwide (1). Although it was once thought to be more common in Western countries, its prevalence tends to increase in Asia, particularly in Southeast Asia (2). The present situation is partly explained by dietary and lifestyle changes and an increase in body mass index (BMI), particularly in conjunction with dramatic socioeconomic development in this region (3). Heartburn and regurgitation are the cardinal symptoms of GERD (4). As the definitive diagnosis of GERD requires objective evidence based on endoscopy or functional investigations that are not widely available, the presence of troublesome gastroesophageal reflux symptoms (tGERS) is commonly used to suggest GERD diagnosis in daily practice (4, 5).

Approximately more than two-thirds of GERD cases are nonerosive reflux diseases (2). Among those with endoscopic esophageal injuries, the majority have mild-grade reflux esophagitis, and complications are infrequent, especially in Asian populations (2). Although GERD is not life-threatening, it tends to recur and significantly affects patients' quality of life (6). Therefore, symptom control is considered a priority in GERD management. Dietary and lifestyle modifications are the first-line therapy recommended in all current guidelines, despite low evidence (4, 7, 8). Notably, dietary and lifestyle habits associated with tGERS vary dramatically across populations (9). Routine recommendations to modify various dietary and lifestyle habits can decrease patients' quality of life and compromise their long-term adherence. Therefore, it is necessary to conduct additional studies to assess the risk factors for tGERS and patients' feedback on specific foods and beverages that trigger tGERS in each population. Such data would help physicians with primary prevention strategies and effective counseling.

Vietnam is a developing country in Southeast Asia with a population of nearly 100 million, and it has diverse cuisines. The prevalence of GERD in Vietnam has been increasing over the past 20 years, and it is now one of the most common upper gastrointestinal disorders (10). Although there have been some studies on GERD in Vietnam, most previous studies are hospital-based, and there have been no population-based studies on the association between dietary and lifestyle habits and tGERS. This study aimed to (1) identify dietary and lifestyle factors associated with tGERS and (2) record the feedback of Vietnamese adults with tGERS on the specific dietary and lifestyle habits, foods, and beverages that associated with tGERS.

Materials and methods

Study design and participants

A cross-sectional online survey was conducted via a widely read national online newspaper and Facebook, one of most popular social media platforms in Vietnam, from March 2023 to May 2023. The survey targeted the general Vietnamese population aged 18 years or above. The questionnaire was built on the web platform https://www.surveymonkey.com/. The consent form was presented on the first page of the survey link. By clicking the "Agree" button on this page, the participants agreed to participate and would complete the survey online. Confidentiality and anonymity were maintained, as no individually identifiable information was obtained during the questionnaire.

The survey was carried out using a convenience sample and included any adult participants who completed the survey questionnaire. Responses were excluded from the analysis if the respondents failed to answer all survey questions completely or the completion time was unreliable according to the software's estimated finishing time. In addition, responses with duplicated internet protocol addresses were also excluded.

Ethics approval was obtained for this study (numbered 011/NDGD-HDDD, signed on March 22, 2023).

Development of the survey questionnaire

One senior investigator with more than 20 years of experience in GERD management (DTQ) drafted the questionnaire. Questions about dietary and lifestyle habits and specific foods and beverages that associated with tGERS were developed based on his expertise in managing GERD in Vietnamese. They were also referenced from a recent systematic review of the dietary and lifestyle factors related to tGERS (9). The other four research team members then pretested the initial survey questionnaire to verify the clarity and comprehension of each question. Following this, a pilot test was conducted on 30 individuals experiencing reflux symptoms to examine the survey's reliability. The reliability was assessed using Cronbach's alpha coefficient, which yielded a value of 0.61, indicating an acceptable internal consistency (11). In addition, the content validity of the survey questionnaire was evaluated using the content validity index, resulting in an index of 0.81, which indicates a good content validity (12, 13). Subsequent adjustments were made as necessary after this evaluation. The final survey questionnaire comprised three sections (Supplementary material S1). The first section collected demographic data, including age, sex, height, weight, education level, current place of residence, and current job. The second section gathered information on dietary and lifestyle habits, including staying up late after midnight, skipping breakfast, eating within 2 h before bed, eating beyond fullness, wearing tight clothing, smoking, anxiety, and insomnia. They were rated on a 5-point Likert frequency scale (never, rarely, occasionally, fairly often, and very often). The third section of the questionnaire determined about the presence and characteristics of tGERS. tGERDS include esophageal and extra-esophageal ones. However, the symptoms which supposed to be extra-esophageal are often non-specific and can be caused by various otorhinolaryngological, maxillofacial and respiratory diseases (4, 8). Therefore, in this survey we only address the typical reflux symptoms (i.e., hearburn and regurgitation). Participants who did not have tGERS within the last month finished the survey after answering the first two sections of the questionnaire. Those with tGERS continued to answer questions about tGERS frequency, the timing of symptom occurrence and symptom duration. The participants were also asked about their self-management methods, medical consultations, and adherence to adjusting their diet and lifestyles. These questions were in multiple-choice, single-select format. In addition, the lifestyles, eating habits, foods, and beverages that associated with tGERS were recorded. For these questions, they could choose multiple options that suited them and/or state other options. Within the scope of this study, we only investigated the factors associated with tGERD but not GERD, the disease. Therefore, objective investigations for GERD diagnosis such as upper gastrointestinal endoscopy and 24 h esophageal pH monitoring measurement were not applied.

Statistical methods

All statistical analyses were performed with SPSS 23 (SPSS Inc., Chicago, IL). Categorical variables are presented as numbers and percentages and were compared using Pearson's chi-squared test. Continuous variables were tested for normality using the Kolmogorov–Smirnov test. Those with a nonnormal distribution are presented as the median (upper and lower quartiles) and were compared using the Mann–Whitney U test. Univariate logistic regression was performed to identify factors associated with tGERS. The dietary and lifestyle habits assessed on the Linkert score were divided into two groups for comparison: group 1 (never, rarely, or occasionally) versus group 2 (fairly often or very often). Variables with p values <0.2 in univariate analysis were used for multiple logistic regression analysis. All p values were two-sided, and those less than 0.05 were considered statistically significant.

Results

Participant characteristics

There were 4,400 valid responses from March 2023 to May 2023, including 2050 responses from participants without troublesome reflux symptoms and 2,350 responses from those with at least one troublesome reflux episode within the past month (Figure 1). The participants' demographic characteristics are presented in Table 1.

Dietary and lifestyle habits associated with tGERS

In multivariate analysis, the factors associated with tGERS included eating beyond fullness (odds ratio [OR] 1.383, confidence interval 95% [CI95%] 1.127–1.698), tight clothing (OR 1.627, CI95% 1.256–2.107), stress (OR 1.566, CI95% 1.363–1.800), and insomnia (OR 1.321, CI95% 1.129–1.546) (Table 2).

Characteristics of tGERS and management patterns

The characteristics of tGERS are presented in Table 3. Regurgitation was more prevalent than heartburn (49.3 and 20.3%, respectively). A total of 30.5% (716/2350) of participants experienced both symptoms, and 62.3% (1,465/2350) of them experienced tGERS for more than 1 year.

The participants' management methods for tGERS are presented in Figure 2. Only 1,217 (51.8%) sought medical consultation, while 1,133 (48.2%) chose self-management methods, including dietary and lifestyle modifications, self-medication, or applying both methods (28.4, 12.3, and 21.7%, respectively). A total of 11.3% (137/1217) of participants who sought medical consultation reported not receiving any advice about dietary and lifestyle modification from their physicians. For those who sought medical consultation and received advice on dietary and lifestyle modification, 89.0% (961/1080) reported that tGERS was reduced to a satisfactory level. However, 55.5% (675/1217) reported that they could not follow the advice for the long term (Figure 3).

Dietary and lifestyle habits reported as triggers in subjects with tGERS

The dietary and lifestyle habits that associated with tGERS are shown in Figure 4. Eating beyond fullness was the most frequently reported habit that triggered tGERS (64.6%). Interestingly, although a short meal-to-bed time and staying up late after midnight were not risk factors for tGERS, they were two common factors that triggered

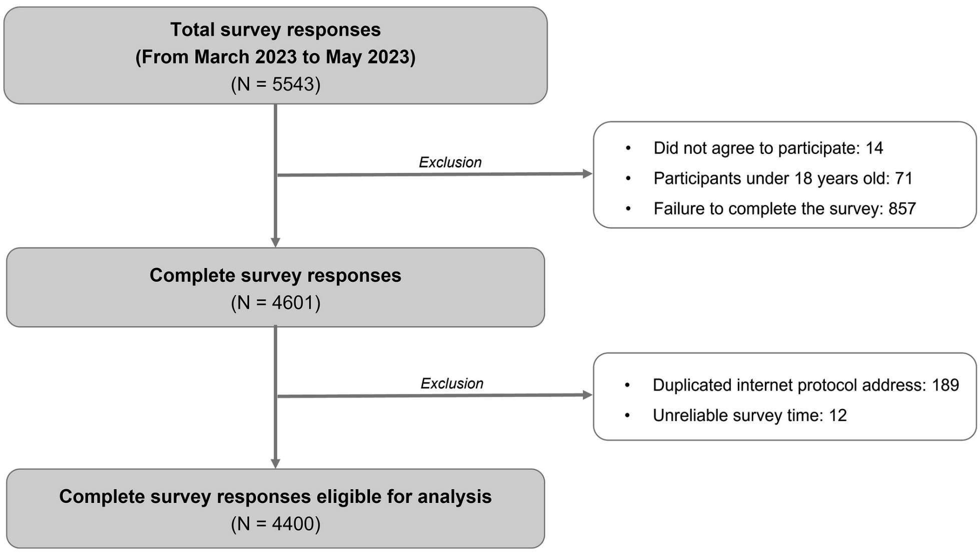

FIGURE 1
Recruitment flowchart of participants in the survey.

TABLE 1 Participants' demographic characteristics.

Characteristics	Participants without tGERS (*N* = 2,050)	Participants with tGERS (*N* = 2,350)	Total (*N* = 4,400)	*p*
Gender				0.185
Male	470 (22.9)	592 (25.2)	1,062 (24.1)	
Female	1,577 (76.9)	1,753 (74.6)	3,330 (75.7)	
Other[a]	3 (0.1)	5 (0.2)	8 (0.2)	
Age				<0.001
18–30	711 (34.7)	679 (28.9)	1,390 (31.6)	
31–40	768 (37.5)	897 (38.2)	1,665 (37.8)	
41–50	344 (16.8)	507 (21.6)	851 (19.3)	
51–60	169 (8.2)	195 (8.3)	364 (8.3)	
Over 60	58 (2.8)	72 (3.1)	130 (3.0)	
Height (cm) (median, IQR)	158 (155–164)	158 (155–164)	158.0 (155–164)	0.900
Weight (kg) (median, IQR)	54 (49–62)	55 (49–63)	55.0 (49–62)	0.008*
BMI (median, IQR)	21.6 (19.9–23.5)	21.9 (20.0–24.1)	21.7 (20.0–23.9)	<0.001*
Level of education				0.012
Primary/secondary/high school	192 (9.4)	217 (9.2)	409 (9.3)	
College/university	1,478 (72.1)	1,613 (68.6)	3,091 (70.2)	
Post-graduate	380 (18.5)	520 (22.1)	900 (20.5)	
Domicile				0.347
Urban	1,670 (81.5)	1940 (82.6)	3,610 (82.0)	
Rural	380 (18.5)	410 (17.4)	790 (18.0)	
Career				0.017
Office work	1,356 (66.1)	1,651 (70.3)	3,007 (68.3)	
Freelance trading/business	241 (11.8)	262 (11.1)	503 (11.4)	
Transportation – delivery	13 (0.6)	24 (1.0)	37 (0.8)	
Agriculture/manual labor	43 (2.1)	43 (1.8)	86 (2.0)	
Student	138 (6.7)	114 (4.9)	252 (5.7)	
Retirement	34 (1.7)	29 (1.2)	63 (1.4)	
Housewife	225 (11.0)	227 (9.7)	452 (10.3)	
Habits (fairly or very often)				
Staying up late after midnight	521 (25.4)	641 (27.3)	1,162 (26.4)	0.162
Skipping meals	361 (17.6)	426 (18.1)	787 (17.9)	0.655
Eating within 2 h before bed	692 (33.8)	855 (36.4)	1,547 (35.2)	0.069
Eating beyond fullness	179 (8.7)	306 (13.0)	485 (11.0)	<0.001
Wearing tight belongings	98 (4.8)	194 (8.3)	292 (6.6)	<0.001
Smoking	58 (2.8)	68 (2.9)	126 (2.9)	0.898
Stress (fairly or very often)	573 (28.0)	935 (39.8)	1,508 (34.3)	<0.001
Insomnia (fairly or very often)	402 (19.6)	649 (27.6)	1,051 (23.9)	<0.001

* Mann–Whitney U test. [a]This "Other" category was provided for those who may identify outside of the binary gender options.

tGERS in symptomatic participants, particularly those with nocturnal reflux symptoms. Regarding foods that triggered tGERS, the top three most common foods were greasy foods (71.9%), sour/spicy soups (64.7%), and citrus fruits (36.0%). In terms of beverages, carbonated soft drinks were at the top tGERS trigger (40.3%), followed by beer (35.7%) and orange juice (30.6%).

Discussion

This is the first study investigating the dietary and lifestyle habits associated with tGERS among the Vietnamese population. A recent systematic review showed that the risk factors for tGERS varied greatly across populations (9). Our study showed that eating beyond fullness,

TABLE 2 Factors associated with troublesome gastroesophageal reflux symptoms in univariate multivariate analysis.

Predictors	Univariable			Multivariable		
	OR	95% CI	*p*	OR	95% CI	*p*
Female	1.135	0.989–1.304	0.072	1.104	0.951–1.281	0.192
Age > 30	1.307	1.150–1.484	<0.001	1.376	1.200–1.578	<0.001
Body mass index	1.037	1.018–1.057	<0.001	1.027	1.006–1.048	0.012
Post-graduate	1.249	1.077–1.448	0.003	1.108	0.949–1.295	0.195
Office work	1.209	1.064–1.373	0.003	1.156	1.011–1.320	0.033
Staying up late after midnight	1.101	0.962–1.259	0.162	1.019	0.880–1.180	0.802
Eating within 2 h before bed	1.122	0.991–1.271	0.069	1.032	0.907–1.175	0.631
Eating beyond fullness	1.565	1.288–1.901	<0.001	1.383	1.127–1.698	0.002
Tight clothing	1.792	1.395–2.302	<0.001	1.627	1.256–2.107	<0.001
Stress	1.703	1.500–1.934	<0.001	1.566	1.363–1.800	<0.001
Insomnia	1.564	1.358–1.802	<0.001	1.321	1.129–1.546	<0.001

wearing tight clothing, stress, and insomnia were significantly associated with tGERS. This is consistent with prior studies in Asia. Meanwhile, a few other factors, which were found to be related to tGERS in previous studies, such as smoking, skipping breakfast, eating within 2 h before going to bed, and staying up late, were not associated with tGERS in our study (14–16). The differences among studies can be due to a variety of factors. First, it may stem from the diversity of diets and lifestyles in differing ethnicities as well as countries worldwide. Second, the definitions and measurements of dietary habits vary widely across studies. In addition, the dietary and lifestyle habits in each individual may change over time. Therefore, it is challenging to assess these factors accurately. Third, recall bias is an additional challenge that makes it difficult to obtain precise measurements.

When considering only the group of participants suffering from tGERS, we found that nearly half of them did not seek medical consultations but opted for various self-management approaches for their symptoms. This finding highlights the need to provide appropriate public health education on the self-management of tGERS. As relapse is the nature of GERD, it requires a long-term management plan in which dietary and lifestyle modifications are the mainstay of treatment (4, 7, 8). Our study showed that more than half of the participants with tGERS could not follow their physicians' advice on dietary and lifestyle modifications. Therefore, identifying exactly the habits that associated with tGERS in a particular population is crucial. This helps avoid unnecessary modifications that may reduce the patient's quality of life and lead to difficulty in their long-term adherence, hence symptom recurrence.

This study found that eating beyond fullness is the most common trigger of tGERS. Interestingly, although the habits of lying down within 2 h after meals and staying up late were not risk factors for tGERS when compared with asymptomatic participants, they were the two most common triggers for the onset of tGERS, especially at night, in symptomatic participants (Figure 4A). In a previous study conducted in Vietnam among pregnant women, we found that a short meal-to-bed time was the most important risk factor for tGERS (17). This is probably explained by a progressive decrease in the pressure of the lower esophageal sphincter and a decrease in gastric motility due to hormonal alterations in pregnancy (18). In another study, we found that subjects with abnormal gastroesophageal flap valves had significantly higher gastroesophageal reflux disease questionnaire (GERDQ) scores than those with normal flap valves (19). Therefore, the difference in findings in our current study may be partly elucidated by the variations in the functional or anatomic antireflux barrier across our participants. With the results of this study, we think that while short meal-to-bed time should be avoided in individuals with tGERS, such advice is probably unnecessary for primary prevention of tGERS in the general population.

TABLE 3 Clinical characteristics of patients with troublesome gastroesophageal reflux symptoms (tGERS) (*N* = 2,350).

Clinical characteristics of troublesome gastroesophageal reflux symptoms (tGERS)	*N* (%)
tGERS	
Regurgitation	1,158 (49.2)
Heartburn	476 (20.3)
Regurgitation and heartburn	716 (30.5)
Frequency of tGERS in the last 7 days (days)	
0	354 (15.1)
1	675 (28.7)
2–3	735 (31.3)
4 or more	586 (24.9)
The time tGERS happened	
During the day	1,089 (46.3)
At night	462 (19.7)
Both during the day and at night	799 (34.0)
First time experience with tGERS	
< 1 month	244 (10.4)
1 to 6 months	321 (13.7)
6 to 12 months	320 (13.6)
2 years to 5 years	800 (34.0)
More than 5 years	665 (28.3)

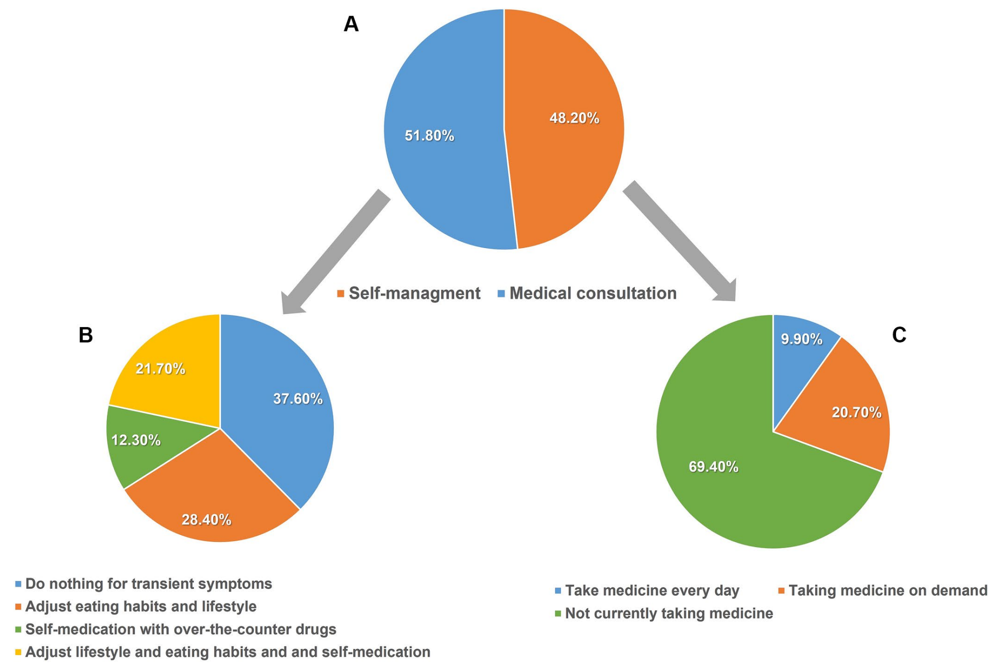

FIGURE 2
Participants' management methods for tGERS. **(A)** Proportions of self-management and medical consultation of participants presenting with tGERS (*N* = 2,350). **(B)** Self-management methods in participants with self-management of tGERS (*N* = 1,133). **(C)** Current medical treatment in participants seeking medical consultation (*N* = 1,217).

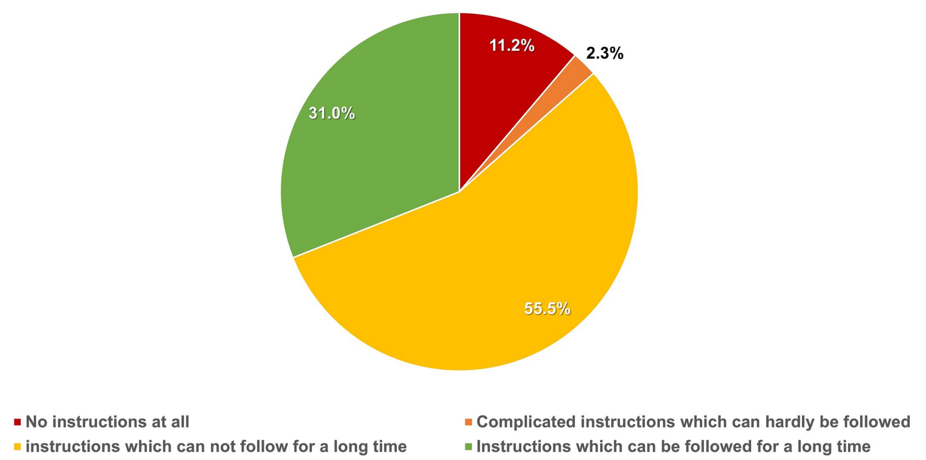

FIGURE 3
Physicians' instructions regarding lifestyle and diet modifications in participants seeking medical consultation (*N* = 1,217).

Our study showed that foods and drinks that trigger tGERS in Vietnamese individuals are diverse. The most common foods were fatty or fried food, spicy soups, citrus fruits and curries, and dishes with coconut milk. For beverages, carbonated soft drinks were the top, followed by beer, alcohol, coffee, and orange juice. This result is similar to previous studies in other populations, but some differences exist. First, previous Asian studies did not find carbonated soft drinks to be associated with tGERS; in our study, this was the most common trigger drink (9). Meanwhile, these beverages were reported to trigger tGERS in many Western populations (9, 20). Second, there are differences in the associations between milk and coffee and tGERS in Asian countries. A study in India showed that occasional milk intake was a risk factor for GERD (21). A recent Taiwanese study reported that coffee added to milk or sugar was not associated with tGERS (22). Both of these studies measured the intake of these beverages in subjects with or without tGERS but were not based on subjective reporting by subjects with tGERS. Although these drinks were not risk factors for tGERS in our study, 26.6% of the participants who had experienced tGERS reported that coffee could trigger tGERS, and the figure for milk was 22.4%. Coffee had little to no effect on the lower esophageal sphincter pressure, but it might have direct irritant effects that trigger tGERS (23, 24). It has also been reported that high-fat milk

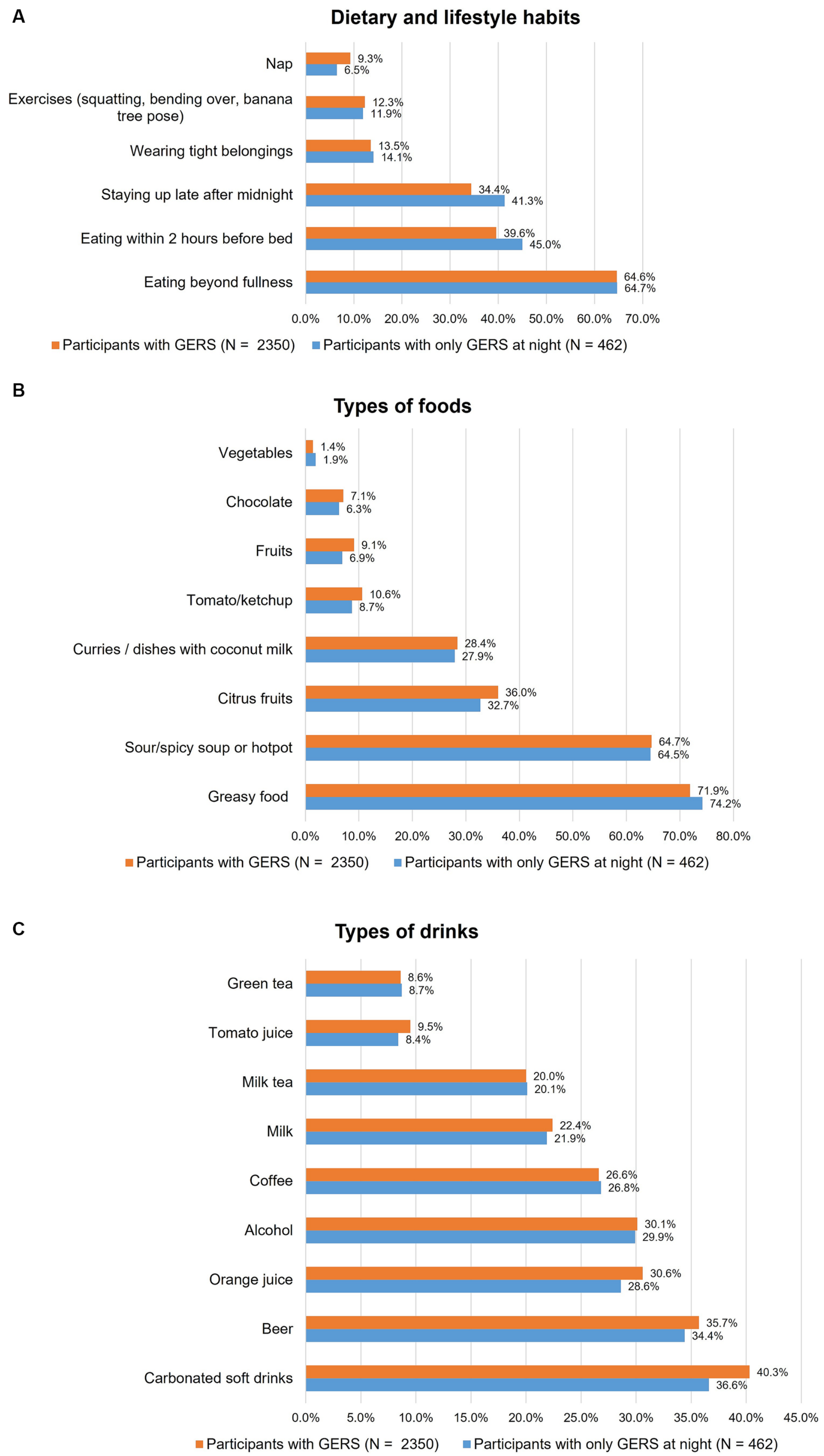

FIGURE 4
Factors that associated with troublesome gastroesophageal reflux symptoms (tGERS) and nocturnal tGERS: **(A)** Dietary and lifestyle habits, **(B)** Food types, and **(C)** Drink types.

and dairy products could worsen heartburn (25). The composition and volume of the drinks as well as the timing of drinking may contribute to the difference across studies.

Our study has some limitations. First, the questionnaire used in this study has not been well validated. Second, the assessment of some variables in the study was subjective depending on the patient's perception, such as tight clothing and eating beyond fullness. In addition, some other factors, such as lack of physical exercise and alcohol consumption, have not been addressed. Third, when analyzing the foods or drinks that could worsen tGERS, the amount ingested, which was certainly related to the symptoms, has not been established. As there are a variety of foods and drinks, it is difficult to measure all in one study due to the overwhelming workload for participants. However, we think that the results of this study will be a premise for more in-depth studies on some of the factors associated with tGERS with more accurate and thorough measurements. Fourth, as the participants were mainly from urban areas, the findings of this study may not represent the entire Vietnamese population.

In conclusion, we reported the dietary and lifestyle habits associated with tGERS in Vietnamese for the first time. The findings of this study will serve as a basis for further studies on the primary prevention and nondrug management of tGERS in Vietnam.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by Ethics Committee in Biomedical Research of Nhan Dan Gia Dinh Hospital, Ho Chi Minh City, Viet Nam (number 011/NDGD-HDDD, signed on March 22, 2023). The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

DQ: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. ML: Data curation, Formal analysis, Investigation, Methodology, Software, Validation, Writing – review & editing. PN: Data curation, Investigation, Writing – review & editing. UV: Investigation, Methodology, Writing – review & editing. CV: Investigation, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fnut.2023.1280511/full#supplementary-material

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Altered dietary behaviour during pregnancy impacts systemic metabolic phenotypes

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Rationale: Evidence suggests consumption of a Mediterranean diet (MD) can positively impact both maternal and offspring health, potentially mediated by a beneficial effect on inflammatory pathways. We aimed to apply metabolic profiling of serum and urine samples to assess differences between women who were stratified into high and low alignment to a MD throughout pregnancy and investigate the relationship of the diet to inflammatory markers.

Methods: From the ORIGINS cohort, 51 pregnant women were stratified for persistent high and low alignment to a MD, based on validated MD questionnaires. ^{1}H Nuclear Magnetic Resonance (NMR) spectroscopy was used to investigate the urine and serum metabolite profiles of these women at 36 weeks of pregnancy. The relationship between diet, metabolite profile and inflammatory status was investigated.

Results: There were clear differences in both the food choice and metabolic profiles of women who self-reported concordance to a high (HMDA) and low (LMDA) Mediterranean diet, indicating that alignment with the MD was associated with a specific metabolic phenotype during pregnancy. Reduced meat intake and higher vegetable intake in the HMDA group was supported by increased levels of urinary hippurate ($p = 0.044$) and lower creatine ($p = 0.047$) levels. Serum concentrations of the NMR spectroscopic inflammatory biomarkers GlycA ($p = 0.020$) and GlycB ($p = 0.016$) were significantly lower in the HDMA group and were negatively associated with serum acetate, histidine and isoleucine ($p < 0.05$) suggesting a greater level of plant-based nutrients in the diet. Serum branched chain and aromatic amino acids were positively associated with the HMDA group while both urinary and serum creatine, urine creatinine and dimethylamine were positively associated with the LMDA group.

Conclusion: Metabolic phenotypes of pregnant women who had a high alignment with the MD were significantly different from pregnant women who had a poor alignment with the MD. The metabolite profiles aligned with reported food intake. Differences were most significant biomarkers of systemic inflammation and selected gut-microbial metabolites. This research expands our understanding of the mechanisms driving health outcomes during the perinatal period and provides additional biomarkers for investigation in pregnant women to assess potential health risks.

KEYWORDS

Mediterranean diet, pregnancy, metabolic phenotype, inflammation, α-1-acid glycoprotein, hippurate, fibre

1 Introduction

Previous research into foetal programming has demonstrated that maternal lifestyle choices and exposures during the gestational period have a lasting impact on the offspring, in term of its association with chronic health conditions in later life, including neurodevelopment, diabetes and cardiovascular disease (1, 2).

The maternal diet is a modifiable lifestyle factor that can have a direct impact on the health of the developing foetus. Low quality diet can lead to poor growth rates and higher rates of birth complications and later life chronic health conditions (3, 4). An increasing interest in the impact of maternal nutrition on lifelong health of the offspring has led to a range of dietary studies either assessing the impact of single foods/nutrients or evaluating dietary patterns during pregnancy. For example, consumption of fish during pregnancy has been associated with benefits in neurocognitive development in the offspring (5), while an association between lower birth weight and diets that are high in processed foods, saturated fats and sugars has been found (6). As nutrients are not consumed in isolation, and the impact of the food matrix cannot be understated, studying the impact of whole diet is more appropriate to community-based interpretation of research outcomes.

The Mediterranean diet is one of the most well-studied diets and numerous investigations have assessed the impact of consuming this diet during pregnancy on birth or childhood development outcomes. It is generally accepted that consumption of a Mediterranean diet during pregnancy is associated with benefits to both the mother and offspring, particularly with reference to systemic inflammation (7, 8). Adherence to the Mediterranean diet during pregnancy has been linked to reduced likelihood of gestational diabetes (9), reduced lipid oxidation and DNA damage in mothers (10), and a reduction in preterm births (6). In the offspring, maternal adherence to consumption of a Mediterranean diet during pregnancy was associated with lower rates of overweight and reduced body fat percentage, including waist circumference (11), improved cognitive and executive function in offspring (9), reduced incidence of atopic diseases (12) beneficial differences in DNA methylation and microRNAs (13) and a lower offspring systolic and diastolic blood pressure (14). Some studies have assessed alignment with a MD, including during pregnancy. Previous studies investigating the impact of the MD during pregnancy have shown that although increasing MD alignment was not associated with a significant change in BMI, it was associated with lower pregnancy weight gain (15, 16). Other studies have demonstrated that greater adherence to the Mediterranean dietary pattern during the first trimester of pregnancy may be favourably associated with communication abilities at 6-month aged infants (17) as well as lower risk of adverse pregnancy outcomes, with evidence of a dose–response association (18). However, despite the general consensus of the benefits of a maternal Mediterranean diet, several studies have not found associations between maternal diet and infant health (19), highlighting the challenges in assessing dietary impact on foetal programming.

One potential mechanism of foetal programming is through maternal systemic inflammation levels. During pregnancy inflammation naturally increases from the time of blastocyst implantation and escalates during parturition (20) and pregnancies with complications such as preeclampsia and gestational diabetes show raised levels of the inflammatory marker C-Reactive Protein (CRP) compared to pregnancies without complications (21). Plasma acute phase glycoprotein glycans (GlycA and GlycB), arising from N-acetylglucosamine/galactosamine and neuraminic (or sialic) acid chains, can be measured using ^{1}H nuclear magnetic resonance (NMR) spectroscopy (22, 23) and have been shown to be more reliable than high sensitivity CRP (24). These signals are associated with acute phase proteins such as α-1-acid glycoprotein, transferrin, haptoglobin, serotransferrin and α-1-antitrypsin (25). Studies in other pregnancy cohorts have shown a direct association between GlycA and BMI (26) and gestational diabetes (27). It is unknown whether reducing inflammation during pregnancy can result in improved pregnancy outcomes.

Diets which are high in saturated fats, meats, processed and sugary foods, as well as being low in whole grains, fruits and vegetables, and healthy fats, tend to be associated with systemic inflammation (28, 29). Conversely, plant-based diets, such as the Mediterranean Diet (MD), high in whole grains and healthy fats such as avocado and olive oil, tend to have lower levels of inflammatory metabolites (29). This style of eating has been adopted as an anti-inflammatory dietary tool in general dietary practice (30). However, the mechanisms by which adherence to a Mediterranean diet achieves this anti-inflammatory effect are not yet fully understood.

Metabolic phenotyping, using high resolution spectroscopic technologies, has proven to be a useful tool in dietary assessment (31–33). It has been used to assess compliance through dietary

Abbreviations: BCAA, Branched Chain Amino Acid; FFQ, Food Frequency Questionnaire; HMDA, High Mediterranean Diet Alignment; LMDA, Low Mediterranean Diet Alignment; TMAO, Trimethylamine-*N*-Oxide; MD, Mediterranean Diet; CRP, C-Reactive Protein; NMR, Nuclear Magnetic Resonance; SPC, Supramolecular Phospholipid Composite; MDI, Mediterranean Dietary Index; TSP, Trimethylsilylpropionic acid; PCA, Principal Component Analysis; OPLS-DA, Orthogonal Projection to Latent Structures-Discriminant Analysis; STOCSY, Statistical Correlation Spectroscopy; COMPASS, Combined Multi-block Principal components Analysis with Statistical Spectroscopy.

metabolite biomarkers and to elucidate metabolic profiles associated with consumption of a Mediterranean diet, either as a lifestyle choice (34) or as a tool for reducing cardiometabolic disease risk (35). Here, we apply ^{1}H nuclear magnetic resonance (NMR) spectroscopy to assess differences between women who were stratified into high and low alignment with a Mediterranean diet throughout their pregnancy and analyse the spectral profiles with respect to foods and food groups identified from Food Frequency Questionnaires (FFQ's). We anticipate significant metabolic differences between those in a high alignment and low alignment with the MD, with those highly aligned to the MD exhibiting lower levels of inflammatory biomarkers.

2 Materials and methods

2.1 Patient enrolment and sample collection

The BIOMOOD study was established retrospectively as a subsidiary of the ORIGINS project, a longitudinal study of family health outcomes, commencing during pregnancy. The study selection criteria and collection protocol are provided as a schematic (Figure 1A) including food data and sample collection details (Figure 1B). The study was approved by the ORIGINS Scientific Committee and Project Management Group (Application ID: ND01905) and Ramsay Health Care Human Research Ethics Committee (Protocol number: ND01905). Sample collection methods have been described in detail elsewhere (36) but include the collection of dietary information socio-demographic and anthropomeric data, and urine and serum samples. Briefly, pregnant women who attended Joondalup Health Campus in Australia for antenatal care were invited to participate in the ORIGINS project at approximately 18 weeks gestation. Initial samples were collected at either 20 weeks or 28 weeks of gestation, dependent on their presentation to the antenatal clinic, and then again at 36 weeks. Participants completed several questionnaires, including a validated Mediterranean Diet Questionnaire (MDQ) (37) and FFQ. The FFQ used was the Australian Eating Survey (38). The MDQ is a validated 14-point assessment which focusses on olive oil use, wine intake, legume consumption, fish intake, and the consumption of chicken over red meats, and has previously been used to assess diet in pregnant women (15). Since alcohol intake is discouraged during pregnancy, this item was excluded from the MDQ scale (see Supplementary Table S1). Items were scored simply as meeting requirement, or not meeting requirement, and therefore the range of potential scores for the MDQ is between 0 and 13. Only participants who completed at least two MDI assessments during their pregnancy were included in the current study.

Participants were assigned to groups dependent on their MDI scores at week 20 and 28 and were stratified according to Ashwin et al., whereby low alignment (LMDA) was considered a score between 0 and 4, medium alignment between 5 and 7 and high alignment (HMDA) between 8 and 13 (39). The inclusion criteria were such that no individual was included if the MDI score deviated more than 2 points between the collections, therefore we accepted participants where at least one of the MDI values met the criteria for low or high alignment with the Mediterranean Diet. Participants were also excluded if they did not have biological samples available for analysis, were on antibiotics at any time during their pregnancy, reported using antidepressants or anti-anxiety medication or had a pre-pregnancy BMI of over 40 kg/m^2. A total of 52 women were determined to be eligible for the BIOMOOD study, with one participant excluded due to dropout, leaving 26 participants assigned to the HMDA group, and 25 assigned to the LMDA group (demographics provided in Table 1). Participants provided urine and blood (serum collected into lithium heparin tubes). Samples were aliquoted to allow for multiple analyses and stored at −80°C at the Telethon Kids Institute in Western Australia as part of their ongoing BioBank. A serum and urine aliquot for each participant was transferred frozen to the Australian National Phenome Centre, where they were again stored at −80°C prior to analysis.

2.2 Sample preparation

In preparation for analysis, the serum samples were thawed at room temperature for 30 min, before undergoing centrifugation at 13,000 g for 10 min at 4°C. Samples were prepared in SampleJet™ NMR tubes of 5 mm outer diameter using a standard preparation method (40) of 300 μL of serum mixed with 300 μL phosphate buffer (75 mM Na_2HPO_4, 2 mM NaN_3, 4.6 mM sodium trimethylsilyl propionate-[2,2,3,3-$^2H_4$] (TSP) in H_2O/D_2O 4:1, pH 7.4 ± 0.1).

Similarly, urine was thawed at room temperature for 30 min, before undergoing centrifugation at 13,000 g for 10 min at 4°C. Samples were prepared in SampleJet™ NMR tubes of 5 mm outer diameter using a standard preparation method (40) of 540 μL of urine mixed with 60 μL phosphate buffer (1.5 mM KH_2PO_4, 2 mM NaN_3, 0.1% TSP, pH 7.4 ± 0.1).

2.2.1 Acquisition and preprocessing of ^{1}H NMR serum spectra

A 600 MHz Bruker Avance III HD spectrometer equipped with a 5 mm BBI probe, utilising a Bruker SampleJet™ robot cooling system set to 5°C, was used to perform NMR spectroscopic analyses. Prior to the analysis, a full quantitative calibration was completed using a previously described protocol (40). Three experiments were performed in automation mode for each serum sample, taking a total experimental acquisition time of 12 min. These experiments were a 1D experiment with solvent pre-saturation (32 scans, 98 K data points, spectral width of 30 ppm), a spin-echo experiment (32 scans, 74 K data points, spectral width of 20 ppm) and a diffusion-relaxation edited experiment (JEDI-PGPE: 64 scans, 98 K data points, spectral width of 30 ppm) (41). For both urine and serum, the standard 1D experiment was acquired using the Bruker In Vitro Diagnostics Research (IVDr) protocol to allow for quantification. All data were processed in automation using Bruker Topspin 3.6.2 and ICON NMR to achieve phase correction and calibration to TSP (δ 0). Bruker IVDr Quantification in Serum/Serum B.I.Quant-PS provided data on 25 low molecular weight metabolite concentrations (acetic acid, acetoacetic acid, acetone, alanine, citric acid, creatine, creatinine, formic acid, glucose, glutamic acid, glutamine, glycine, histidine, D-3-hydroxybutyric acid, isoleucine, lactic acid, leucine, lysine, N,N-dimethylglycine, methionine, phenylalanine, pyruvic acid, trimethylamine-*N*-oxide, tyrosine, and valine) and B.I.LISA provided 112 lipoprotein parameters. For serum a CPMG spin-echo experiment (42), which performs differential T2 relaxation to filter the spectrum, was used to remove signals from large molecules with fast relaxing protons and the JEDI-PGPE employed diffusion and relaxation spectral editing to enhance the signals from

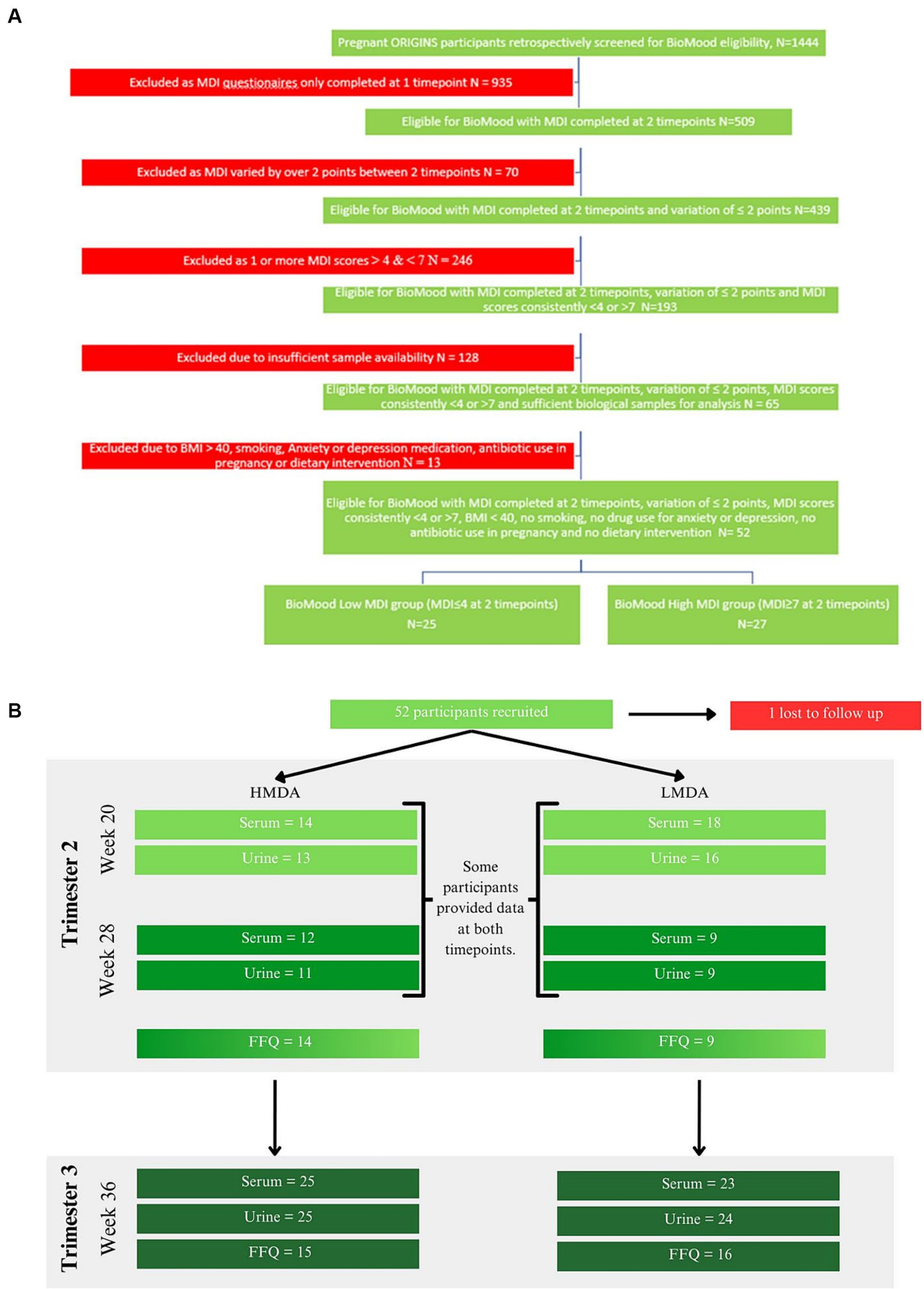

FIGURE 1
(A) Study selection criteria and collection protocol, **(B)** food data and sample collection cohorts for each hospital visit timepoint.

the inflammatory panel (GlycA, GlycB, and the supramolecular phospholipid composite (SPC) peak) (41).

Upon completion of spectral acquisition, processing using in house developed R scripts included: division of spectral data points for each of the three NMR experiments (standard 1D with water suppression, spin echo, JEDI-PGPE) by the eretic factor (electronic quantitation standard) (42). Both the standard 1D and CPMG NMR spectral datasets were calibrated to the α-anomeric proton signal of glucose at δ 5.23, while no calibration was necessary for the JEDI experiments. Spectral regions corresponding to the residual water resonance signal (δ 4.60–4.85) or predominantly noise ($\delta < 0.5$ and $\delta > 9.5$) were excluded from analyses and the spin-echo spectrum was corrected for baseline distortions using an asymmetric least squares routine using the R package metabom8 (version 1.0.0), available from GitHub.[1] To estimate the signal intensities of GlycA and GlycB peaks, spectral regions were integrated (GlycA: δ 2.03; GlycB: δ 2.07) from the JEDI-PGPE spectra. The GlycA signal (δ 2.03) is a composite of

1 github.com/tkimhofer/metabom8

TABLE 1 Demographic information of participants in the BIOMOOD study.

	Low Mediterranean diet alignment (n = 25)	High Mediterranean diet alignment (n = 26)	p-value
Age in years (SD)	31.28 (3.75)	32.92 (3,93)	0.133**
Pre-pregnancy weight, kg (SD)	74.40 (11.57)	70.54 (15.13)	0.312**
Pre-pregnancy BMI, kg/m^2 (SD)*	28.00 (4.17)	25.28 (5.43)	0.056**
Parity (%)			0.331***
0	20.00 (80.00%)	16.00 (61.54%)	
1	4.00 (16.00%)	7.00 (26.92%)	
2	1.00 (4.00%)	3.00 (11.54%)	
Education (%)			0.689***
Year 10	1.00 (4.00%)	0.00 (0.00%)	
Year 12	4.00 (16.00%)	1.00 (3.85%)	
Trade	2.00 (8.00%)	3.00 (11.54%)	
Bachelor	10.00 (40.00%)	12.00 (46.15%)	
Postgrad	6.00 (24.00%)	8.00 (30.77%)	
Other	2.00 (8.00%)	2.00 (7.69%)	
Employment (%)			0.629***
Not seeking work	0.00 (0.00%)	1.00 (3.85%)	
Home duties	3.00 (12.00%)	4.00 (15.38%)	
Periodic work	0.00 (0.00%)	1.00 (3.85%)	
Casual work	1.00 (4.00%)	2.00 (7.69%)	
Part time work	7.00 (28.00%)	3.00 (11.54%)	
Full time work	14.00 (56.00%)	14.00 (53.85%)	
Other	0.00 (0.00%)	1.00 (3.85%)	

Values reported as mean with (standard deviation) or number of participants (percentage). * Missing BMI data for two participants (one in HMDA and one in LDMA). p-values reported for ** two-sided independent t-test and *** two-sided Fisher's test.

N-acetyl signals from five proteins: α-1-acid glycoprotein (major component), α-1-antitrypsin, α-1-antichymotrypsin, haptoglobin, and transferrin. The GlycB acetyl signal (δ 2.07) arises from glycoprotein N-acetylneuraminidino groups (41). The region containing the supramolecular phospholipids composite peak (SPC) was also integrated from the JEDI-PGPE spectra (δ 3.20–3.30). This composite peak was further subdivided into 3 markers, SPC1 (δ 3.2–3.236) corresponding predominantly to small HDL (HDL4) phospholipids, SPC2 (δ 3.236–3.252) corresponding to larger HDL phospholipid particles (HDL1-3) and SPC3 (δ 3.252–3.3) corresponding to LDL phospholipids (43). In addition, the sum of Glyc (Glyc A + Glyc B) and SPC (SPC1, SPC2, and SPC3) ratios were calculated of Glyc A /Glyc and SPC (total) / Glyc (total).

2.2.2 ^{1}H NMR spectroscopy data acquisition and processing parameters for urine samples

The same spectroscopic platform (see Section 2.2.1) was used to record spectra of urine samples. Prior to analysis, a full quantitative calibration was completed using a previously described protocol (40). A standard 1D experiment, acquired using the Bruker In Vitro Diagnostics Research (IVDr) methods, was performed in automation mode for each urine sample using solvent pre-saturation, taking a total experimental acquisition time of 4 min; 32 scans; 65 K data points; spectral width of 20 Hz. All spectra were processed in automation using Bruker Topspin 3.6.2 and ICON NMR to achieve phase and baseline correction, and calibration to TSP (δ = 0).

Further processing was undertaken using in house developed R scripts: For each spectrum, the regions corresponding to the residual water resonance signal (δ 4.75–4.85) or predominantly noise (δ < 0.5 and δ > 9.5) were excluded and each data point was divided by the eretic factor to obtain quantitative values. The concentrations of urinary metabolites associated with alignment to the Mediterranean Diet were obtained either from the Bruker IVDr Quantification procedure B.I.Quant-UR b or an in-house curve resolution algorithm in the cases where the metabolite was not found in the B.I.Quant-UR b data. Combined Multi-block Principal components Analysis with Statistical Spectroscopy (COMPASS) (44) was used to estimate the concentrations of 4-cresol sulfate (δ = 2.35) and phenylacetylglutamine (PAG) (δ = 7.36–7.45) and expand the B.I.Quant-UR b panel.

2.3 Statistical analysis

All computation and data visualisation were performed using R (4.1.0) and RStudio IDE. Comparison of cohort demographics between the two diet groups was assessed using two-sided independent t-test (continuous variables) or two-sided Fisher's test (categorical variables) (Table 1). Multivariate modelling was achieved using the open-source

R package metabom8 (release 1.0.0), available from GitHub (see text footnote 1) and Combined Multi-block Principal components Analysis with Statistical Spectroscopy (COMPASS) was achieved using the scripts openly available (41). Principal Component Analysis (PCA) and Orthogonal projection to latent structures-discriminant analysis (OPLS-DA) (45) were used to model variance in the data and to extract discriminating features between the two diet groups. Metabolite identification was undertaken using statistical correlation spectroscopy (STOCSY) (46), by comparison with reference standards found either in house or in databases including HMDB (47) and by using 2-dimensional NMR experiments including COSY, TOCSY, HMQC and J-Resolved carried out on representative samples to confirm tentative assignments from databases (48).

Based on the OPLS-DA model, the concentrations of nine low molecular weight metabolites were used for further univariate analysis (arginine, citric acid, creatine, creatinine, dimethylamine, glycine, hippuric acid, *N,N*-dimethylglycine, and trigonelline).

Dietary data obtained during the second trimester were available for 23 participants (9 LMDA and 14 HMDA). At the third trimester, dietary data were recorded for 31 participants (16 LMDA and 15 HMDA). Seven participants in each diet group had data available at both timepoints. PCA using Pareto scaling, eruption plots and OPLS was performed with 83 dietary components at both time points. For multivariate analysis dietary components were grouped together into related food groups (see Supplementary Table S2 for full list of dietary items). A final set of 40 variables were identified, which included the MDI score obtained at weeks 20 or 28 and at week 36, the amount of fibre expressed as grams per 1,000 kJ, 24 food frequency variables, ten variables related to percentage of energy, and three variables related to percentage of fat intake (see Supplementary Table S3 for further details). Spearman pairwise rank correlation analysis was used to investigate relationships between dietary components as well as between dietary components and metabolites. Whereas all participants attended the visit at 36 weeks in trimester 3, with the exception of a few participants, attendance in the second trimester was either at week 20 or 28. While data from both available trimesters were investigated, associations between diet and metabolic profiles were drawn solely from trimester three data. However, for the FFQ data we explored the consistency of the reported data across both trimesters to ascertain the reproducibility of dietary reporting (Figure 2).

Post-partum outcomes were not assessed as part of the BIOMOOD study.

3 Results

3.1 Cohort characteristics

In the group of 51 pregnant women enrolled in the study, the mean age was 32.12 (SD 3.89) years, with an average pre-pregnancy BMI of 26.62 kg/m^2 (SD 4.99 kg/m^2). No significant differences were noted between the demographics of the two groups (Table 1).

3.2 Dietary analysis

Of the 51 women for whom urine and serum samples were available, 41 provided food frequency questionnaires (FFQ's) for at least one timepoint, from which the estimated intake of total energy and nutrients was obtained. Nutrients were expressed as a percentage of total energy and dietary fibre per 1,000 kJ. As these participants either provided their initial biological sample at week 20 or week 28, the sample cohort for these time points was significantly reduced for both groups. As such, we decided to focus the nutritional analysis on the week 36 timepoint, for which 31 participants had provided dietary data. Figure 2 demonstrates the dietary differences between the groups in the second and third trimesters, with further details in Supplementary Tables S4A,B. As the dietary patterns remained consistent between the two time points, this supported our decision to use the more complete dietary data from the week 36 timepoint.

Principal Component Analysis (PCA) is an unsupervised multivariate method that finds the largest degrees of variance in a dataset. It is therefore suitable for evaluating the overall data quality, identifying outliers or of unexpected sources of variance, and confirming the presence of trends in the data, i.e., separation between groups. Such a trend can be observed in the PCA scores depicted in Figures 2A,D, where the HMDA and LMDA groups naturally separate. One limitation of PCA is that it cannot be used to model a specific source of variance, such as the one of interest (diet group) in our experimental design. In contrast, Projections to Latent Structures (PLS) is a family of supervised methods that require prior knowledge of categories or groups to model a single degree of variance. Once a model is trained and validated its scores will reflect the selected variance (predicted) on the x dimension, while unrelated source of variance (orthogonal) will be displayed on the y-axis. Therefore, Orthogonal Projection to Latent Structures Discriminant Analysis (OPLS-DA) models were calculated for alignment to the Mediterranean diet using the participants with available FFQ data. The resulting scores demonstrated clear separation between the two dietary alignment groups (Figures 2C,F) (Trimester 2, $R^2X = 0.21$, CV-AUROC = 0.96; Trimester 3, $R^2X = 0.17$, CV-AUROC = 0.82). The model loadings were used to identify the variables that contributed most to explaining the score for each individual participant. An eruption plot of the FFQ's or "nutrigram" was created from the loadings to contrast univariate non-parametric pair testing and Cliff's deltas (Figures 2B,E). The nutrigram shows that, as expected, participants in the HMDA group were consuming the anticipated foods based on a typical Mediterranean diet profile (Figures 2C,F). The variables with a Cliff's delta statistic $-0.4 > cd > 0.4$ are listed for both trimesters in Supplementary Tables S5A,B, and are color coded according to food group. A significantly higher intake of vegetables was evident for the HMDA group overall, especially green vegetables such as celery, cabbage and spinach, and higher intakes of fresh fish and nuts. Comparatively, the LMDA group demonstrated a diet driven by highly processed foods such as muffins and takeaway foods, and especially soft drink consumption (Figure 2E and Supplementary Tables S4A,B). Dietary elements such as overall dairy intake, canned and dried fruits and eggs did not contribute to the difference between the two dietary groups. These dietary patterns are consistent with the anticipated dietary intakes for people based on their level of alignment with the Mediterranean diet and the patterns remained relatively consistent between trimester 2 and trimester 3, supporting the analysis, which demonstrated minimal dietary change over the course of gestation.

Correlation maps of the dietary variables based on all participants (Supplementary Figure S1) showed expected relationships between

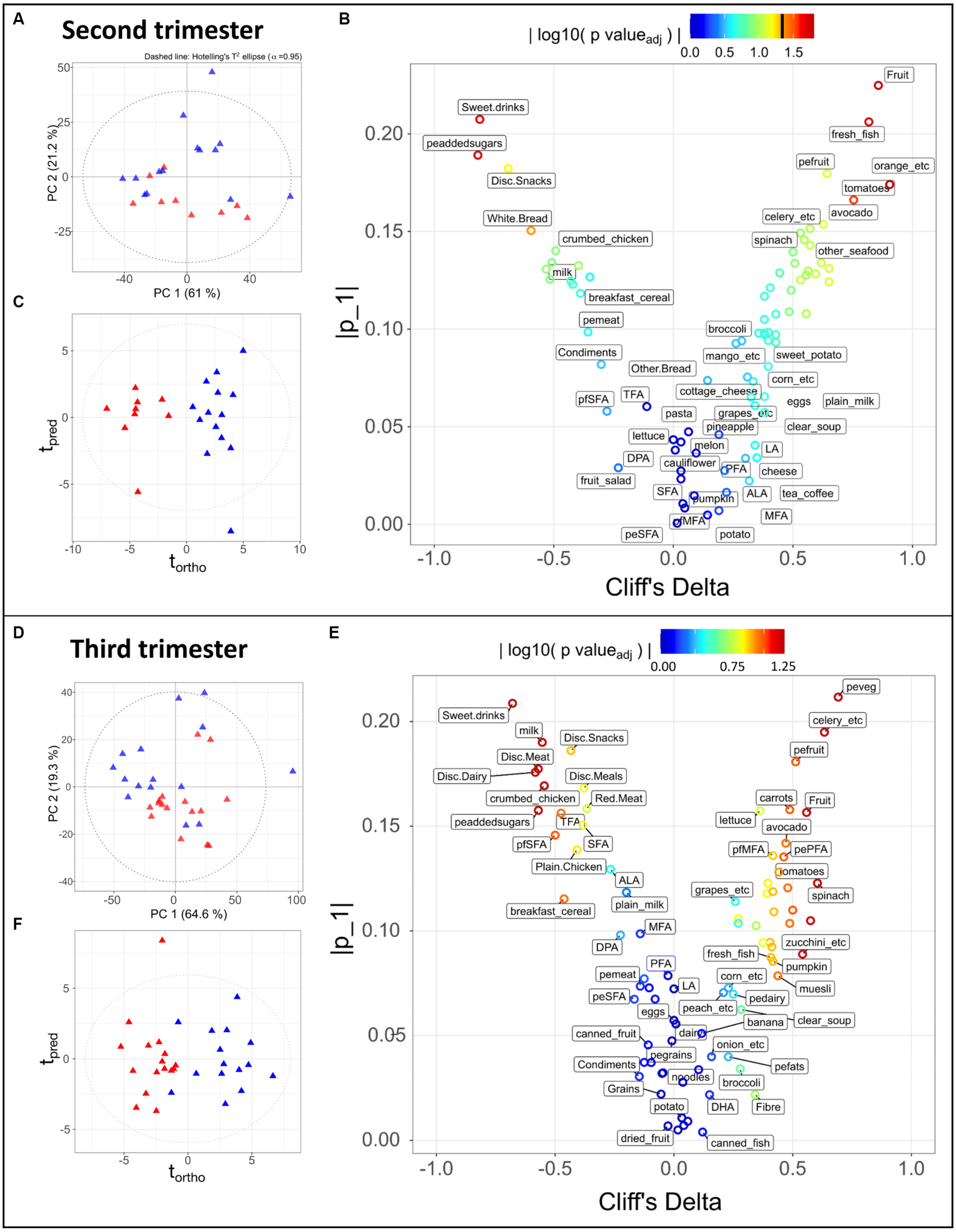

FIGURE 2

Statistical analysis of 83 dietary components obtained during the second trimester **(A–C)** for 9 LMDA, 14 HMDA participants; and third trimester **(D–F)** for 16 LMDA, 15 HMDA participants. **(A,D)** PCA scores plot of dietary components, classified by dietary adherence (low-red triangles or high-blue triangles), **(B,E)** OPLS-DA scores plots of dietary components, classified by dietary adherence (low-red triangles or high-blue triangles), **(C,F)** Eruption plots of dietary components, demonstrating the driving components in the model differentiating the two dietary adherence groups. For figures **(B,E)**, the color represents the magnitude of the reconstructed loadings, the vertical axis represents the univariate statistics, while the Cliff's delta is represented on the *x*-axis. This latter is used as non-parametric estimator of the effect size, with values outside of the ±1 interval representing samples

(Continued)

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FIGURE 2 (Continued)
with no overlap. pefats, percentage of energy from fats; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; DPA, docosapentaenoic acid; ALA, alpha-linolenic acid; LA, linoleic acid; MFA, monounsaturated fatty acids; peMFA, percentge of energy from monounsaturated fatty acids; peaddedsugars, percentage of energy from added sugars; PFA, polyunsturated fatty acids; pePFA, percentage of energy from polyunsaturated fatty acids; pfpolyfats, percentage of fat from polyunsaturated fat; pfSFA, percentage of fats coming from saturated fatty acids; peSFA, percentage of energy from saturated fatty acids; SFA, saturate fatty acids; TFA, transaturated fatty acids; pemeat, percentage of energy from meat; pefruit, precentage of energy from fruit; peveg, percentage of energy from vegetables; pedairy, percentage of energy from dairy; pegrains, percentage of energy from grains; Disc, discretionary.

food components. For example, added sugars expressed as percentage of energy intake significantly correlated with sweet drinks, discretionary snacks (such as soft drink, juice, cordials, potato chips, jelly, and chocolate etc.) and inversely correlated with fresh fruits; fresh vegetables were correlated with vegetables and percentage energy and starch; monounsaturated dietary fats correlated with saturated dietary fats; and nuts and legumes correlated with vegetables.

3.3 Alignment to Mediterranean diet is reflected in the serum NMR profiles

Serum samples taken at 36 weeks were available for 48 participants (23 LMDA, 25 HMDA). The CPMG/spin-echo serum ^{1}H NMR profiles of the HMDA and LMDA group demonstrated a number of systematic differences in the OPLS-DA models (Figure 3A), which was driven by significantly higher concentrations of the amino acids: valine, alanine, glutamine and tyrosine, as well as increased levels of acetone and acetate for the HMDA group (Figure 3B). Conversely glycine was present in higher concentrations in the LMDA group. Histidine and methylhistidines also differed between groups but this was not apparent from the OPLS-DA loadings due to the high degree of chemical shift. Standard comparison of the spectra showed these histidines to be present in relatively higher concentrations in the HMDA group and histidine was correlated with foods associated with HMDA in the metabolite-food plot (see Supplementary Figure S2).

Similarly, the two dietary groups were completely differentiated in the models using the JEDI-PGPE spectra that enhances the contribution from the *N*-acetylated glycoproteins and Supramolecular Phospholipid Composite Peaks (SPC) (CV-AUROC = 0.68) (Figure 3C). These differences were almost entirely driven by the stronger presence of GlycA (p-value = 0.020) and GlycB (Figures 3D,E; p-value = 0.016) in the LMDA group. The composite supramolecular phosphocholine peak SPC (δ 3.20–3.30), was not significantly different between the two diets but showed a trend towards higher concentrations in the HMDA score.

Systematic differences between the two dietary alignment groups were also visible in the OPLS-DA model calculated using the quantified metabolites extracted using the IVDr procedure (Figure 3F). Here the main differences in metabolite composition were visualised using an eruption plot (Figure 3G). The HMDA group was characterised by *N,N*–dimethylglycine, glutamine and acetate for the HMDA group, whereas creatine was significantly higher in the LMDA group. Although the quantified branched chain amino acids were not significantly different between groups, there was a trend towards higher levels in the HMDA group, matching the results established using the multivariate OPLS-DA analysis of the spectral profiles. Similarly, alanine and tyrosine were associated with the HMDA group but did not achieve significance in the univariate analysis after adjusting for multiple testing.

3.4 Differential urine ^{1}H NMR profiles between HMDA and LMDA groups

A differential urinary signature was found for the HMDA versus the LMDA group based on the OPLS-DA model scores and loadings plot (Figures 4A,B respectively) built from the ^{1}H NMR spectra of urine samples obtained at 36 weeks of gestation (23 LMDA, 24 HMDA) yielding a CV-AUROC of 0.84. The loadings coefficients for the model (Figure 4B) indicated that hippurate dominated the separation between the two dietary groups, being present in significantly higher concentrations in the urine of those individuals who were highly adherent to the Mediterranean diet. Analysis of the quantified low molecular weight metabolites provided by the IVDr method (Figure 4C,D and Supplementary Figure S4) also supported increased hippurate in the HMDA, as well as trigonelline. Like the serum profiles, creatine was again noted as being present in significantly higher concentrations in those who were least adherent to the Mediterranean diet (Figure 4E). Sarcosine, alanine, and citrate were additionally identified as being present in higher concentrations in the LMDA group, although the difference was not significant due to a high degree of inter-individual variation (Supplementary Figures S5, S6 and Figures 4C,E,F).

3.5 Metabolite and diet-metabolite correlations underlying the differences in alignment with a Mediterranean diet pattern

Correlations between individual metabolites are highlighted in Figure 5 (see Supplementary Figure S7 for metabolite correlation matrices stratified according to diet). A number of direct correlations were observed between metabolites that were related by compound class or pathway. For example, GlycA with GlycB for both dietary patterns ($p < 0.001$); SPC2 with SPC3 ($p < 0.001$); serum branched chain amino acids (BCAAs) (valine, leucine, isoleucine) with tyrosine and serum glucose with pyruvate ($p < 0.001$). In the LMDA group, a strongly significant anti-correlation was found between lysine (serum) and the two GlycA and GlycB (serum) ($p < 0.05$).

The three calculated SPC components, although part of the same composite phospholipid peak, showed a different correlation structure with other serum and urinary metabolites. SPC1 correlated with the total SPC concentration but showed little or no correlation with SPC 2 and SPC3, which were strongly correlated with each other ($p < 0.01$) (Figure 5). This is consistent with the lipoproteins that

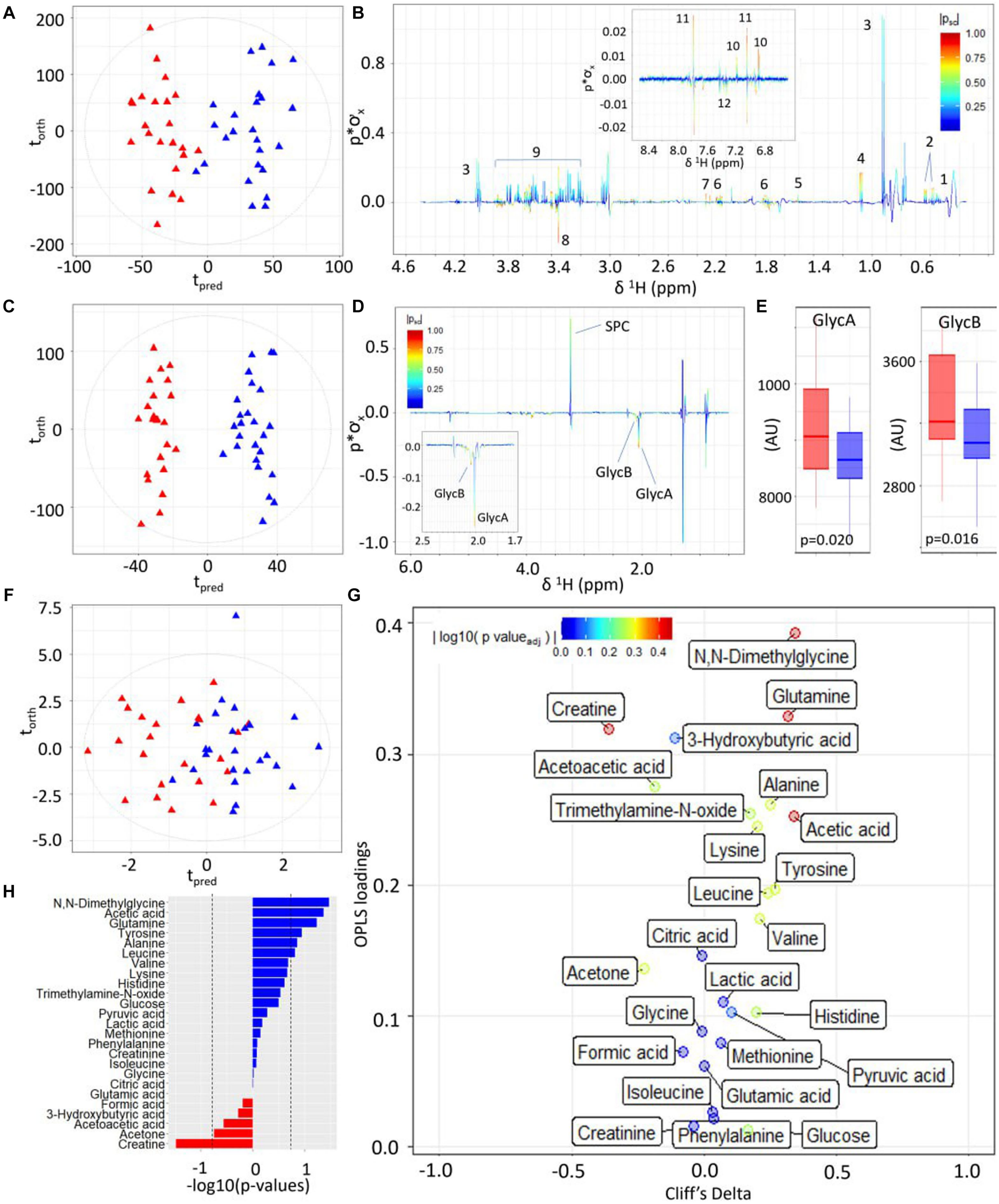

FIGURE 3
Statistical comparison of third-trimester serum metabolite profiles of participants with high versus low alignment to the Mediterranean Diet showing higher concentrations of inflammatory-associated metabolites and lower concentrations of amino acids and ketone bodies. **(A)** OPLS-DA scores plot of 1D ¹H CPMG NMR profiles of serum samples taken at trimester three, classified by HMDA (blue triangles) or LMDA groupings (red triangles) (R^2X = 0.04, CV-AUROC = 0.68), **(B)** ¹H NMR backscaled coefficients plot from OPLS-DA model based on ¹H CPMG NMR showing significant metabolite peaks at trimester 3, with insert of aromatic region indicating a significant increase of hippurate in the HMDA group. Key: 1-leucine, 2-valine, 3-lactate, 4-alanine, 5-acetic acid, 6-glutamine, 7-citrate, 8-glycine, 9-glucose, 10-tyrosine, 11-histidine, 12-phenylalanine. **(C)** OPLS-DA scores plot of JEDI-PGPE NMR data (R^2X = 0.03, CV-AUROC = 0.68), **(D)** backscaled coefficients plot for JEDI-PGPE model, **(E)** box plots of GlycA and GlycB concentrations, **(F)** OPLS-DA scores plot of small molecule metabolites (R^2X = 0.09, CV-AUROC = 0.63), **(G)** Eruption plot of quantified small molecule concentrations, **(H)** −log10 *p*-values of all the small molecules. Blue bars represent metabolites that are increased in the HMDA group, while those in red are increased in the LMDA group. SPC, supramolecular phospholipid composite; GlycA, acute phase glycoprotein glycan A; GlycB, acute phase glycoprotein glycan B.

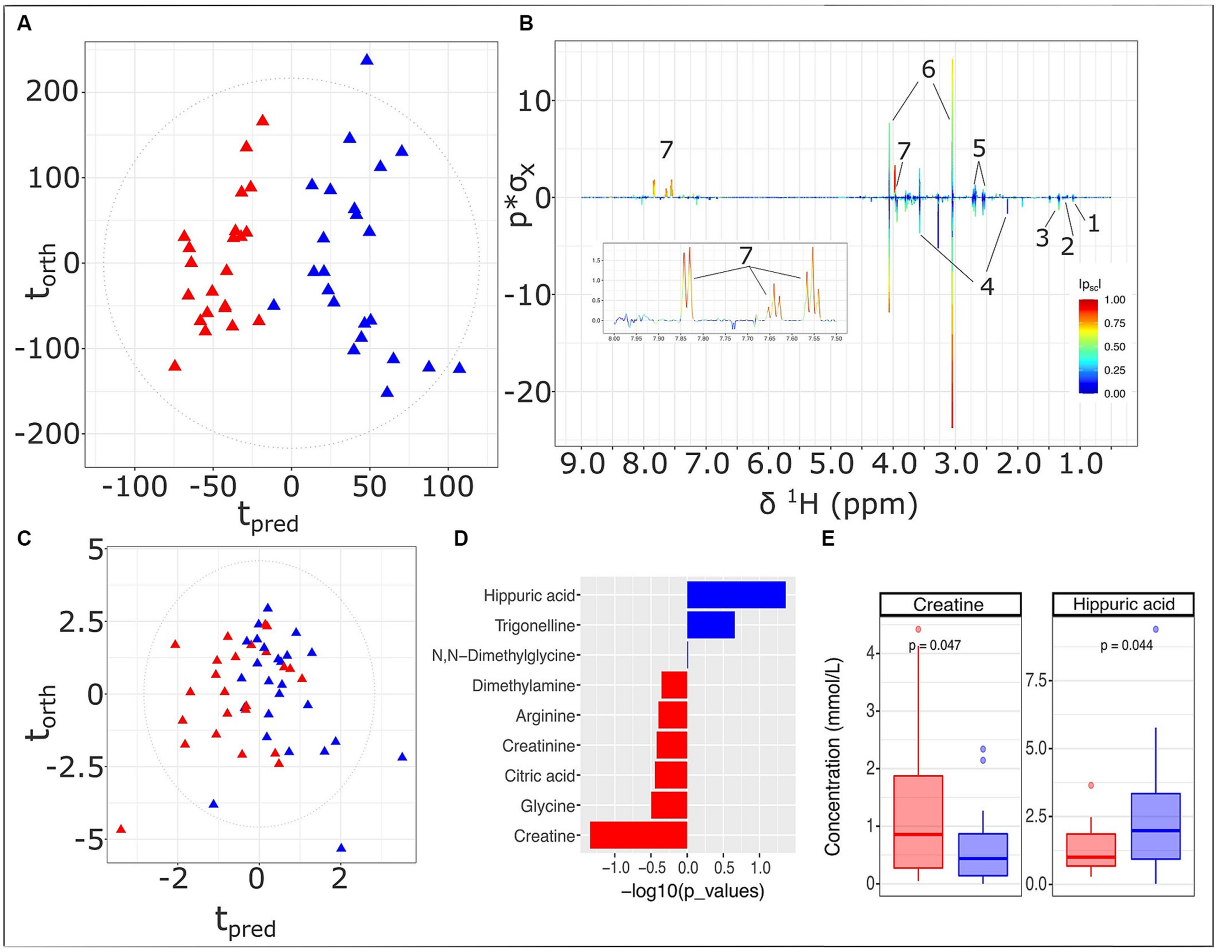

FIGURE 4
Urine metabolite analysis for samples obtained at 36 weeks, LMDA (n = 22) in red and HMDA (n = 23) shown in blue. **(A)** OPLS-DA scores plot of standard 1D ¹H NMR profiles of urine samples taken at trimester three, classified by HMDA or LMDA groupings (R^2X = 0.05,CV-AUROC = 0.84), **(B)** ¹H NMR backscaled coefficients plot showing significant metabolite peaks of 1D OPLS-DA at trimester 3, with insert of aromatic region to highlight the increase of hippuric acid in the HMDA group; **(C)** OPLS-DA scores plot of small molecules (R^2X = 0.31, CV-AUROC = 0.72). **(D)** –log10 p-values of the nine small molecules. Metabolites denoted by blue bars are increased in the HMDA group, while those in red are increased in the LMDA group. **(E)** Boxplot of creatine and Hippurate, with statistical significance in differentiating the LMDA and HMDA groups. Key: 1. 0.4-Deoxyerythronic acid, 2. 4-Deoxythreonic acid, 3. Lactate, 4. p-Cresol sulfate, 5. Citrate, 6. Creatinine, 7. Hippurate.

contribute to the SPC components, with SPC1 being composed mainly of HDL4, SPC2 mainly of HDL1-3, and SPC3 of LDL particles. In keeping with this observation, the total SPC concentration is inversely correlated with the total Glyc concentration, but positively correlated with metabolites associated with plant-based diets, such as hippurate. Other notable correlations were observed between other various urinary gut metabolites, hippuate inversely associated with paracresol sulfate and formate, and positively correlated with PAG and dimethylamine.

These correlations between microbial metabolites were generally stronger for the LMDA group than the HMDA group (see Supplementary Figures S7A,B). A correlation plot (Figure 6) was created to allow for associations to be drawn between specific metabolites and particular dietary components identified in the FFQ's (see also Supplementary Figures S6, S7). Of particular interest were the food correlations with SPC1, corresponding predominantly to small HDL phospholipid particles (HDL-4), which is recognised as a protective lipoprotein entity in cardiovascular disease (49). SPC1 was mildly, although not significantly, negatively associated with saturated fat intake, and significantly negatively associated with red meat ($p < 0.05$) and condiments ($p < 0.05$). SPC1 was non-significantly positively associated with vegetable intake (% energy). Conversely, SPC3, reflecting LDL phospholipid particles, was positively correlated with discretionary meats ($p < 0.01$), and starch vegetables, including potato ($p < 0.05$).

Of note, the serum amino acids valine, tyrosine, glutamine, methionine and leucine were associated with increased fat intake and with nuts and legumes. Inflammatory markers GlycA and GlycB demonstrated negative associations with cottage cheese, noodles and pasta. Urinary hippurate, a gut microbial-host co-metabolite, was strongly associated with some vegetables, fruit and muesli, and had strong negative associations with white bread, chicken and sweet drinks, as well as condiments. Excretion of acetate, a short chain fatty acid, predominantly of microbial origin, was strongly associated with dietary intake of polyunsaturated fats, noodles and some fruits, while being negatively correlated with saturated fats.

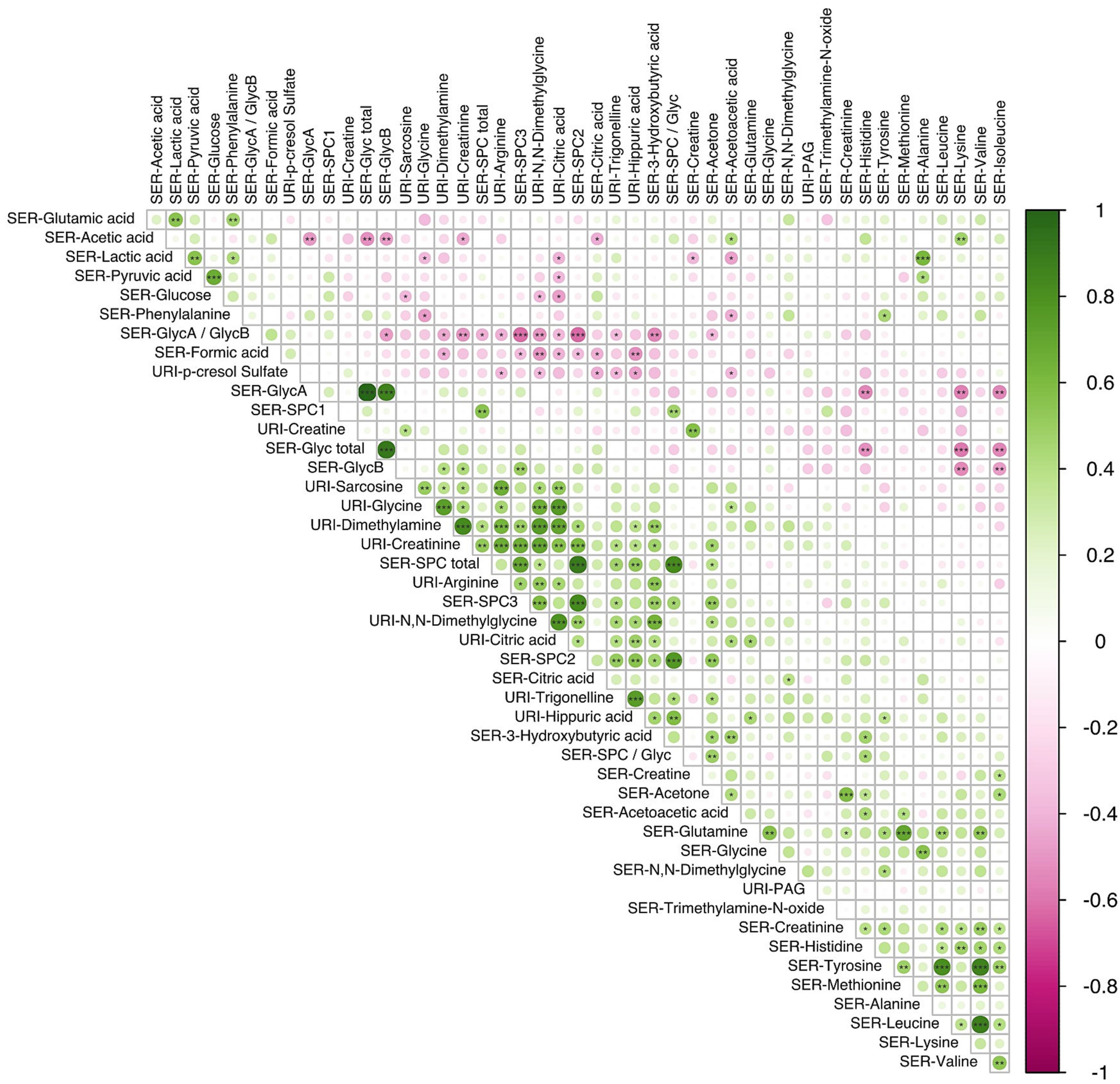

FIGURE 5
Correlation analysis using the Spearman pairwise rank method showing relationship between small molecules identified in serum ($n = 34$) and urine ($n = 12$) samples obtained during the third trimester of pregnancy (16 LMDA and 15 HMDA). The molecules are clustered using the angular order of the eigenvectors. Associations ranked from 1 (green), representing positive correlation, to −1 (pink), representing negative correlation (significance level according to Spearman correlation coefficients: $p < 0.001$ = ***; $p < 0.01 <$ **; $p < 0.05$ = *). SER, serum; URI, urine; SPC, supramolecular phospholipid composite; Glyc, acute phase glycoprotein glycan; PAG, phenylacetylglutamine.

4 Discussion

This study compared the metabolic phenotypes of women whose dietary patterns were self selectively aligned, or not, with the Mediterranean diet (characterised by consumption of fruits, vegetables, nuts, fish, olive oil and wholegrains, with minimal intake of processed foods, red meat and saturated fats). The diet-related differences between the LMDA and HMDA groups were reflected in both the urine and the serum profiles, indicating that alignment with the Mediterranean diet is associated with a specific metabolic phenotype during pregnancy. The MDI was inversely associated with inflammatory markers GlycA and GlycB but positively associated with SPC1 (reflecting HDL-4 concentration), which suggests that the women following the Mediterranean diet had a lower level of systemic inflammation.

Comparison of the FFQ data, between trimesters 2 and 3 showed a remarkable consistency in terms of reporting of dietary composition with clear differences in the food and nutrient composition between the two dietary groups relating to high and low alignment to the Mediterranean diet at both time points. Although the MDI scores were used to select participants who had no more than 2 points difference, the FFQ is made up of 40 different food groups and so the similarity between the two time points in terms of the finer dietary profile was noteworthy. The MDI showed direct correlation across both time points with the urinary gut microbial metabolites hippurate, phenylacetylglutamine and acetate and inverse correlations with both

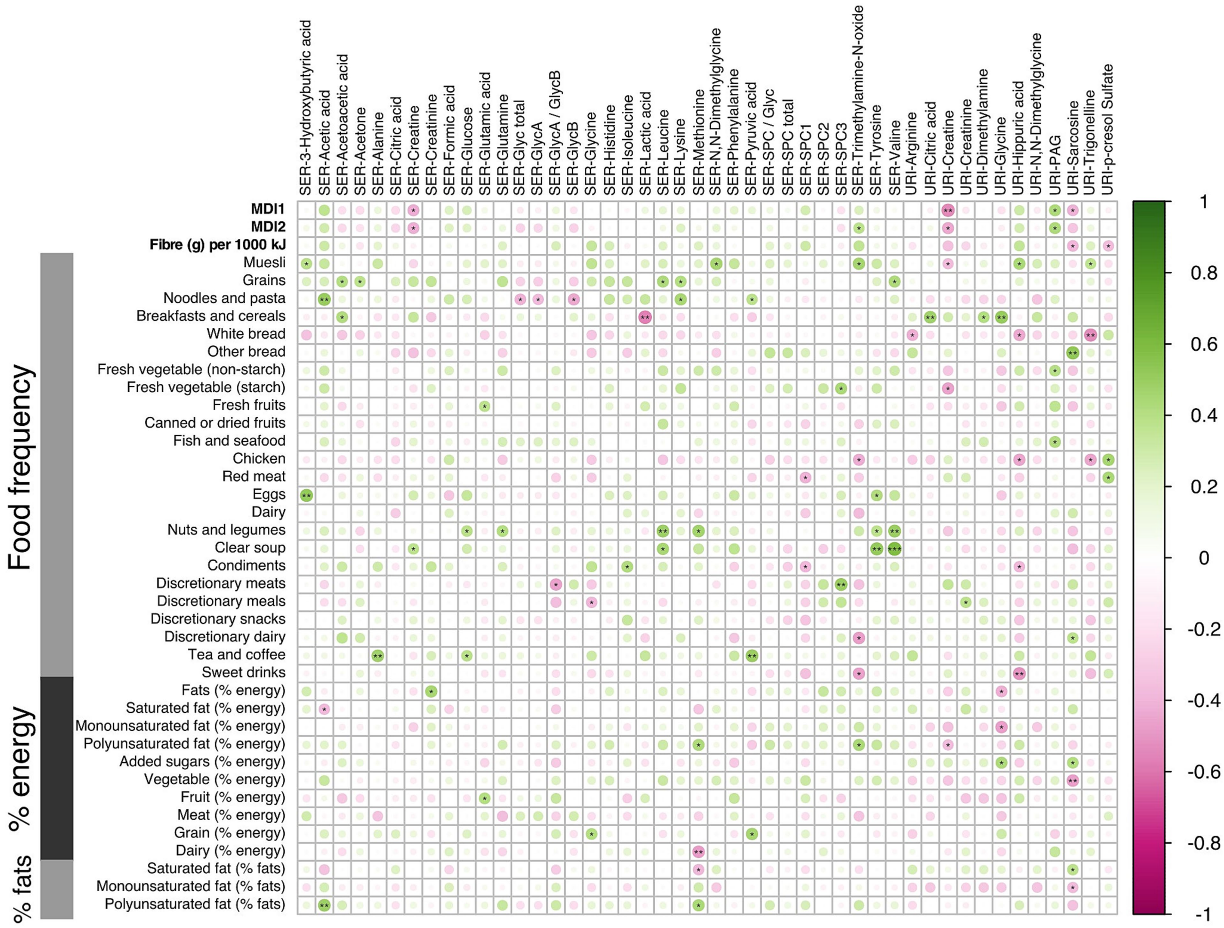

FIGURE 6
Correlation analysis using the Spearman pairwise rank method for dietary scores and small molecules during the third trimester of pregnancy (16 LMDA and 15 HMDA). Associations ranked from 1 (green), representing positive correlation, to −1 (pink), representing negative correlation (significance level according to Spearman correlation coefficients: $p < 0.001$ = ***; $p < 0.01 <$ **; $p < 0.05$ = *). SER, serum; URI, urine; SPC, supramolecular phospholipid composite; Glyc, acute phase glycoprotein glycan; PAG, phenylacetylglutamine.

serum and urine creatine and with sarcosine, which are associated with more meat-based diets.

4.1 An inflammatory metabolic profile is associated with low alignment with a Mediterranean dietary pattern

One of the most striking differences between the low and high alignment with Mediterranean diet in the current study was the presence of higher concentrations of the inflammatory markers GlycA and GlycB in the serum of women in the LMDA group, as well as the difference in SPC patterns between the groups. The ^{1}H NMR signals from GlycA and GlycB underlie a combination of acute phase glycoproteins, with alpha-1-acid glycoprotein being the most prominent but also encompassing haptoglobin, transferrin and alpha-1-antitrypsin (25). GlycA and GlycB are known to be highly correlated markers of inflammation and have been shown to be associated with a wide range of inflammatory health conditions (50). GlycA has been reported to be more sensitive and more stable than the more commonly used high sensitivity C-reactive protein, used as a gold standard marker of inflammation (34), and is elevated in obesity (24). Both GlycA and GlycB are associated with coronary heart disease (51) and other vascular inflammatory states (50). One study demonstrated that GlycA is associated with all-cause mortality (52, 53).

The supramolecular phosphocholine composite (SPC) signal, which contains the choline headgroups of lysophosphatidylcholines on glycoproteins and phospholipids in LDL and HDL, has been shown to be negatively correlated with inflammatory conditions (41, 43). Clear differences in the SPC patterns between the dietary adherence groups indicated that the SPC1, the resonance deriving from cardioprotective HDL-4 (54), was increased for those in the HMDA group and was negatively correlated with many dietary components that are not present in the Mediterranean dietary pattern, such as intake of red meat, discretionary foods (chocolate, chips etc.) and sweet drinks (such as soft drinks and juices). Conversely, SPC2 and SPC3 were increased in those participants in the LMDA group and this was associated with increasing discretionary meats (ham, bacon, salami etc.). The SPC3 signal derives from LDL phospholipids, which are generally considered to be proinflammatory, while SPC2 derives from larger HDL(1-3) phospholipid particles. This study demonstrates for the first time that SPC signals are associated with specific dietary patterns and may be manipulated by a change in eating habits.

These findings of metabolite profiles consistent with lower inflammation in the HMDA group are concordant with previous studies demonstrating that plant-based diets consumed during pregnancy by overweight or obese mothers have been associated with a reduction in the low-grade inflammation and with a higher gut microbial diversity. This is likely related to the increased fibre content in the plant-based diet (55). Since GlycA and GlycB are positively associated with LMDA but were not strongly associated with any specific dietary parameter, this indicates that the Mediterranean diet pattern (whole grains, pasta and noodles, fresh fruit, and vegetables) suggests that the whole dietary profile high in fibre is more important than individual components. Several weak associations between specific nutrients/foods and the acetylated glycoproteins indicated that the balance of animal protein to carbohydrate content may be important and is worth pursuing further. These results suggest that a Mediterranean diet may support both mother and child physically via a reduction in inflammation.

4.2 Adherence to a Mediterranean diet pattern affects the gut microbial metabolite phenotype

Hippurate was the strongest metabolic differentiator between the urine profiles of the HMDA and LMDA groups. Produced as a co-metabolite of microbial (production of benzoic acids) and human (glycine conjugation in the hepatic mitochondria) metabolism, hippurate is associated with reductions in blood pressure, obesity, visceral fat, and non-alcoholic fatty liver disease in adult populations (49, 56). Hippurate is an established surrogate marker for metabolic health, gut function and microbial diversity (57, 58). The composition of the gut microbiome is important during pregnancy as it has demonstrated impacts on foetal outcomes, as well as long-term health implications for both mother and child including the regulation of glucose metabolism and gestational diabetes, obesity, and risk of preeclampsia during pregnancy (59). Our study demonstrated significantly increased urinary hippurate levels in those closely adhering to the Mediterranean diet. Hippurate intake is known to be associated with higher intakes of whole grains, coffee, fruit and vegetables, and a diet which is overall high in fibre and polyphenols (56, 57, 60, 61). As such, higher levels of hippurate are generally associated with a healthier eating pattern and leaner body mass (56). Hippurate has previously been associated with dietary fibre intake (61), again concordant with the dietary intake of those on a Mediterranean Diet. However, it should be mentioned that not all healthy dietary patterns are associated with higher levels of hippurate. For example, although the traditional Japanese diet is known to be inversely associated with cardiovascular disease and is high in plant-based phenolics, hippurate excretion, in general, is lower in Japanese individuals compared to participants from the U.K., U.S.A and People's Republic of China (61).

Hippurate directly correlated with phenylacetylglutamine, a product of aromatic amino acid breakdown by the colonic bacteria. Phenylacetylglutamine correlated with the MDI and was specifically associated with fresh vegetables, fruits and fish, adding weight to the observed impact of the Mediterranean diet on the gut microbiome. Increased levels of phenylacetylglutamine have previously been reported in individuals showing high adherence to the Mediterranean diet (62) and after consumption of foods that are rich in polyphenols (63).

We observed further dietary impact on microbial metabolites with higher concentrations of acetate, a short chain fatty acid typically produced from the metabolism of indigestible carbohydrates, or fibre, found in the serum of women with high adherence to a Mediterranean diet pattern. The short chain fatty acids are associated with gut microbial function and this relationship between the Mediterranean diet and circulating acetate levels has been reported previously (64). High fibre foods include fruits and vegetables, wholegrain foods, nuts and seeds, all of which are highly prevalent in the Mediterranean diet. Circulating acetate concentrations are associated with lower body weight, reduced risk of cardiovascular disease and increased immune functioning (65, 66). In addition, acetate levels during pregnancy may have a lasting impact on the developing foetus. Hu and colleagues found that low serum acetate was associated with increased risk of pre-eclampsia (67). Similarly, Brantsæter and colleagues found a reduced risk of pre-eclampsia in pregnant women who regularly consumed probiotic products, which were capable of increasing acetate levels in the gut environment (68). The relationship between fibre intake and acetate levels during pregnancy and the subsequent impact on offspring health, specifically ectopic conditions have been further demonstrated in mouse models (69). In the current study we found a modest association, although not significant, between serum acetate and percentage of dietary polyunsaturated fats, whereas there was an inverse correlation between serum acetate and saturated fats ($p < 0.01$). This supports the concept that high dietary fibre intake is likely indicative of a healthy dietary profile.

Adding to the body of evidence that the Mediterranean diet beneficially influences the gut microbiome is the observed inverse correlation between serum GlycA and serum acetate, which were present in higher and lower relative concentrations, respectively, in the samples of women in the LMDA group. GlycA has been reported to have an inverse correlation with dietary fibre and gut microbiome diversity (20).

4.3 Creatine and meat intake is associated with low adherence to a Mediterranean diet pattern: balance of animal to plant-based diets

Creatine was noted as the most significant serum metabolite driving the difference between the two diet groups, being present in higher concentrations in the serum profiles of the LMDA group and a strongly correlation between serum and urinary creatine was identified. Creatine can be derived from dietary sources, such as fish, meat and dairy, or can be synthesized endogenously (70). Creatine is required to facilitate the developing foetus, as well as the uterine and placental tissues, particularly in the third trimester, and is necessary for adequate foetal growth (71). Human studies demonstrate that pregnant women have lower serum levels of creatine by approximately 35%, compared to non-pregnant women, and the excretion of creatine reduces as the pregnancy progresses. Although, unlike other studies (70) we find no significant correlation between serum creatinine and red meat in the current study, serum creatine was weakly associated with all types of meat and fish in the LMDA group but not the HMDA group (Supplementary Figure S3) and urine creatinine was inversely correlated with vegetable and fruit intake in the LMDA group. Consumption of meat is associated with increased excretion of urinary creatine and creatinine (70) but the effects are relatively small with a 13% increase in creatinine excretion observed following a meal of cooked red meat (72). We found a small but significant increase in serum concentrations of creatine in the HMDA and trend towards higher urinary creatine concentrations in the LMDA group. The failure to reach significance is likely due to the relatively small number of participants enrolled in the study. The correlation of urinary creatine to urinary creatinine, sarcosine, dimethylglycine and dimethylamine and serum creatine adds confidence in the association of these metabolites with protein intake. Considering the combined urine and serum metabolomes, we observe different patterns between the HMDA and LMDA reflective of discordance in the ratio of meat to plant-based dietary protein. For example, serum creatine was inversely associated with trigonelline, which is an indicator of bean and pea consumption (73, 74). A low creatine to trigonelline ratio is therefore consistent with adherence to a Mediterranean dietary pattern, as there is a focus on plant-based protein sources such as legumes. Trigonelline has been associated with a range of health benefits, and is credited with hypoglycaemic, hypolipidemic, and neuroprotective properties (75, 76). As such, a Mediterranean dietary pattern, which is lower in meat consumption than a Western dietary pattern, is likely to rely on a greater percentage of plant-based sources of protein.

4.4 Association of fish intake, urinary methylamines, and the Mediterranean diet

Consistent with a Mediterranean dietary pattern, participants reported higher consumption of fish in the HMDA group. Urinary trimethylamine-*N*-oxide (TMAO) and its precursor trimethylamine are markers of fish consumption, particularly deep dwelling marine fish (77) but are also synthesized from bacterial degradation of dietary choline and carnitine found in red meats (56, 77). Less commonly, urinary TMAO can also be related to legume intake (78). Urinary and serum TMAO have been proposed as biomarkers of cardiovascular disease (79), however caution must be exercised in interpreting its role in dietary health. This is due to the fact that there are dietary sources of this metabolite, including fish (77), which is generally associated with alignment to a Mediterranean-style diet. In the current study, TMAO was positively associated with increased polyunsaturated fats, muesli intake, and nuts and legumes. This indicates that the source of choline in the HMDA group is more likely to be from plant-based sources, such as legumes and whole grains, and that fish intake, although increased in the HMDA group, does not significantly account for urinary or serum concentrations of methylamines in this case. In the current study the median spectrum of urinary TMAO (Supplementary Figure S6E) was higher in the HDMA group, but this difference was not significant in either the univariate or multivariate models due to the relatively small group size and the fact that TMAO was overlapped with multiple signals from betaine and choline species. In contrast to our observation, De Filippis and co-workers found that adherence to a Mediterranean diet was linked to lower urinary trimethylamine-*N*-oxide concentrations (80).

4.5 The Mediterranean diet is associated with differences in amino acid metabolism

Alignment with a Mediterranean diet was associated with generally lower levels of serum amino acids, with the exception of glycine, which associated with the HMDA group. The Branched Chain Amino Acids (BCAA's) valine and leucine were found in higher concentrations in the HMDA group, as was tyrosine. These metabolites showed significant inter-correlation and were also associated with intake of legumes and nuts, key components of the Mediterranean diet. The implications of BCAA's in chronic disease are, as yet, unclear, with contradictory studies indicating for their benefit or detriment. However, the consensus from most studies is that BCAA's play an anti-inflammatory role in the body and can reduce levels of proinflammatory mediators interleukin-6 and cyclooxygenase-2 (81). Indeed, one study which examined the metabolome, as omnivorous participants moved to a vegan diet for 48 h, demonstrated that BCAA's were notably increased in the vegan metabolome, as part of an overall improved metabolic profile (82).

Other differences between the urine profiles of the two diet groups were the lower concentrations of alanine in the LMDA group along with two products of threonine metabolism, 4-deoxyerythronic acid and 4-deoxythreonic acid. Urinary concentrations of these products of threonine catabolism have been shown to increase over the course of pregnancy (83) and have been found to be correlated with BMI (84). In non-pregnant cohorts 4-deoxythreonic acid is associated with major depressive disorder (85). In a dietary study comparing the impact of a Mediterranean diet with that of an ultra-processed food diet, 4-deoxythreonic acid was inversely associated with the Mediterranean diet (85), consistent with the results we observe here.

4.6 Limitations

The main limitation of this study was the relatively small sample size of the cohort when stratified by diet, which prohibits overinterpretation of the results. Not all participants completed the food frequency questionnaire at all time points and as such the Mediterranean diet screening that was conducted may not be fully reliable. The cohort were self-selected and while every effort was made to ensure there was no bias between the two diet groups, because the groups were self-selected and the diets were not randomised, it is possible that there is an inherent bias between the two groups. However, there was no statistical difference after adjusting for multiple testing in age, parity, education, work status, pre-pregnancy weight/BMI, and socioeconomic indexes for areas factors. On the other hand, because the diets were self-selected, it could be possible that adherence may be better than when randomising participants to different diets. Nevertheless, using the FFQ's to confirm the expected food correlations between the two groups indicated consistency of the dietary patterns established by the MDQ within each group and between timepoints. Since it would have been difficult to obtain ethics for fasting samples in this pregnancy cohort, the biological samples were not taken in a fasting state, which may distort the biofluid composition based on the last meal consumed. However, the differences in metabolic phenotype between the two groups was convincing and based on the metabolite-metabolite and metabolite-diet correlations, the metabolic consequences were in keeping with a lower inflammatory profile in the HMDA group.

5 Conclusion

We demonstrated a clear difference between the metabolite profiles of pregnant women who had a high versus low Mediterranean diet score. These metabolite profiles align with their reported choice of food. High adherence to a Mediterranean diet was associated with lower serum markers of inflammation, creatine and an altered amino acid profile, together with increased concentrations of gut-microbial metabolites, indicating greater functional diversity associated with adherence to a Mediterranean diet. This may have long term health benefits for both mother and child. The combination of serum inflammatory markers and hippurate as a marker of dietary fibre intake may provide an effective biomarker panel for assessing adherence to Mediterranean diet in pregnancy.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding authors.

Ethics statement

The studies involving humans were approved by ORIGINS Scientific Committee and Project Management Group (Application ID: ND01905); Ramsay Health Care Human Research Ethics Committee (Protocol number: ND01905). The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

ND'V: conceptualization and methodology. CR, SL, SE, and JW: investigation. CR, GF, and EH: writing – original draft preparation. EH, GF, JN, ND'V, CC, and TO'S: validation, resources, and writing – review and editing. ND'V and JN: funding acquisition. ND'V, EH, and GF: supervision. All authors contributed to the article and approved the submitted version.

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Conflict of interest

GF and EH are directors of Melico Ltd. outside the scope of the submitted work and CR is a director for Habits for Health, also outside the scope of the submitted work.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fnut.2023.1230480/full#supplementary-material

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Feasibility pilot study of a Japanese teaching kitchen program

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Background: This pilot study examined the feasibility of a new lifestyle modification program involving a “Teaching Kitchen” in Japan. Our goal was to explore (1) feasibility of the program; (2) acceptability for class frequency (weekly vs. bi-weekly); and (3) changes in biometrics, dietary intakes, and lifestyle factors.

Methods: A total of 24 employees with obesity in a Japanese company were recruited. Participants were randomly divided into two groups (weekly or bi-weekly group), each attending the program consisting of four two-hour classes (lectures on nutrition, exercise, mindfulness, and culinary instructions). Participants were observed for changes in dietary intakes, biometrics, and health related quality of life over the subsequent 3 months. We tested the between-group differences in changes using linear mixed-effect models.

Results: The program completion rates were 83.3% in total (91.7% for weekly group and 75.0% for bi-weekly group). From baseline to post-intervention, significant decreases were observed in weight ($p < 0.001$), body mass index ($p < 0.001$), diastolic blood pressure ($p = 0.03$), body fat mass ($p < 0.001$), and dietary intakes in total fat ($p = 0.03$) and sodium ($p = 0.008$) among 17 participants who were available for measurements. Improvements in biometrics remained significant 1 month after the intervention (all $p \leq 0.03$ in 14 participants). Participants’ health related quality of life was significantly improved in bodily pain, general health, vitality, and mental component score (all $p \leq 0.047$).

Conclusions: The new Japanese Teaching Kitchen program is feasible with high program completion rates in Japanese office workers with obesity. While this was a small feasibility study, significant multiple improvements in dietary intakes, biometrics, and health related quality of life suggest that this line of inquiry warrants further exploration to address obesity and obesity-related diseases in Japan.

KEYWORDS

teaching kitchen, diet, obesity, lifestyle modification, behavior modification program

1 Introduction

The increase of obesity and obesity-related diseases is a severe global problem in both Western and Asian countries. Recently, a new lifestyle modification program referred to as a "Teaching kitchen" was developed and led by the researchers at the Harvard T.H. Chan School of Public Health (1, 2). Core components of Teaching Kitchen include: (1) nutrition lectures based on the latest scientific evidence; (2) hands-on culinary instruction to prepare healthy, delicious, and easy-to-prepare meals; (3) movement and exercise lectures; (4) mindfulness lectures; and (5) motivational interviewing and health coaching to sustain behavior change (2). Based on this concept, Teaching Kitchens are currently being held in a variety of settings, including hospitals, schools, and corporations, primarily in Western countries, with various program lengths and topics to suit the participants (2). Several previous studies on the efficacy of Teaching Kitchens reported that the curricula resulted in significant decreases in weight, waist circumference, blood pressure, and total cholesterol in the US individuals with obesity (3) and decreases in weight and HbA1c in Canadian patients with diabetes (4).

The traditional Japanese diet has been known to be healthy (5, 6). However, westernization of the Japanese diet and other lifestyle factors has led to a gradual increase in the Japanese population with obesity and obesity-related diseases since the 1960s (7). To modify lifestyles including diet, health guidance has recently been provided to Japanese individuals aged 40–74 who are enrolled in the National Health Insurance and have a risk of lifestyle related diseases (8). Similarly, companies provide their employees annual health checkups and lifestyle counseling to reduce their metabolic risk. In addition, many hospitals provide nutritional guidance for patients with diabetes by registered dietitians. Traditionally, most guidance is based on the Food Exchange Lists-Dietary Guidance for Persons with Diabetes (9), which provides a rough estimate of the amount of energy and nutrients contained in each food (10). Such strategy aims to restrict patients' calorie intake, restrain themselves from the consumption of snacks, and ensure macronutrient balance. However, the latest report from the Japanese National Institute of Health and Nutrition showed that the number of people with metabolic syndrome is continuing to increase in Japan (11). Therefore, more effective approaches are needed in addition to the current guidance to improve the diets and health outcomes of Japanese adults.

A previous US study reported that each 30 min decrease of food preparation time was associated with the increase in body mass index (BMI) of 0.5 between 1965 and 1995 (12). Another study in Japan with 9,143 men and 10,595 women aged more than 65 years showed that women had higher levels of cooking skills than men, and that both men and women with low level of cooking skills were more likely to have lower frequency of home cooking and unhealthy dietary behaviors than those with a high level of cooking (13). Several other studies have also consistently reported that there is a positive association between home cooking skills and diet quality (14–16). Therefore, it is considered that the acquisition of cooking skills at home is useful for motivating Japanese people to improve their diet. In addition, the National Health and Nutrition Survey in Japan showed that the obesity rate has increased rapidly among Japanese males in their 20s when most of them start living alone (17), implying that they do not have sufficient cooking skills to prepare healthy meals.

Therefore, if we can customize the US Teaching Kitchen curriculum developed by investigators from Harvard and the Teaching Kitchen Collaborative (18) for Japan and spread it into clinical practice and workplaces as a social implementation, this approach may serve as a powerful strategy to address, and potentially mitigate, the increasing obesity/obesity-related diseases rate and rising medical costs in Japan. To meet such critical needs, in the current study we developed a new Japanese Teaching Kitchen program by building the professional team with Japanese physicians specialized in diabetology and metabolism, public health specialists, registered dietitians, culinary specialists (a.k.a., cooks), and companies that specialized in behavior modification (Cancerscan, Inc) and the production of Japanese traditional foods (Kubara Honke Group Co., Ltd). Our goal was (1) to examine the feasibility of a potentially replicable Teaching Kitchen program/curriculum as applied to a Japanese population of worksite employees; (2) to determine if a frequency of classes of once per week vs. once per 2 weeks was accepted by participants over four classes; and 3) to investigate and report on changes in relevant lifestyle factors, biometrics, and health related quality of life (HR-QoL), before and after the program intervention.

2 Materials and methods

2.1 Recruitment

The participants of the current study are the employees in the NISSIN Foods Holdings Co., Ltd (Tokyo, Japan) working at that company's main office (Shinjuku, Tokyo) and at the company's research center (Hachioji, Tokyo). The NISSIN Foods Holdings Co., Ltd had no conflict of interest to this study. Subject recruitment criteria included: those with the ages of 20 to 74 and with BMI$\geq$25 and/or waist circumstance $\geq$85 cm for men and $\geq$90 cm for women (consistent with the diagnostic criteria of metabolic syndrome in Japan). The exclusion criteria were those who needed special dietary therapy such as protein restriction and/or severe food allergy, those with severe hypertension (systolic blood pressure $\geq$160 mmHg and diastolic blood pressure $\geq$110 mmHg), those with severe hypertriglyceridemia ($\geq$1000 mg/dl), those who required exercise restriction (e.g., those with heart failure and/or unstable angina), those who were pregnant, planning to become pregnant, or were breastfeeding, and those who the researchers judged difficult to participate in the program (e.g., those who were going to be absent due to a long trip). Based on the most recent health checkup data, employees who met the criteria were invited to participate in this study via e-mails from the staffs of the company. After signing the informed consent, participants were randomly divided into two groups: the weekly group, who attended four weekly classes; and the bi-weekly group, who attended four classes every other week. We employed a stratified randomization method which controlled for age, sex, BMI, and working place (Supplementary Table 1). On stratification, the participants were not asked their preference regarding the frequency of classes.

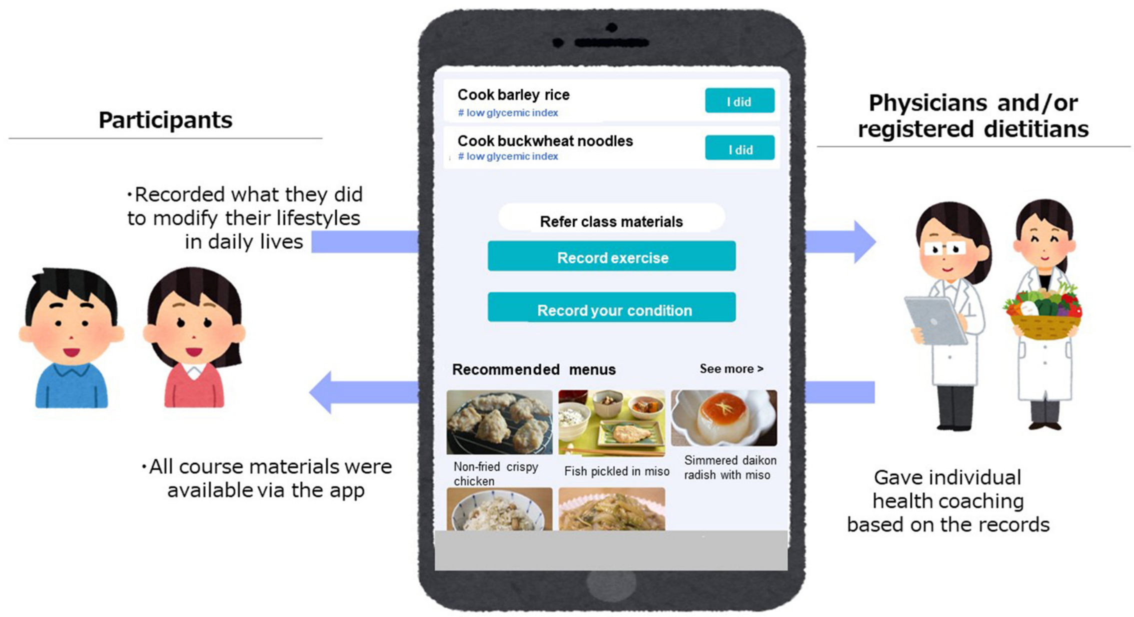

FIGURE 1
The overview of the web application.

The current study was approved by the Institutional Ethics Review Board of Osaka University Hospital (approved number 21335) and informed consent was obtained from all participants.

2.2 Interventions

Based on the concept of a Teaching Kitchen which includes hands-on culinary instruction and lifestyle guidance based on the scientific evidence (2), the Japanese Teaching Kitchen program has been developed by building the team with Japanese physicians specialized in diabetology and metabolism, public health specialists, registered dietitians, culinary specialists, and companies specialized in behavior modification (Cancerscan, Inc, the Japanese start-up company providing preventive healthcare service to local governments) and the production of Japanese traditional foods (Kubara Honke Group Co., Ltd). In developing the Japanese Teaching Kitchen program, all healthy recipes created for the program were based on the healthy Japanese diet, using foods that are available in Japan on a daily basis and using cooking methods commonly used in Japan (e.g., boiling, steaming, and baking). In addition, since the Japanese diet has a higher sodium intake than that of Western countries (19), the Japanese Teaching Kitchen program particularly focused on how to reduce salt intake. Specifically, we made use of *dashi*, a fish soup stock that contains a lot of umami, which is traditionally used in Japan, as well as spices and seasonings to reduce salt intake while maintaining food satisfaction.

The intervention included four 2-hour face-to-face classes (one month for four weekly classes and 2 months for four biweekly classes). All classes took place at the kitchens owned by ABC Cooking Studio Co. Ltd (Tokyo, Japan) and were facilitated by the researchers (physicians, registered dietitians, and chefs). The example of timetable for the face-to-face class was shown in Supplementary Table 2. During the classes, participants attended lectures on nutrition, physical activity, and mindfulness, as well as hands-on culinary lessons working in assigned teams of 4–6 people to cook the healthy meals with chefs and then eat the foods they prepared by themselves. Each class had a specific topic (how to lower calorie intake, how to lower salt intake, how to lower glycemic index, and healthy party menus including appetizers and snacks) and participants learned the nutrition evidence and practical skills related to the topic in lectures and cooking experience. The participants also used a web application (app) designed for this study by the researchers and Cancerscan, Inc during the intervention. The app had mainly two functions. First, participants could access all class materials including the recipes and recommended menus that helped participants to cook healthy dishes at home and to choose healthy menus when they ate out (Figure 1). Second, participants could record what they did in their daily lives to modify their lifestyles (e.g., cooked healthy dishes they learned, chose healthy menus, did exercise) by posting the text and/or pictures via the app and researchers (physicians and/or registered dietitians) replied with encouraging advice as an individual health coaching (Figure 1).

2.3 Outcome assessments

Feasibility was assessed through recruitment, program completion rate, and satisfaction with classes as a primary outcome. We assessed acceptability for class frequency and

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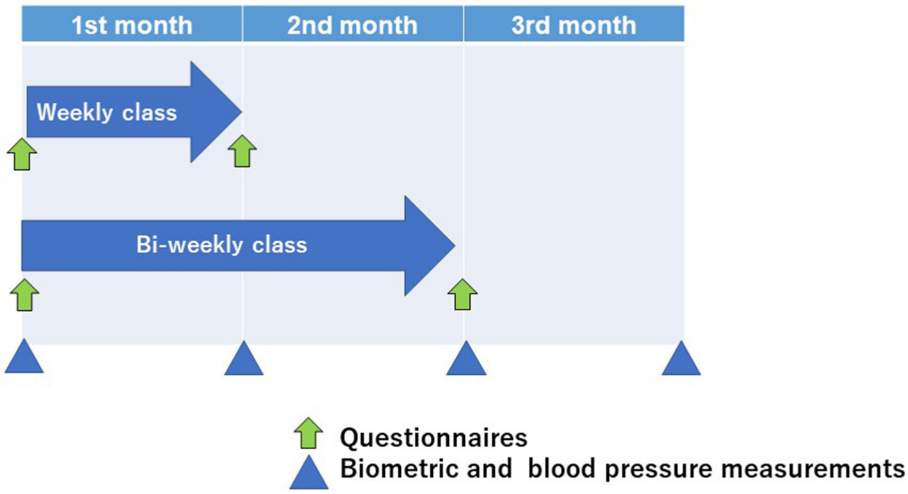

FIGURE 2
The timeline of assessments.

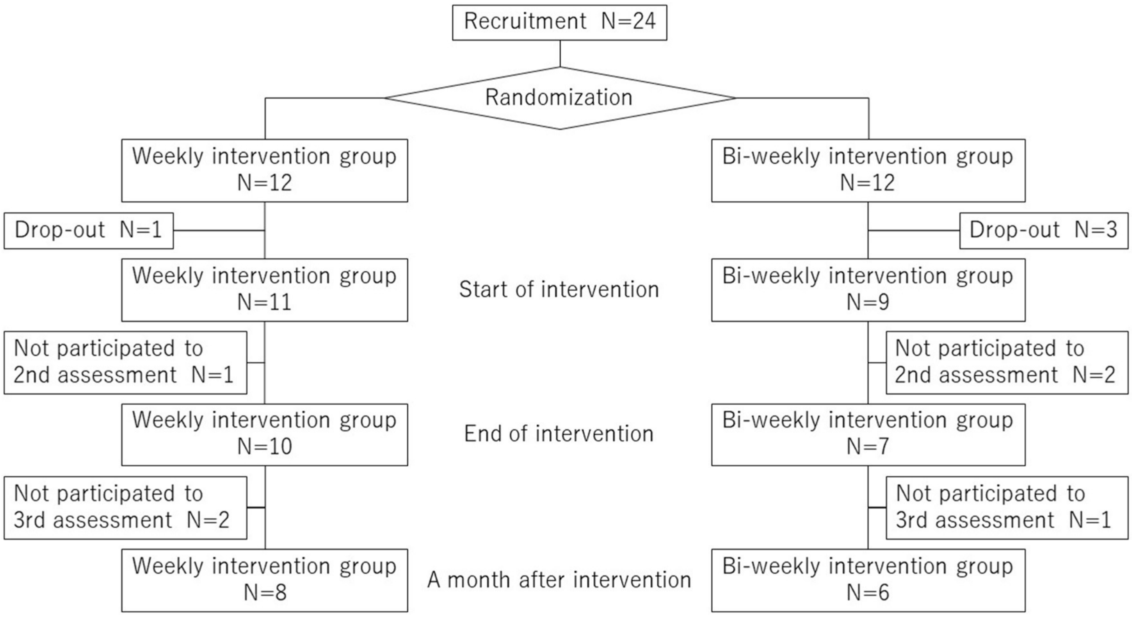

FIGURE 3
A flow diagram with the recruitment, randomization, intervention, and follow-up.

changes in biometrics, dietary intakes, and lifestyle factors as secondary outcomes. The timeline of assessments was shown in Figure 2 and all instruments used in this study were listed in Supplementary Table 3. Biometric outcomes and blood pressure were assessed four times: at baseline, 1 month later, 2 months later, and 3 months later. Body weight and the amounts of body fat mass and lean mass were evaluated using body composition analyzer (MC-780A-N, TANITA Co. Ltd, Tokyo, Japan). Weights were measured to one decimal place, with participants wearing light clothing, shoes removed, and 0.5 kg subtracted for the weight of clothing. Blood pressure was measured in the sitting position by the researchers (physician) using a digital sphygmomanometer (TERUMO, Tokyo, Japan). Changes in biometric and blood pressure at baseline, end of the intervention, and 1 month after the intervention were assessed using the baseline values, values at the end of the program (four weeks later for the weekly group and 8 weeks later for the bi-weekly group), and values at the end of the one-month follow-up (8 weeks later for the weekly group and 12 weeks later for the bi-weekly group). Several validated questionnaires were used to assess the difference of participants' diets, physical activity, sleep difficulty, and HR-QoL between baseline and at the end of the program (four weeks later for the weekly group and 8 weeks later for the bi-weekly group). Dietary intakes were examined using the self-administered long-food frequency questionnaire (FFQ) developed for Japanese individuals (20). Food intake was calculated by multiplying the frequency of consumption (never, 1–3 times/month, 1–2 times/week, 3–4 times/week, 5–6 times/week, once/day, 1–2 times/day, 4–6 times/day, 7+ times/day) by relative portion size (small, medium, and large), and participants were asked to report dietary intake in the previous year for the baseline and dietary intake during the intervention for the post-intervention assessment. Obesity-related eating behavior was quantified using the questionnaire of the guideline for obesity issued by the Japan Society for the Study of Obesity to identify the problems in various eating behaviors, following previous studies (21–23). This questionnaire consists of 55-item questions of seven major scales as follows: 1. Recognition for weight and constitution (e.g., "Do you think it is easier for you to gain weight than others?", "Do you think you gain weight because of less exercise?"), 2. External eating behavior (e.g., "If food smells and looks good, do you eat more than usual?", "If you walk past the supermarket, do you have the desire to buy something delicious?", "If you see others eating, do you also have the desire to eat?"), 3. Emotional eating behavior (e.g., "Do you have the desire to eat when you are irritated?", "Do you have a desire to eat when you have nothing to do?"), 4. Sense of hunger (e.g., "Do you get irritated when you feel hungry?", "Do you often regret because you have eaten a lot of food?"), 5. Eating style (e.g., "Do you eat fast?", "Are you known to eat a lot of food?"), 6. Food preference (e.g., "Do you often eat snack bread?", "Do you like meat?", "Do you like noodles?"), 7. Regularity of eating habits (e.g., "Is your dinner time too late at night?", "Do you gain body weight during holidays?"). All items were rated on a four-point scale ranging from 1 (seldom) to 4 (very often) and higher scores mean poorer eating behaviors. Physical activity was assessed using International Physical Activity Questionnaire (IPAQ). Sleep difficulty was quantified using Athens Insomnia Scale. HR-QoL was evaluated using the medical Outcomes Study 36-Item Short-Form Health Survey (SF-36), version 2 (24). In addition, participants put smart bands (Mi Band 6, Xiaomi, China) to assess their physical activity and sleep duration during the study period. Participants' cooking frequency (times/week) and the percentage of skipping meals more than once a week were asked by the self-reported questionnaire before and after the intervention. Further, after the intervention, participants reported their satisfaction for each content of the face-to-face classes (nutrition lecture, cooking, exercise lecture, and mindfulness lecture) by choosing the numbers from 0 to 10 (0; not satisfied and 10: most satisfied) and whether they felt their diet have improved or not.

2.4 Statistical analyses

The program completion rate was determined by the percentage of participants who completed the study. To compare the program completion rate, satisfaction rating, and characteristics of participants between weekly and bi-weekly groups, t-tests were used for continuous variables and Fisher's exact test was used for categorical variables. We confirmed the normality of each continuous variable by drawing a probability plot and found that age, alcohol intake, and satisfaction rating for the nutrition class were not in the normal distribution. For these three variables, we tested the between-group difference by the Willcoxon rank test. The changes in biometrics, HR-QoL, and lifestyles between

TABLE 1 Baseline characteristics of participants in weekly group and bi-weekly group.

	Weekly group	Bi-weekly group	p
N	11	9	
Age, year	38 [35, 52]	39 [38, 43]	0.30
Sex (male/female)	10/1	8/1	1.00
Weight, kg	80.3 ± 10.4	81.6 ± 13.5	0.81
BMI, kg/m^2	27.2 ± 2.3	27.4 ± 4.1	0.93
Body fat mass, kg	22.1 ± 6.6	24.9 ± 8.3	0.42
Lean mass, kg	55.2 ± 7.7	53.8 ± 7.5	0.69
Systolic blood pressure, mmHg	131.7 ± 10.0	137.4 ± 16.5	0.35
Diastolic blood pressure, mmHg	86.7 ± 7.0	87.3 ± 8.9	0.87
Physical activity, MET-h/week	23.5 ± 15.3	23.4 ± 17.9	0.98
Athens Insomnia Scale	4.5 ± 1.8	7.4 ± 4.4	0.08
Living alone, %	18.2	44.4	0.34
Office (main office/research center), %	81.8/18.2	88.9/11.1	1.00
Smoking (current, past, none), %			0.25
Current	0	11.1	
Past	54.6	22.2	
None	45.5	66.7	
Alcohol intake, g/day*	2.1 [0.5, 11.5]	4.9 [0.5, 16.9]	0.32
Hypertension, %	36.4	11.1	0.32
Hyperlipidemia, %	18.2	11.1	1.00
Diabetes, %	9.1	0	1.00
Sleep Apnea Syndrome, %	0	22.2	0.19
Program completion rate, %	91.7	75.0	0.59

Values are means ± standard deviations (SDs) for continuous variables and percentages for categorical variables. The differences between weekly and bi-weekly groups were tested using t-tests for continuous variables other than age and alcohol intake, the Willcoxon rank test for age and alcohol intake, and Fisher's exact test for categorical variables. $p < 0.05$ indicates statistically significant. BMI, body mass index; MET, metabolic equivalent; n, the number of participants. * Values are median [interquartile range] and tested by using the Wilcoxon rank test.

TABLE 2 Participants' satisfaction ratings of each content of classes in weekly group and bi-weekly group.

	Weekly group	Bi-weekly group	P
n^a	10	6	
Nutrition lecture	9.5 [8, 10]	8.5 [7, 10]	0.32
Cooking class	7.1 ± 1.7	8.2 ± 1.7	0.25
Exercise lecture	6.9 ± 2.0	7.7 ± 2.1	0.48
Mindfulness lecture	5.3 ± 2.1	7.7 ± 1.2	0.03

Values are means ± standard deviations (SDs) or median [interquartile range]. The differences between weekly and bi-weekly groups were tested using the Willcoxon rank test for the Nutrition lecture and t-tests for the others. $p < 0.05$ indicates statistically significant.
[a]n = 16 instead of 17 because of missing values.

before and after the program intervention were examined by using linear mixed effect models. Changes in outcomes from baseline to post-intervention (when the program finished) were examined in the participants who finished biometric measurements both at baseline and after the intervention. The changes from baseline to 1 month after the program were examined in the participants who finished measurements three times (baseline, when they finished the program, and after the 1 month follow up). All All analyses were conducted using SAS version 9.4 (SAS Institute, Inc, Cary, NC) with statistical significance defined as two-sided $p < 0.05$.

3 Results

3.1 Program completion rates and baseline characteristics of participants in weekly and bi-weekly groups

Approximately 300 employees who met the criteria were sent e-mails for recruitment into the study, and 24 participants were recruited within 3 weeks. By inviting employees who met the criteria, the recruited participants were predominantly male (22 males and 2 females, Supplementary Table 1). A flow diagram with the recruitment, randomization, intervention, and follow-up was shown in Figure 3. Baseline characteristics of the participants and program completion rates in weekly and bi-weekly groups are summarized in Table 1. Within the 12 participants in each group, one participant in the weekly group and three participants in the bi-weekly group dropped out from the program. All participants who quit the program expressed their withdrawal before they attended the first class. Reasons for their dropping out were one for family matter and three relating to their work schedules. Consequently, the program completion rates were 83.3% in total, with 91.7% in the weekly group and 75.0% in the bi-weekly group. When participants were asked for their ratings with respect to the content of the classes, with a range from 0 (not satisfied) to 10 (most satisfied), their approval scores (mean±SD) in all participants were 8.6 ± 1.7 for the nutrition lectures, 7.5 ± 1.8 for the cooking classes, 7.2 ± 2.0 for the exercise lectures, and 6.2 ± 2.1 for the mindfulness lectures. When we compared the satisfaction ratings for each content of the classes in the weekly and bi-weekly groups, there were no significant differences between the two groups, except for the mindfulness lecture (Table 2).

3.2 Changes in biometrics from baseline to post-intervention

From baseline to post-intervention (four weeks for the weekly group and 8 weeks for bi-weekly group), significant decreases were observed in weight, BMI, systolic blood pressure, diastolic blood pressure, and body fat mass (Table 3). On the other hand, the lean mass remained unchanged (Table 3). These significant biometric improvements were maintained by participants 1 month after the intervention (Supplementary Table 4). There were no differences in biometric improvements between the weekly and the bi-weekly groups (Table 3 and Supplementary Table 4). Percent changes in biometrics were shown in Supplementary Tables 5, 6.

3.3 Changes in dietary habits

Compared to the baseline, in total, there were significant decreases in total fat intake and sodium intake ($p = 0.03$ and 0.008, respectively, Table 4). When we compared the changes in dietary intakes between the weekly and the bi-weekly groups, the tendencies of changes were almost identical except for fruit intake (p for interaction=0.04). Percent changes in dietary intakes were shown in Supplementary Table 7. As shown in Figure 4, participants' obesity-related eating behaviors tended to improve from baseline to post-intervention in total score and significantly improved in the sense of hunger ($p = 0.04$, the decreased score means the improvement of eating behaviors). In addition, based on the self-reported questionnaire, the percentage of skipping breakfast tended to decrease from 41.2 to 17.6% ($p = 0.23$) whereas there were no differences in skipping lunch (5.9 to 5.9%, $p = 1.00$) and dinner (0 to 0%, $p = 1.00$). For cooking frequency, we observed no differences from baseline until the end of the intervention (from 6.6 times/week to 6.3 times/week, $p = 0.62$).

3.4 Changes in physical activity

As shown in Table 5, the amount of physical activity assessed using the IPAQ tended to increase from 21.6 ± 3.7 MET-h/week at baseline to 25.6 ± 4.3 MET-h/week in the post-intervention assessment ($p = 0.20$). The mean changes of physical activity from baseline to post-intervention were 4.6 ± 3.3 MET-h/week in weekly group and 2.8 ± 7.2 MET-h/week in bi-weekly group (p for interaction=0.79). Percent changes in physical activity were shown in Supplementary Table 8. We also assessed the amount of physical activity including dairy activities during the intervention by using smart bands. As shown in Supplementary Table 9, the amount of physical activity assessed by the smart bands were 29.0 ± 4.4 MET-h/week in total, 36.4 ± 6.7 MET-h/week in weekly group, and 20.5 ± 3.1 MET-h/week in bi-weekly group (p for interaction = 0.07).

TABLE 3 Changes in biometrics at baseline and post-intervention.

	Baseline	Post-intervention	Mean change	*p*	p for interaction
Weight, kg					
Weekly ($n = 10$)	81.2 ± 3.3	80.0 ± 3.4	−1.2 ± 0.3	<0.001	
Bi-weekly ($n = 7$)	84.1 ± 5.5	82.4 ± 5.0	−1.8 ± 0.8	0.04	
Total ($n = 17^a$)	82.4 ± 2.9	80.9 ± 2.8	−1.4 ± 0.4	<0.001	0.42
BMI, kg/m^2					
Weekly ($n = 10$)	27.3 ± 0.8	26.9 ± 0.8	−0.4 ± 0.1	<0.001	
Bi-weekly ($n = 7$)	27.6 ± 1.7	27.0 ± 1.5	−0.6 ± 0.3	0.04	
Total ($n = 17$)	27.4 ± 0.8	26.9 ± 0.8	−0.5 ± 0.1	<0.001	0.45
SBP, mmHg					
Weekly ($n = 10$)	134 ± 3	132 ± 6	−2 ± 4	0.60	
Bi-weekly ($n = 7$)	140 ± 7	127 ± 4	−13 ± 5	0.02	
Total ($n = 17$)	136 ± 4	130 ± 4	−7 ± 2	0.05	0.09
DBP, mmHg					
Weekly ($n = 10$)	88 ± 2	83 ± 3	−5 ± 2	0.03	
Bi-weekly ($n = 7$)	87 ± 4	84 ± 4	−2 ± 3	0.46	
Total ($n = 17$)	87 ± 2	83 ± 2	−4 ± 2	0.03	0.49
Body fat mass, kg					
Weekly ($n = 10$)	22.5 ± 2.2	21.5 ± 2.2	−1.0 ± 0.2	<0.001	
Bi-weekly ($n = 7$)	25.0 ± 3.4	22.9 ± 2.7	−2.1 ± 0.8	0.03	
Total ($n = 17$)	23.5 ± 1.8	22.1 ± 1.7	−1.5 ± 0.4	<0.001	0.15
Lean mass, kg					
Weekly ($n = 10$)	55.6 ± 2.5	55.5 ± 2.5	−0.2 ± 0.3	0.63	
Bi-weekly ($n = 7$)	56.1 ± 2.2	56.3 ± 2.2	0.3 ± 0.7	0.71	
Total ($n = 17$)	55.8 ± 1.7	55.8 ± 1.7	0.0 ± 0.4	0.96	0.54

Values are means ± standard errors (SEs). [a]n = 17 instead of 20 because measurements were not available for three participants because of work commitments. The baseline and post-intervention differences were tested using linear mixed effect models. $p < 0.05$ indicates statistically significant. BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure.

3.5 Changes in sleeping habit

From the baseline to post-intervention, the Athens Insomnia Scale changed from 5.8 ± 0.9 to 4.8 ± 1.1 ($p = 0.19$, Table 5). Percent changes in the Athens Insomnia Scale were shown in Supplementary Table 8. The sleep duration during the intervention assessed by using smart bands was 6.3 ± 0.3 hour in all participants, 6.7 ± 0.3 hour in weekly group, and 5.9 ± 0.4 hour in bi-weekly group (p for interaction = 0.20, Supplementary Table 9).

3.6 Changes in health-related quality of life

Changes in the summary scores and each domain score of HR-QoL were shown in Supplementary Table 10. From the baseline to post-intervention, there was a significant improvement in mental component score ($p = 0.01$). For the eight domains of HR-QoL, bodily pain, general health, and vitality were significantly improved ($p = 0.03$, 0.006, and $p = 0.047$, respectively). Percent changes in HR-QoL scores were shown in Supplementary Table 11. There was no difference in the improvements of summary scores and domains of HR-QoL between weekly and bi-weekly group (all p for interaction ≧ 0.33).

4 Discussion

To our knowledge, the current study is the first feasibility study of a Japanese Teaching Kitchen program involving Japanese employees with obesity. Our results suggest that the Japanese Teaching Kitchen program is feasible in this workplace with high program completion rates (91.7% for the weekly group and 75.0% for the bi-weekly group); and, that this program led to improvements in participants' biometrics, lifestyle behaviors, and HR-QoL.

In line with Teaching Kitchen programs originally developed in the US (1, 2), our Japanese Teaching Kitchen program offers a comprehensive approach to modify participants' diet, exercise,

TABLE 4 Changes in energy, nutrient and food intakes at baseline and post-intervention.

	Baseline	Post-intervention	Mean change	p	P for interaction
Total energy intake, kcal					
Weekly ($n = 10$)	2176 ± 71	2133 ± 63	−43 ± 49	0.39	
Bi-weekly ($n = 7$)	2247 ± 55	2162 ± 40	−85 ± 28	0.01	
Total ($n = 17$)	2205 ± 47	2145 ± 40	−60 ± 30	0.06	0.52
Protein, g					
Weekly ($n = 10$)	86.3 ± 1.8	85.2 ± 1.9	−1.2 ± 1.2	0.33	
Bi-weekly ($n = 7$)	88.9 ± 1.8	86.6 ± 0.9	−2.3 ± 1.1	0.07	
Total ($n = 17$)	87.4 ± 1.2	85.8 ± 1.1	−1.6 ± 0.8	0.05	0.50
Total fat, g					
Weekly ($n = 10$)	64.0 ± 1.1	63.1 ± 1.1	−1.0 ± 0.9	0.3	
Bi-weekly ($n = 7$)	65.9 ± 0.8	63.8 ± 0.9	−2.1 ± 0.7	0.01	
Total ($n = 17$)	64.8 ± 0.7	63.4 ± 0.7	−1.4 ± 0.6	0.03	0.38
Carbohydrate, g					
Weekly ($n = 10$)	286.6 ± 14.8	283.2 ± 12.8	−3.3 ± 10.0	0.75	
Bi-weekly ($n = 7$)	288.3 ± 11.3	282.0 ± 6.1	−6.3 ± 6.4	0.34	
Total ($n = 17$)	287.3 ± 9.6	282.7 ± 7.8	−4.5 ± 6.3	0.48	0.82
Total dietary fiber, g					
Weekly ($n = 10$)	17.9 ± 0.5	17.7 ± 0.5	−0.2 ± 0.4	0.66	
Bi-weekly ($n = 7$)	19.2 ± 1.2	18.8 ± 0.9	−0.4 ± 0.6	0.51	
Total ($n = 17$)	18.4 ± 0.6	18.2 ± 0.5	−0.3 ± 0.3	0.41	0.73
Sodium, g					
Weekly ($n = 10$)	10.7 ± 0.4	10.3 ± 0.4	−0.4 ± 0.3	0.15	
Bi-weekly ($n = 7$)	11.7 ± 0.7	10.8 ± 0.4	−0.9 ± 0.3	0.02	
Total ($n = 17$)	11.1 ± 0.4	10.5 ± 0.3	−0.6 ± 0.2	0.008	0.24
Vegetables, g					
Weekly ($n = 10$)	338.6 ± 9.1	349.5 ± 15.5	10.9 ± 16.1	0.51	
Bi-weekly ($n = 7$)	390.7 ± 35.2	412.0 ± 24.6	21.3 ± 30.9	0.5	
Total ($n = 17$)	360.1 ± 16.1	375.2 ± 15.2	15.2 ± 15.3	0.33	0.75
Fruits, g					
Weekly ($n = 10$)	131.9 ± 4.8	129.3 ± 4.7	−2.6 ± 1.4	0.09	
Bi-weekly ($n = 7$)	140.7 ± 14.6	150.6 ± 20.5	9.9 ± 6.8	0.17	
Total ($n = 17$)	135.5 ± 6.4	138.1 ± 8.9	2.5 ± 3.2	0.43	0.04
Fish and shellfish, g					
Weekly ($n = 10$)	101.1 ± 2.2	101.9 ± 3.2	0.8 ± 2.3	0.73	
Bi-weekly ($n = 7$)	106.1 ± 5.1	105.3 ± 3.7	−0.9 ± 6.2	0.89	
Total ($n = 17$)	103.2 ± 2.5	103.3 ± 2.4	0.1 ± 2.8	0.97	0.78
Meats, g					
Weekly ($n = 10$)	73.8 ± 2.6	72.1 ± 4.8	−1.7 ± 5.0	0.74	
Bi-weekly ($n = 7$)	79.3 ± 5.0	69.1 ± 4.9	−10.1 ± 3.8	0.02	
Total ($n = 17$)	76.1 ± 2.5	70.9 ± 3.4	−5.2 ± 3.4	0.14	0.22

(Continued)

TABLE 4 (Continued)

	Baseline	Post-intervention	Mean change	p	P for interaction
Eggs, g					
Weekly ($n = 10$)	35.5 ± 0.4	34.9 ± 0.7	−0.6 ± 0.7	0.38	
Bi-weekly ($n = 7$)	37.3 ± 1.7	36.7 ± 0.6	−0.6 ± 1.3	0.66	
Total ($n = 17$)	36.2 ± 0.7	35.6 ± 0.5	−0.6 ± 0.6	0.36	0.98
Dairy, g					
Weekly ($n = 10$)	194.1 ± 42.7	162.4 ± 22.2	−31.7 ± 43.7	0.48	
Bi-weekly ($n = 7$)	195.7 ± 38.8	187.4 ± 17.1	−8.3 ± 34.2	0.81	
Total ($n = 17$)	194.8 ± 28.9	172.7 ± 14.8	−22.1 ± 28.7	0.45	0.70
Alcoholic beverages, g					
Weekly ($n = 10$)	8.9 ± 4.4	4.3 ± 1.7	−4.7 ± 3.6	0.21	
Bi-weekly ($n = 7$)	11.2 ± 4.9	9.6 ± 4.2	−1.6 ± 0.9	0.11	
Total ($n = 17$)	9.9 ± 3.2	6.5 ± 2.0	−3.4 ± 2.2	0.12	0.64
Confectionaries, g					
Weekly ($n = 10$)	24.5 ± 5.2	19.2 ± 4.7	−5.3 ± 3.6	0.16	
Bi-weekly ($n = 7$)	30.6 ± 7.3	21.7 ± 10.2	−8.9 ± 7.1	0.24	
Total ($n = 17$)	27.0 ± 4.2	20.2 ± 4.8	−6.8 ± 3.5	0.06	0.63

Values are means ± standard errors (SEs). The baseline and post-intervention differences were tested using linear mixed effect models. $p < 0.05$ indicates statistically significant.

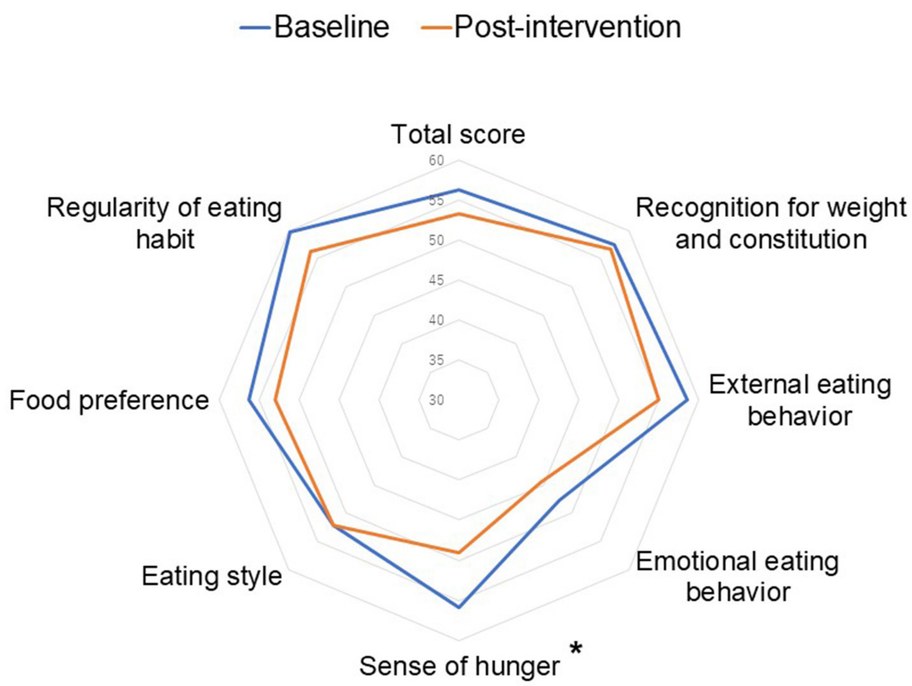

FIGURE 4
Comparisons of obesity-related eating behaviors between baseline and post-intervention ($n^a = 16$). The baseline and post-intervention differences were tested using linear mixed effect models. $^a n = 16$ instead of 17 because of the missing value. *indicates $p < 0.05$.

and mindfulness, incorporating both didactic and experimental learning. In face-to-face classes, lecturers introduced various recent scientific evidence on nutrition, physical activity, and sleeping habits to deepen participants' understanding of healthy lifestyles. In addition, lecturers offered simple and practical measures to modify their diet and other lifestyle factors. For example, the participants learned to better assess the differences in calories in each type of meat (e.g., learned the calories of loin vs. filet

TABLE 5 Changes in physical activity and Athens insomnia scale at baseline and post-intervention.

	Baseline	Post-intervention	Mean change	*p*	p for interaction
Physical activity, MET-h/week					
Weekly ($n = 10$)	22.8 ± 5.0	27.4 ± 6.1	4.6 ± 3.3	0.17	
Bi-weekly ($n = 5$)	19.2 ± 5.1	22.0 ± 5.1	2.8 ± 7.2	0.71	
Total ($n = 15$)	21.6 ± 3.7	25.6 ± 4.3	4.0 ± 3.1	0.20	0.79
Athens Insomnia Scale					
Weekly ($n = 10$)	4.4 ± 0.6	3.4 ± 1.1	−1.0 ± 0.9	0.30	
Bi-weekly ($n = 6$)	8.4 ± 1.9	7.0 ± 2.2	−1.2 ± 1.6	0.48	
Total ($n = 16$)	5.8 ± 0.9	4.8 ± 1.1	−1.1 ± 0.8	0.19	0.92

Values are means ± standard errors (SEs). Physical activities were assessed using the international physical activity questionnaire (IPAQ). n = 15 for physical activity and 16 for Athens insomnia scale instead of 17 because of missing values. The baseline and post-intervention differences were tested using linear mixed effect models. $p < 0.05$ indicates statistically significant. MET, metabolic equivalent.

of beef) and learned the difference in calories when employing different cooking methods (e.g., learned the calories of dishes made when frying vs. grilling ingredients) that enabled them to choose healthier foods and dishes to lower calorie intakes. In addition, participants learned about aerobic and resistance exercises that are appropriate for them in the exercise lectures and breathing techniques for relaxation in the mindfulness lecture. Following these lectures, participants made dishes using these techniques, and enjoyed the simplicity and deliciousness of what they cooked. This type of educational approach integrating lectures and culinary experience effectively motivated participants to incorporate what they learned into their daily lives. It is noteworthy that this approach enabled participants to improve their dietary intakes without strict prohibitions and concomitant feelings of perceived deprivations which often accompany usual diet related therapies, the majority of which are restrictive in nature.

One of the originalities of the Japanese Teaching Kitchen program is that the program made use of the effectiveness of *dashi*, the fish soup stock traditionally used in Japan, to increase food satisfaction of the participants. *Dashi* contains a lot of umami, which is one of the basic tastes (25). Umami stimulates the amygdala in the brain to increase food satisfaction (26) and suppresses overeating (27). In addition, *dashi* contains multiple umami components such as glutamic acid (mainly from kelp), inosinic acid (bonito flakes), and guanylic acid (shiitake mushrooms), and strong umami stimulation is obtained by synergistic effects of multiple umami components (28, 29). Actually, in this study we observed the significant decrease in sodium intake by Japanese Teaching Kitchen program, which is in line with a previous study reported that consumption of umami-rich diets decreased salt intake (30). In addition, the improvements in other dietary intakes as well as sodium intake and obesity-related eating behaviors shown in this study indicate that the program contents were effective for the population.

Another original approach in the Japanese Teaching Kitchen program is that we have developed a web app and used it in conjunction with the face-to-face classes. The app enabled participants to access class materials, record what they did to improve their lifestyles, and receive message from physicians and dietitians based on their records. In the current study the participants could only use the app during the intervention (four weeks for weekly group and eight weeks for bi-weekly group) to assess the feasibility of this app-based approach. As the next step, we will modify the app to maintain the efficacy of the Japanese Teaching Kitchen program even after the intervention finishes and examine its' effectiveness and potential for improvement in another study.

In this study, we randomly divided participants into weekly and bi-weekly groups independent from their preferences to see which is more feasible and effective. The weekly group showed higher program completion rates than the bi-weekly group and may be more acceptable to Japanese adults. There were no significant differences in satisfaction with class contents between the two groups, except for the mindfulness lecture. This difference may be influenced by the small number of participants who completed the satisfaction questionnaire ($n = 6$) in the bi-weekly group. It is worth noting that the completion rates and patients' satisfaction with the program in total were relatively high regardless of their preferences for weekly vs bi-weekly classes. However, at the same time, the participants' preferences may have affected the completion rates and satisfaction. We will assess these factors in another intervention study in which designing all participants will take classes at the same frequency.

The current study is the first feasibility study of Japanese Teaching Kitchen program and showed the feasibility and effectiveness of the program in various aspects. However, there are several limitations that should be noted. First, all participants were employees of one Japanese company (NISSIN Foods Holdings). Although the company had no input into the design of the study, or analysis of the data collected, their cooperation in recruiting participants (sending emails for recruitment and allowing participants to take the Teaching Kitchen program in their working time) will need to be reassessed in subject populations from other employers and work settings. Second, as the current study had a short-term intervention and follow-up period, we could not evaluate the long-term efficacy of the intervention. Third, the questionnaires used in the study to examine the lifestyle behaviors, HR-QoL, and satisfaction were based on self-report. Although most of the questionnaires were highly validated and consistent with previous studies on Teaching Kitchen programs in Western countries (1, 3, 4, 31, 32), there may be self-reporting bias. Fourth, as a pilot study, the current study design had a small sample size with the lack of a control group. In addition, the participants of this study were predominantly male. However, the previous studies of lifestyle intervention for obesity in Japanese subjects showed that the effectiveness of such an approach was independent of gender (33, 34), which implies that the Japanese Teaching Kitchen is expected to be effective for women as well. Based on these limitations, the interpretation and generalizability of what we found in this study might be limited. As a next step, we will conduct a randomized controlled trial with a longer intervention and follow-up phase, with an adequate sample size of participants from diverse backgrounds. Such a follow-on trial will be necessary to establish scientific evidence in support of the long-term effectiveness of the Japanese Teaching Kitchen program, leading to further research development and social implementation of this novel approach in Japan and other Asian countries.

5 Conclusions

The current study showed that the Japanese Teaching Kitchen program used in this pilot study is feasible and may positively impact the disease risk profiles of Japanese adults with obesity, high blood pressure, and other chronic diseases associated with sub-optimal diets and lifestyles. These findings from an initial feasibility study of a teaching kitchen curriculum in Japan suggest that future studies in this area are worth pursuing to address obesity and obesity-related diseases.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by the Institutional Ethics Review Board of Osaka University Hospital. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

MB: Conceptualization, Funding acquisition, Investigation, Methodology, Project administration, Resources, Visualization, Writing—original draft. SK: Data curation, Investigation, Resources, Writing—review & editing. AN: Investigation, Writing—review & editing. TH: Investigation, Writing—review & editing. HO: Data curation, Investigation, Resources, Writing—review & editing. CI: Writing—review & editing. YH: Writing—review & editing. YukF: Writing—review & editing. YuyF: Investigation, Writing—review & editing. HN: Investigation, Writing—review & editing. JK: Writing—review & editing. IM: Data curation, Formal analysis, Software, Writing—review & editing. YusF: Investigation, Visualization, Writing— review & editing. AY: Investigation, Writing—review & editing. TS: Writing—review & editing. TK: Writing—review & editing. IS: Funding acquisition, Supervision, Writing—review & editing. DE: Conceptualization, Methodology, Supervision, Writing—review & editing.

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Conflict of interest

MB and HO are members of the Department of Lifestyle Medicine, a sponsored course endowed by Kubara Honke Group Co., Ltd. YusF and AY were employed by the Cancerscan, Inc, Tokyo, Japan. TS and TK were employed by Kubara Honke Group Co., Ltd, Fukuoka, Japan.

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The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2023.1258434/full#supplementary-material

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Dietary behaviors of rural residents in northeastern China: implications for designing intervention information and targeting high-risk population

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Background: Dietary behavior is a pivotal modifiable determinant in reducing the occurrence of obesity/overweight and chronic non-communicable diseases. Improving the dietary behavior of rural residents in China is imminent due to the poor performance of their dietary behavior. Nutrition knowledge and health literacy are considered as elements that are linked intimately to healthy dietary behaviors but lack research in the Chinese setting.

Purpose: The study is designed to explore the relationship between nutritional knowledge, health literacy and dietary behaviors and to analyze the performance under different demographic characteristics.

Methods: A face-to-face survey of 400 rural residents on their nutrition knowledge, functional health literacy and dietary intake of five food categories consisting of 32 items was conducted based on a validated questionnaire. Descriptive analysis, difference test including ANOVA, *t*-test and non-parametric test, and multivariate linear regression were used for data analysis.

Results: The results indicate that declarative nutrition knowledge, individuals' information application capacity, and dietary behaviors, especially the intake of fruits, dairy and beans, and vegetable are not ideal and requires improvement. Male, elder, low-income, unmarried, and low-education populations performed significantly worse and were the high-risk group. Procedural nutrition knowledge, information access capacity, information understanding capacity, and information application capacity have remarkable effects on better dietary behavior.

Conclusion: This study provides evidence-based guidance for prioritizing information and populations for healthy dietary interventions.

KEYWORDS

dietary behavior, health literacy, nutrition knowledge, behavior intervention, health promotion

1 Introduction

The Chinese population is switching from a plant-based diet to western-style diets high in fat and animal-based foods (1), and malnutrition has significantly decreased. But, the proportion of residents with an imbalanced diet and overnutrition has gradually increased, and there is a significant expansion in the prevalence of overweight, obesity and patients with chronic non-communicable diseases (2). The proportion of adults with a BMI ≥ 25 kg/m^2 have increased from 20% (about 150 million) in 1992 to nearly 50% (about 550 million) in the most recent national survey (3). Dietary behavior is one of the key modifiable determinants for reducing obesity/overweight and chronic disease prevalence in China (4, 5). The Chinese government pays significant attention to improving the residents' dietary and successively formulated the Outline of the Health China 2030 Plan (6) and the National Nutrition Plan (2017–2030) (7).

Currently, the incidence of chronic diseases is higher in urban areas than in rural areas in China, and the growth rate of rural areas is higher than that in urban areas, which is related to poor dietary behavior in rural residents (8). China, however, is a developing country with a rural population of over 500 million, and policy implementation capacity in rural areas is extremely limited (9). It is necessary to identify priority intervention contents and groups in order to conduct interventions more effectively.

To prioritize the intervention information, two domains that are closely associated to dietary behavior, nutritional knowledge and health literacy, were considered. The prevailing research state that nutrition knowledge has an important role in health behavior (10, 11), including dietary behavior (12, 13). But some intervention experiments based on knowledge courses have yielded mixed results, and such differences may be due to interventions targeting different types of knowledge. Some studies have indicated that knowledge is not a simple structure, but multiple types (14). In cognitive psychology, knowledge can be classified as declarative knowledge or procedural knowledge. Declarative knowledge is knowing about facts and objects, while procedural knowledge is pertaining to the execution of behavior (15). Several scholars have analyzed the relationship with dietary behavior using procedural nutrition knowledge (PNK) and declarative nutrition knowledge (DNK), respectively (16, 17), but limited studies have considered both types of knowledge, especially for Chinese populations.

Health literacy has become increasingly important in recent years because evidence supports its association with healthy behaviors (18). Health literacy also plays an important role in health education and promotion (19) and is negatively correlated with national healthcare utilization and expenditure (20). The U.S. Department of Health and Human Services has defined health literacy as the ability of individuals to access, process, and understand health information to make decisions about treatment and their health in general (21). Regarding dietary behaviors, some studies have found that health literacy motivates individuals to make healthier dietary food choices (22, 23), but others have demonstrated the reverse effect (18). The role of health literacy in the promotion of dietary behavior of the Chinese residents remains to be clarified. Functional health literacy (FHL) is the most common type of health literacy assessment, and this study is based on the FHL scale to evaluate individuals' capacity to access, understand, and apply health information (24–26).

Priority intervention populations were identified by examining differences in nutrition knowledge, health literacy, and dietary behavior between groups. Previous studies have indicated that FHL, nutrition knowledge, and dietary behavior are affected by demographic characteristics. Characteristics such as gender (27), age (28), region (urban or rural) (29), occupation (30), education level, household income, and self-reported health status (31) were found to affect health literacy. Xu et al. (32) found that significant differences in nutritional knowledge across demographic characteristics, which in turn influenced their dietary habits and health. Education level, gender, BMI, and exposure to chronic disease were found to influence individuals' nutritional knowledge and dietary behavior (32–35). To identify priority intervention populations in a multi-dimensional way, a wide range of demographic variables, including gender, age, education, marital status, income, body mass index (BMI), and chronic disease status, were selected to identify high-risk groups.

In summary, this study collected data on the nutrition knowledge, FHL, and dietary behavior of rural residents in China to serve three objectives: (1) to assess the current dietary behavior, FHL, and nutrition knowledge of rural residents in China; (2) to examine the differences in dietary behavior, FHL, and nutrition knowledge between different populations; and (3) to analyze the relationship between health literacy and nutrition knowledge and dietary behavior. This study provides guidelines for determining the priority intervention information and populations for healthy dietary intervention programs in rural China. Figure 1 shows the research framework.

2 Materials and methods

2.1 Questionnaire design

To investigate the nutrition knowledge, FHL, and dietary behavior, we designed a questionnaire for the target population. The questionnaire in this study had four parts: (1) demographic characteristics; (2) nutrition knowledge; (3) FHL; and (4) a food frequency questionnaire (FFQ). Demographic characteristics included gender, age, marital status, education level, annual household income, BMI, and chronic disease status. Nutrition knowledge included the PNK and DNK, and their items are from the studies of Dickson-Spillmann et al. (36) and Ju (37), respectively. The form of categorical judgment was chosen as the response to the nutrition knowledge, and all nutrition knowledge questions had only one correct answer. FHL included information access capacity (IACC), information understanding capacity (IUC), and information application capacity (IAPC). We selected the FHL questions from the health literacy questionnaire proposed by Osborne et al. (38) and FHL was measured using a five-point Likert scale. The original PNK and FHL questions were written in English. The questions were translated into Chinese, and two bilingual experts on dietary behavior corrected the semantics of the questionnaire and ensured translation equivalence. An initial set of items was formed consisting of seven items for measuring PNK, six items for measuring DNK, and nine items for measuring FHL.

The FFQ was used as the *dietary intake questionnaire* to investigate food consumption frequency and intake in the past week in the subject. Food was divided into five categories (i.e., meat, poultry, fish, and eggs; dairy and beans; grain; fruit; and vegetable), and specific

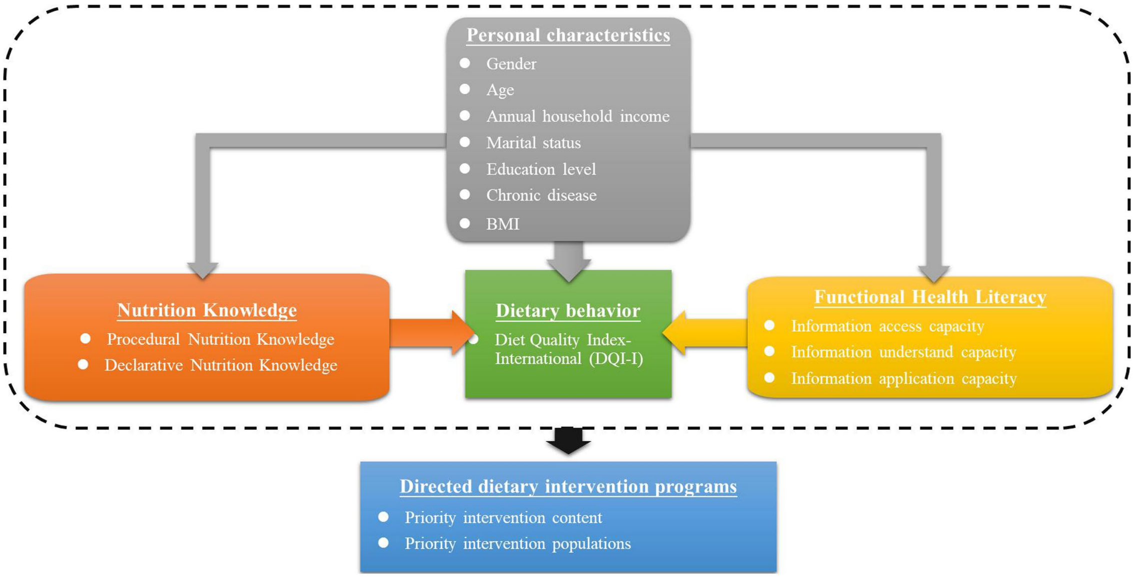

FIGURE 1
Research framework.

food names were listed in every category as a reference for the subject to fill in the food consumption frequency and food intake. To increase the suitability of the questionnaire, the types of food consumed with high frequency in the survey area were pre-survey by a group of 30 rural residents. The 24 most commonly consumed foods were listed in the food frequency questionnaire, and a blank area was present for the subject to add in foods that were not mentioned. Two forms were used for food consumption frequency. Foods with a high consumption frequency were written as "X times/day," and foods with a low consumption frequency were written as "W times/week (7 days)." The question was not filled in if the food was not consumed in the past week. When filling in the food intake, the *schematic diagram of standard food weight* provided by the investigator was used to estimate the weight of the food consumed each time. See Appendix for *schematic diagram of standard food weight* (Supplementary Figure S1) and *dietary intake questionnaire* (Supplementary Table S1).

Three instruments, i.e., content validity, internal consistency, and test–retest reliability, were applied to evaluate the reliability of the questionnaire. First, an expert group was organized to assess the content validity of the questionnaire. The group is composed of two professors, one assistant professor, and three doctoral candidates, whose research areas are focused on nutrition and consumer behavior. Explain to the expert group the study objectives, questionnaire content, and assessment procedure via email or WeChat (a kind of instant messaging social software), and invite participation after receiving consent (39). The assessment included question clarity and understanding, relationship to the study objective, overlap between questions, answer rationality, and conformance to China's context. In the light of the expert group's comments, we deleted some questions that were not clearly stated. For example, one item which asked *whether it was unhealthy to eat an excessive proportion of fruits and vegetables in the daily diet* was deleted because it mentioned the intake of both fruits and vegetables, which is a double-barrelled question, and this may have confused respondents. Some questions were optimized, i.e., the item "*A balanced diet is one that has the same intake of all nutrients*" was modified to "*A balanced diet is one that has the same intake of all types of food*," as nutrients are academic jargon that are difficult to understand for rural residents. Subsequently, a preliminary study was carried out on 30 rural residents. Each respondent completed the questionnaire from 30 to 45 min. We used Cronbach's α coefficient to assess the internal consistency. Cronbach's α coefficient of FHL (including information access capacity, information understanding capacity, and information application capacity) was above 0.8, and the Cronbach's α coefficients of PNK and DNK were 0.597 and 0.538, respectively. In some studies involving the internal consistency of the items, especially for knowledge items, it was considered acceptable if it was close to the threshold ($\alpha = 0.6$) (40, 41). Nunnally (42) first version of the introduction to Cronbach's α coefficients suggested that the minimum accepted ranges in preliminary studies were 0.5 to 0.6. Thus, the internal consistency of items measuring the FHL, PNK, and DNK is acceptable. To further evaluate the stability of the questionnaire over time, 20 subjects were randomly selected for a telephone interview 3 days after the first investigation, and 10 questions in the questionnaire were randomly selected for the interviewee to answer. The two investigations were conducted 3 days apart to decrease memory bias, and 10 questions were randomly selected to reduce sequence bias. The Pearson correlation coefficient of the two scores was 0.86 ($p < 0.01$), showing that the questionnaire has high test–retest reliability.

2.2 Data collection

2.2.1 Survey site

Three provinces in northeastern China, which are Heilongjiang, Jilin, and Liaoning, were selected as survey areas. Northeastern China has the highest latitude and cold climate, and these three provinces are the main grain-producing regions of China and are major agricultural

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provinces, which have shaped unique dietary patterns. The daily diet of residents in northeastern China contained excess salt, and long-term high salt intake is an important factor causing chronic diseases (43, 44). Moreover, due to the long and cold winters in northeastern China, residents usually consume grains and meat with high calorific value to withstand the cold weather, leading to a lower proportion of fresh fruits and vegetables in their diet. Hu et al. (45) found that increasing fruit and vegetable intake in northeastern China could decrease the risk of lung cancer. Considering the high health risks associated with this unique dietary pattern, there is a great tendency to conduct healthy eating interventions in these regions.

2.2.2 Questionnaire survey

Ten investigators were recruited to conduct the survey. The survey was carried out in the form of face-to-face interviews. To ensure the credibility and reliability of the survey, training for investigators was implemented. The training included an introduction to the purpose of the survey, an explanation of the meaning of each question and how it should be answered, procedures for conducting the survey, and tips for dealing with unexpected situations that they may encounter during face-to-face interviews. The survey was conducted in the homes of the respondents. To ensure the representativeness of the sample, ten villages in three provinces were selected as survey locations by stratified random sampling. The sampling pattern is to select one city in each province and the corresponding village in each city. As Liaoning Province has the largest number of residents living in rural areas, four villages were selected in Liaoning Province and three villages were selected in the other two provinces. Forty residents in each village were recruited to conduct the survey. To increase randomness, one family was chosen to visit in every geographically separated 3 households. The questionnaire survey was completed from June to August 2019.

Based on the Bartlett et al. (46) formula shown below, the required sample size was estimated to be 323. Given the non-response rate, a total of 400 questionnaires were distributed (Eq. 1).

$$n = \frac{\dfrac{Z^2_{\frac{\alpha}{2}} pq}{d^2}}{1 + \dfrac{1}{N}\left(\dfrac{Z^2_{\frac{\alpha}{2}} pq}{d^2} - 1\right)} \tag{1}$$

where n denotes the required sample size, d denotes a 5% margin with error (the standard value = 0.05), Z denotes a 95% confidence interval $\left(Z_{\frac{\alpha}{2}} = 1.96\right)$, p denotes the proportion of the target population ($p = 0.7$), and q denotes $1 - p$ ($q = 0.3$). N represents the population size, which, according to the 2018 statistics, is 34.84 million rural residents in the three provinces of Northeast China, i.e., $N = 348{,}400{,}000$.

Three hundred and seventy questionnaires were returned, of which 344 were valid questionnaires with no missing values, with a response rate of 92.5% (370/400) and a validity rate of 93.0% (344/370). Three hundred and forty-four valid samples are above the threshold number of required sample size ($n = 323$).

2.3 Data analysis

Amos (version 22.0) and SPSS (version 23.0) were applied for statistical analysis. The frequency (count and percentage) of every option was calculated, and the mean score and standard deviation (S.D.) of every question was calculated. Kurtosis and skewness were used to test the normality of the variables. It is considered that the variables are normally distributed when the absolute values of kurtosis index and skewness index are less than 7 and 2, respectively (47). ANOVA and *t*-test was used to compare the differences when data were normally distributed and variance was homogeneous. In other situations, nonparametric tests (Mann–Whitney U test or Kruskal–Wallis test) were used. Ordinary least squares (OLS) were used to analyze the relationship between nutrition knowledge, FHL, and dietary behavior. Variance inflation factor (VIF) was applied to check the multicollinearity of each fitted model (48).

For knowledge questions, 1 point and 0 point were given for a correct and incorrect answer, respectively. The PNK score was from 0 to 7 and the DNK score was from 0 to 6, and total nutrition knowledge was from 0 to 13. The five-point Likert scale was scored ranging from one to five. The FHL scale contains 9 items with scores ranging from 9 to 45. The three subscales, IACC, IUC, and IAPC, each contained three items scored from 3 to 15. Referring to Nakayama et al. (49), four levels of health literacy were defined based on average FHL scores: 9–23 as inadequate, 24–31 as problematic, 32–38 as sufficient, and 39–45 as excellent.

The scientific community has given diverse instruments for diet assessment from different perspectives. The Dietary Quality Index-International (DQI-I), one of the composite measures that enable a more precise identification of the relationship between overall diet quality scores and the risk of diet-related diseases, was adopted because it is considered a valid tool to make comparisons across countries and regions (50–52). Notably, the DQI-I in the study was calculated depending on the intake of the five food groups in accordance with the recommended values without reference to micronutrients and macro-nutrients. The reason for this calculation format is that the dietary pattern recommended by the Chinese Dietary Guidelines mainly focuses on the intake of these five food groups, and that the adequate intake of these five food groups may, to a certain extent, meet the body's needs for various types of nutrients and reduce chronic diseases (53). The first category (meat, poultry, fish, and eggs) included eight types of foods; the second category (dairy and beans) included five types of foods; the third category (grain) included seven types of foods; the fourth category (fruit) included six types of foods; and the fifth category (vegetable) included six types of foods. The daily intake for each food category (y_i) was equal to the sum of all food intake under that category. Refer to Eqs. (2–6). For high consumption frequency food, the respondent would write the number of times the food was consumed each day (X_i) and the amount of each intake (M_i). For less consumption frequency food, the respondent would write the number of times the food was consumed each week (W_i) and the amount of each intake (M_i), y_i is the daily intake of each category of food:

$$y_{meat,poultry,fish,and\ eggs} = \sum_{i=1}^{i=8}\left(M_i \times X_i + M_i \times W_i / 7\right) \tag{2}$$

$$y_{dairy\ and\ beans} = \sum_{i=9}^{i=13} \left(M_i \times X_i + M_i \times W_i / 7 \right) \quad (3)$$

$$y_{grain} = \sum_{i=14}^{i=20} \left(M_i \times X_i + M_i \times W_i / 7 \right) \quad (4)$$

$$y_{fruit} = \sum_{i=21}^{i=26} \left(M_i \times X_i + M_i \times W_i / 7 \right) \quad (5)$$

$$y_{vegetable} = \sum_{i=27}^{i=32} \left(M_i \times X_i + M_i \times W_i / 7 \right) \quad (6)$$

The 2022 Chinese Dietary Guideline recommends that the recommended intake for five food categories (i.e., meat, poultry, fish, and eggs; dairy and beans; grain; fruit; and vegetable) is 150 g/day, 300 g/day, 250 g/day, 200 g/day, and 300 g/day, respectively. If the intake of a category was lower than the recommended intake; it was scored as 0; otherwise, it was scored as 3. The range of DQI-I is from 0 to 15.

3 Results

3.1 Profile of samples

The sample characteristics of the survey is shown in Table 1. There were slightly more female respondents (57%) in the sample than male respondents (43%), 59% of respondents were between the ages of 35 and 54 years old, nearly 50% of the respondents having an annual household income range from RMB 36,000–84,000, equivalent to US$ 4,956–11,565.[1] The proportion of married respondents (73%) in the sample is substantial, and more than 50% of the respondents have a junior high school education and below, which is consistent with the lack of young and well-educated people in rural China (54). A significant proportion of the sample, about 36%, were suffering from chronic diseases, and more than 50% of the respondents were not at a healthy weight, which is consistent with the results of previous studies that suggest that the health status of rural residents in Northeast China is a matter of concern (55).

3.2 Descriptive data analysis results

As shown in Table 2, the mean PNK score was 4.66 (range from 0 to 7), and the question with the lowest accuracy rate was *meat should be the basis of our daily diet* (45.9%), which the highest accuracy rate was *fat is always bad for your health, so you should avoid it as much as possible* (70.6%). The mean DNK score was 2.53 points (range from 0 to 6), and the question with the lowest accuracy rate was *daily salt intake should not exceed* (27.6%), which the question with the highest accuracy rate was *which of the following food groups contains the most protein* (65.7%). The mean score of total nutritional knowledge was 7.19 (range from 1 to 13).

As shown in Table 3 and Figure 2, the average FHL score was 26.52 (range from 9 to 45, S.D. = 6.49), with 80% of respondents ($n = 275$) having a health literacy status of inadequate/problematic, and only 3% of respondents ($n = 9$) having excellent health literacy. For the three sub-structures of the FHL, the highest mean score was IACC (9.78 ± 3.55), followed by the IUC (9.19 ± 3.05), with the lowest mean score for the IAPC (7.55 ± 2.81). The question with the highest mean score was *I can obtain the healthy diet information that I need from text search* (3.35 ± 1.27), and the question with the lowest mean score was *I have sufficient healthy diet information to manage my diet* (2.49 ± 1.13).

As shown in Table 4, the mean DQI-I score was 10.37 (range from 0 to 15). In particular, the proportion of respondents whose average daily intake of food categories met the recommended values at least four or more 50.87%. The percent of respondents whose average daily grain intake meet the recommendations was the highest, at 87.8%. While, only 55% of respondents ate the recommended amount of fruits and 62.8 and 67.7% of respondents ate the recommended amount of dairy and beans, and vegetable, respectively.

3.3 Difference analysis under different demographic variables

As shown in Table 5, the difference analysis of dietary knowledge of rural residents under different populations revealed that the overall nutrition knowledge level differed significantly by gender, annual

TABLE 1 Participant characteristics ($n = 344$).

Characteristics		n	%
Gender	Male	148	43
	Female	196	57
Age	18–34	97	28.2
	35–44	108	31.4
	45–54	95	27.6
	Above 55	44	12.8
Annual household income	Below 36,000	129	37.5
	36,000–84,000	170	49.4
	Above 84,000	45	13.1
Marital status	Unmarried	79	23
	Married	251	73
	Other	14	4.1
Education	Primary and below	72	20.9
	Junior high school	111	32.3
	High school	94	27.3
	Junior college or above	67	19.5
Chronic disease	Yes	125	36.3
	No	219	63.7
BMI	Underweight (< 18.5)	50	14.5
	Healthy weight (18.5–23.9)	171	49.7
	Overweight (24 to 27.9)	78	22.7
	Obesity (≥28)	45	13.1

1 On November 1, 2022, 1U.S. dollar equals approximately 7.264 RMB.

TABLE 2 Nutrition knowledge passing rate and mean score (n = 344).

Items	Options	*n*	%
Procedural nutrition knowledge (Min = 0 Max = 7 Mean = 4.66 S.D. = 1.74 Skew. = – 0.538 Kurt. = – 0.553)			
1. Fruit can be fully replaced by vitamin and mineral supplements	A. Agree	54	15.7
	B. Disagree	**228**	**66.3**
	C. Not sure	62	18.0
2. A healthy diet means nothing other than eating vitamins	A. Agree	61	17.7
	B. Disagree	**235**	**68.3**
	C. Not sure	48	14.0
3. Meat should be the basis of our daily diet	A. Agree	145	42.2
	B. Disagree	**158**	**45.9**
	C. Not sure	41	11.9
4. Instead of eating fruit you can drink fruit juice	A. Agree	68	19.8
	B. Disagree	**238**	**69.2**
	C. Not sure	38	11.0
5. Fat is always bad for your health, so you should avoid it as much as possible	A. Agree	44	12.8
	B. Disagree	**243**	**70.6**
	C. Not sure	57	16.6
6. A balanced diet implies eating all foods in the same amounts	A. Agree	55	16.0
	B. Disagree	**228**	**66.3**
	C. Not sure	61	17.7
7. For healthy nutrition, dairy products should be consumed in the same amounts as fruit and vegetables	A. Agree	75	21.3
	B. Disagree	**177**	**51.5**
	C. Not sure	92	26.7
Declarative nutrition knowledge (Min = 0 Max = 6 Mean = 2.53 S.D. = 1.51 Skew. = 0.237 Kurt. = – 0.638)			
1. The units of heat, KCAL (kilocalorie) and KJ (kilojoule) are the same	A. Agree	38	11
	B. Disagree	**130**	**37.8**
	C. Not sure	176	51.2
2. The reasonable supply of three meals a day requires that the proportion of calories for breakfast, lunch and dinner is	A. 20%, 50%, 30%	49	14.2
	B. 30%, 40%, 30%	**154**	**44.8**
	C. 30%, 30%, 40%	40	11.6
	D. Not sure	101	29.4
3. The main nutrient provided by animal food is	**A. Protein**	**140**	**40.7**
	B. Carbohydrate	23	6.7
	C. Fibrin	118	34.3
	D. Vitamin	8	2.3
	E. Not sure	55	16
4. Which of the following foods is a major source of iron?	A. Milk	12	3.5
	B. Spinach	148	43
	C. Animal liver	**125**	**36.3**
	D. Orange	10	2.9
	E. Not sure	49	14.2
5. Daily salt intake should not exceed	A. 3 g	49	14.2
	B. 5 g	72	20.9
	C. 6 g	**95**	**27.6**
	D. 8 g	26	7.6
	E. Not sure	102	29.7

(Continued)

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TABLE 2 (Continued)

Items	Options	*n*	%
6. Which of the following food groups contains the most protein	A. Red beans, milk, mung beans	32	9.3
	B. Milk, chicken, fish	**226**	**65.7**
	C. Meat, lettuce, beans	35	10.2
	D. Bread, beef, spinach	10	2.9
	E. Not sure	41	11.9
Total nutrition knowledge (Min = 0 Max = 13 Mean = 7.19 S.D. = 2.59 Skew. = −0.085 Kurt. = −0.396)			

Correct answers are shown in bold.

TABLE 3 Descriptive statistics on functional health literacy (*n* = 344).

	Items	Min.	Max.	Mean	S.D.	Skew.	Kurt.
IACC[A]	IACC1 I have the ability to get information about healthy diet from different sources	1	5	3.15	1.28	−0.084	−0.984
	IACC2 I was able to find information about healthy diet that I was interested in	1	5	3.27	1.28	−0.289	−0.990
	IACC3 I can find healthy diet information by text	1	5	3.35	1.27	−0.374	−0.891
	Total	3	15	9.78	3.55	−0.227	−0.875
IUC[B]	IUC1 I can read and understand all the information about healthy diet	1	5	3.21	1.17	−0.316	−0.731
	IUC2 I was able to fully understand the information I was getting about healthy diet	1	5	2.89	1.22	0.081	−0.885
	IUC3 When I see information about healthy diet, I judge	1	5	3.09	1.17	−0.203	−0.812
	Total	3	15	9.19	3.05	−0.141	−0.672
IAPC[C]	IAPC1 I feel better informed about healthy diet	1	5	2.51	0.98	0.149	−0.543
	IAPC2 I have mastered enough healthy dietary information to manage my own diet	1	5	2.49	1.13	0.522	−0.458
	IAPC3 I have enough healthy diet information to help me achieve a healthy diet	1	5	2.55	1.14	0.435	−0.575
	Total	3	14	7.55	2.861	0.334	−0.662
FHL		10	44	26.52	6.491	−0.211	0.104

IACC, information access capacity; IUC, information understanding capacity; IAPC, information application capacity; FHL, functional health literacy. Different letters indicate significant differences in scores based on paired sample *t*-tests.

household income, and education level. The PNK level of the residents varies as a function of the annual household income and education level. Three demographic dimensions, age, annual household income and education level, are important indicators for determining the different DNK levels of the residents.

For the health literacy status of rural residents, the overall FHL varies mainly by annual household income and education level. Regarding the three sub-dimensions of FHL, there are also differences in their influencing factors. Gender was identified as shaping the differences in residents' IUC and IAPC. The education level contributes to the different IACC and IUC. Moreover, residents' IUC and IACC are influenced by annual household income and marital status, respectively.

We identified significant differences in dietary variety between different education levels, that is, the higher the education level, the healthier the dietary behavior. The average DQI-I score for individuals in high school and above was over 11, while the average score for individuals in primary school and below was less than 10.

The results of the above analysis showed that male, elder, low-income, unmarried, and low-education groups performed significantly worse than their counterparts on one or more dimensions of knowledge, health literacy, and dietary behavior. Of these, male is showing significantly worse performance than female in three dimensions, namely nutrition knowledge, IUC, and IAPC. The 55 and older group performs significantly worse than the younger group in one dimension, i.e., DNK. The high-income group performs significantly better than the low-income group in five dimensions, i.e., PNK, DNK, nutrition knowledge, IUC, and FHL. The married group performs significantly better than the unmarried group in one dimension, i.e., IACC. Except for IAPC, the low-educated group was significantly worse than the high-educated group in the remaining dimensions. Given these findings, male, older adult, low-income, unmarried, and low-education groups are

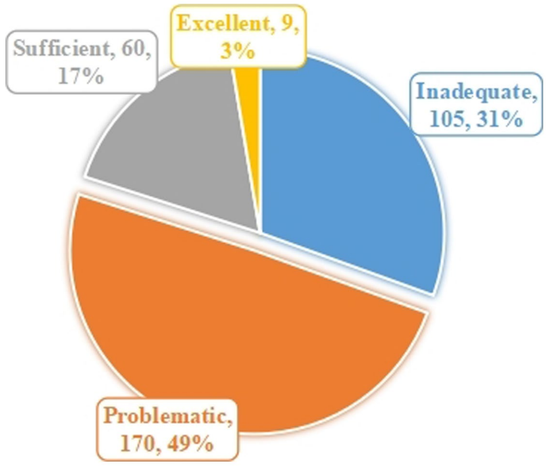

FIGURE 2
Scores on functional health literacy.

TABLE 4 Descriptive statistics of dietary behavior ($n = 344$).

Category	Meet the recommended intake	Not meet the recommended intake
Meat, poultry, fish, and eggs≥150 g	287 (83.4%)	57 (16.6%)
Dairy and beans≥300 g	216 (62.8%)	128 (37.2%)
Grain≥250 g	302 (87.8%)	42 (12.2%)
Fruit≥200 g	190 (55.2%)	154 (44.8%)
Vegetable≥300 g	233 (67.7%)	111 (32.3%)
	Score	**N (%)**
DQI-I Mean = 10.73 S.D. = 2.582 Skew. = −0.001 Kurt. = −0.398	15	53 (15.4%)
	12	122 (35.5%)
	9	141 (41.0%)
	6	26 (7.6%)
	3	2 (0.6%)
	0	0 (0)

considered high-risk groups in terms of healthy diet and warrant prioritization in the design of intervention programs.

3.4 Relationship between nutrition knowledge and health literacy with dietary variety

Table 6 shows the results of the regression analysis. The VIF values were all below 1.5, indicating that there was no multicollinearity. The regression results showed that nutrition knowledge and health literacy could explain 31.5% of variance in dietary behavior. IACC, IUC, IAPC, and PNK significantly and positively affected DQI-I. Of these, the effects of IACC ($\beta = 0.291$) and IAPC ($\beta = 0.277$) on dietary behavior were the most influential. The coefficient of DNK on DQI-I was positive but not significant. After adding age, marital status, gender, annual household income, and education level as control variables, the effect of the above variables on DQI-I remains significant, showing that the test results are robust. The effects of control variables on dietary behavior were not significant.

4 Discussion

In this study, a validated questionnaire was developed to measure the nutrition knowledge (including PNK and DNK), FHL, and DQI-I of rural residents in northeastern China. Based on survey data through face-to-face approach, we were informed about the baseline status of dietary knowledge, health literacy and dietary behavior of rural residents. By examining the differences in different demographic characteristics, high-risk groups with poorer performance in terms of knowledge, literacy, and behavior were identified. In addition, factors associated with dietary behavior were also uncovered by evaluating the effect of dietary knowledge and health literacy. Based on these results, we were able to give evidence-based guidance on the priority content and populations for healthy dietary interventions.

4.1 The picture of consumers' nutrition knowledge, FHL, and dietary behavior

The study showed the average correct scores of PNK, DNK and overall knowledge scores of rural residents in the three northeastern provinces were 66.57% (4.66/7), 42.17% (2.53/7) and 55.31% (7.19/13), respectively. This indicates that the level of nutritional knowledge of the residents is not sufficient and needs to be further promoted. This is consistent with the outcomes of other studies on Chinese residents, e.g., Hou et al. (56) and Zhang et al. (57). The relationship analysis between dietary knowledge and behavior showed that PNK had a positive effect on dietary behavior, while DNK had a non-significant effect on dietary behavior, indicating that different types of knowledge showed different effects on behavior and that the priority of different types of knowledge should be weighed in designing intervention programs.

The results of this study suggest that improvements in behavior may be insignificant if the intervention is targeted to residents' descriptive knowledge. Previous studies that found a weak relationship between dietary knowledge and behavior may also have resulted from a failure to distinguish between different types of knowledge (58–60). Accordingly, integrating content related to procedural knowledge in intervention information development is an effective way to bridge the knowledge–behavior gap in dietary interventions.

The FHL score was generally low, and only 3% of the respondents showed excellent health literacy. This result is significantly lower than the health literacy of the residents of Denmark (35.2 ± 4.0, rang from 9 to 40) (61), Australia (Mean = 30.31, range from 9 to 40) (62) and Netherlands (Mean = 30.06, range from 9 to 40) (63). Li et al. (64) surveyed the Chinese population and found that the proportion of urban residents with adequate health literacy was 24%, while the proportion of the rural population with adequate health literacy in this study was only 20% (17% sufficient and 3% excellent). These suggest that the health literacy of Chinese rural residents is poor and needs to be improved. Furthermore, the ability to apply information

TABLE 5 Relationship between demographic characteristics and nutrition knowledge, functional health literacy, and dietary behavior.

Characteristics		*N*	PNK	DNK	Nutrition knowledge	IACC	IUC	IAPC	FHL	DQI-I
Gender	Male	148	4.47 ± 1.77	2.38 ± 1.46	**6.85 ± 2.6**	10.05 ± 3.57	**8.74 ± 2.93**	**7.04 ± 2.8**	25.84 ± 6.62	10.52 ± 2.60
	Female	196	4.80 ± 1.57	2.64 ± 1.54	**7.44 ± 2.57**	9.57 ± 3.53	**9.53 ± 3.1**	**7.93 ± 2.85**	27.02 ± 6.51	10.88 ± 2.56
	p-value[A]		0.089	0.108	**0.037**	0.207	**0.018**	**0.004**	0.099	0.198
Age	18–34	97	4.91 ± 1.59	**2.78 ± 1.33a**	7.69 ± 2.36	9.64 ± 3.72	9.4 ± 3.14	7.28 ± 2.78	26.32 ± 7.4	10.76 ± 2.7
	35–44	108	4.57 ± 1.73	**2.51 ± 1.60ab**	7.08 ± 2.69	9.89 ± 3.58	9.16 ± 3.21	7.44 ± 2.95	26.49 ± 6.54	10.64 ± 2.73
	45–54	95	4.56 ± 1.90	**2.53 ± 1.54b**	7.08 ± 2.66	9.81 ± 3.47	9.34 ± 2.82	7.82 ± 2.95	26.97 ± 5.86	10.83 ± 2.33
	55 and above	44	4.52 ± 1.75	**2.02 ± 1.52b**	6.55 ± 2.61	9.73 ± 3.34	8.48 ± 2.93	7.8 ± 2.63	26 ± 6.38	10.64 ± 2.54
	p-value[C]		0.423	**0.038**	0.83	0.966	0.377	0.533	0.849	0.95
Annual household income	36,000 and bellow	129	**4.55 ± 1.84a**	**2.44 ± 1.56a**	**6.99 ± 2.77a**	9.58 ± 3.61	**8.46 ± 3.24a**	7.26 ± 2.98	**25.3 ± 6.91a**	10.4 ± 2.43
	36,000–84,000	170	**4.58 ± 1.72a**	**2.37 ± 1.32a**	**6.95 ± 2.3a**	9.79 ± 3.43	**9.66 ± 2.86b**	7.75 ± 2.81	**27.21 ± 6.2b**	10.99 ± 2.48
	84,000 and above	45	**5.24 ± 2.24b**	**3.38 ± 1.76b**	**8.62 ± 2.7b**	10.27 ± 3.8	**9.49 ± 2.86b**	7.58 ± 2.69	**27.33 ± 6.64b**	10.67 ± 3.23
	p-value[A]		**0.05**	**0.001**	**0.001**	0.536	**0.002**	0.341	**0.03**	0.137
Marital status	Unmarried	79	4.91 ± 1.60	2.82 ± 1.52	7.73 ± 2.5	**8.67 ± 3.47a**	9.18 ± 2.94	7.62 ± 2.79	25.47 ± 6.99	10.71 ± 2.57
	Married	251	4.55 ± 1.79	2.47 ± 1.49	7.02 ± 2.63	**10.05 ± 3.53b**	9.18 ± 3.09	7.54 ± 2.83	26.76 ± 6.44	10.69 ± 2.59
	Other	14	5.21 ± 1.37	1.93 ± 1.73	7.14 ± 2.25	**11.14 ± 3.134b**	9.5 ± 3.08	7.21 ± 3.77	27.86 ± 6.46	11.57 ± 2.59
	p-value[A]		0.126	0.061	0.1	**0.003**	0.927	0.886	0.230	0.458
Education level	Primary and below	72	**4.37 ± 1.70a**	**2.11 ± 1.43a**	**6.49 ± 2.46a**	**9.61 ± 3.446a**	**8.44 ± 2.88**	7.14 ± 2.77	**25.19 ± 5.03a**	**9.83 ± 1.96a**
	Junior high school	111	**4.4 ± 1.87ab**	**2.29 ± 1.42a**	**6.69 ± 2.68ab**	**9.86 ± 3.333a**	**9.2 ± 2.87**	7.85 ± 2.77	**26.9 ± 6.1a**	**10.78 ± 2.6ab**
	High school	94	**4.7 ± 1.74bc**	**2.87 ± 1.57b**	**7.64 ± 2.64ab**	**9.62 ± 3.744a**	**9.23 ± 3.07**	7.28 ± 2.93	**25.53 ± 7.08a**	**11.07 ± 2.64b**
	Junior college or above	67	**5.22 ± 1.42c**	**2.90 ± 1.50b**	**8.12 ± 2.15bc**	**10.88 ± 3.506b**	**9.91 ± 3.37**	7.87 ± 2.95	**28.66 ± 7.54b**	**11.1 ± 2.86b**
	p-value[C]		**0.008**	**0.001**	**0.001**	**0.011**	**0.044**	0.225	**0.01**	**0.008**
Chronic disease	No chronic disease	219	4.63 ± 1.73	2.58 ± 1.47	7.21 ± 2.6	9.8 ± 3.538	9.36 ± 2.89	7.7 ± 2.85	26.86 ± 6.55	10.67 ± 2.59
	With chronic disease	125	4.71 ± 1.77	2.44 ± 1.58	7.15 ± 2.6	9.74 ± 3.579	8.9 ± 3.3	7.27 ± 2.86	25.9 ± 6.61	10.82 ± 2.58
	p-value[B]		0.659	0.140	0.854	0.874	0.291	0.179	0.196	0.598
BMI	Underweight	50	4.60 ± 1.59	2.52 ± 1.61	7.12 ± 2.68	10.1 ± 3.524	8.6 ± 3.01	7.5 ± 2.53	26.2 ± 5.57	11.04 ± 2.67
	Healthy weight	171	4.70 ± 1.68	2.53 ± 1.42	7.22 ± 2.45	9.73 ± 3.558	9.11 ± 2.99	7.53 ± 2.97	26.36 ± 6.54	10.72 ± 2.56
	Overweight	78	4.82 ± 1.71	2.71 ± 1.59	7.53 ± 2.52	10.01 ± 3.5	9.51 ± 3.17	7.18 ± 2.74	26.71 ± 6.89	10.81 ± 2.53
	Obesity	45	4.29 ± 2.14	2.24 ± 1.60	6.53 ± 3.09	9.18 ± 3.657	9.6 ± 3.09	8.31 ± 2.92	27.09 ± 7.32	10.27 ± 2.68
	p-value[C]		0.622C	0.449	0.236	0.56	0.298	0.21	0.89	0.525

[A]Analysis of variance (ANOVA) was conducted, [B]Mann–Whitney U test was conducted, [C]Kruskal–Wallis test was conducted. Mean scores denoted by the same letter are not significantly different from each other at the 5% significance level based on Bonferroni *post hoc* analysis. Significant differences ($p < 0.05$) are in bold. PNK, procedural nutrition knowledge; DNK, declarative nutrition knowledge; IACC, information access capacity; IUC, information understanding capacity; IAPC, information application capacity; FHL, functional health literacy; DQI-I, Diet Quality Index-International.

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TABLE 6 Multiple linear regression analysis results for dietary behavior.

Variables	DQI-I			DQI-I		
	β	*t*	VIF	*β*	*t*	VIF
Constant	0.029**	6.765		−0.055**	3.768	
IACC	0.291**	6.25	1.073	0.286**	5.968	1.128
IUC	0.211**	4.241	1.227	0.209**	4.116	1.263
IAPC	0.277**	5.778	1.134	0.272**	5.57	1.169
PNK	0.115**	2.45	1.087	0.107**	2.323	1.118
DNK	0.077	1.596	1.141	0.07	1.433	1.188
Age				0.05	0.97	1.279
Marital status				−0.005	−0.11	1.077
Gender				0.009	0.187	1.064
Annual household income				−0.039	−0.82	1.101
Education level				0.096	1.825	1.373
$R^2 = 0.315$ $F(5,338) = 31.146$, $p < 0.001$				$R^2 = 0.323$ $F(10,343) = 15.87$, $p < 0.001$		

**$p < 0.05$. PNK, procedural nutrition knowledge; DNK, declarative nutrition knowledge; IACC, information access capacity; IUC, information understanding capacity; IAPC, information application capacity; FHL, functional health literacy; DQI-I, Diet Quality Index-International.

to manage dietary was the lowest. FHL was evidenced to be significantly associated with the residents' dietary behavior. Specifically, residents with stronger IACC, IUC, and IAPC had higher DQI-I scores. This is consistent with the findings of a systematic review, which showed that FHL was the most important predictor variable of dietary behavior (65). Some studies also proved that health literacy was a predictor of fruit and vegetable intake (66, 67). This signifies that diet-related health literacy is the priority to be addressed when designing intervention programs, including improving individuals' ability to access, understand, and apply health information.

The dietary behavior met the recommendations (score = 15) accounted for only 15.41% of the residents, and nearly 50% of the individuals were those who had two food categories with less than the recommended intake. Among them, there was a high proportion (87.8%) of participants that met the recommended grain intake value. The reason for this phenomenon is that northeastern China is a major food-producing region where farmers mainly grow rice. The cost for farmers to obtain grain through self-sufficiency is relatively low. Besides, the proportion of fruits, dairy products and beans, and vegetables consumed up to the recommended values is quite low. Previous studies have also found that Chinese consumers' intake of these food groups is grossly inadequate (68, 69). Fruits and vegetables can provide dietary fiber, which is strongly associated with a low incidence of cardiovascular disease and obesity (70). This implies that there is a great urgency to improve the dietary patterns of the Chinese residents, and intervention information should focus on increasing the population's intake of specific foods (e.g., fruits, vegetables, beans, and dairy products).

4.2 Conditions under different demographic characteristics

This study revealed significant differences in dietary knowledge, health literacy, and behavior across demographic variables, which provides the empirical evidence for identifying high-risk groups in relation to healthy diets. One of the significant factors contributing to the differences in nutritional knowledge and FHL was gender. Females have more nutritional knowledge, information understanding and information application capacity than males. Dickson-Spillmann et al. (36) also found that PNK was significantly higher in females than in males. However, some previous studies found no significant relationship between health literacy by gender (71, 72) or that males have higher health literacy than females (73). The reason for this different outcome may be that the dietary decision makers in Chinese households are generally females, who spend more time and energy on food choices and therefore generate more health literacy than males (74). This also suggests that Chinese males are poor performers in terms of health behaviors and are a priority group for dietary interventions.

Age affects DNK, i.e., the elder the respondent, the lower the DNK, which is consistent with previous studies concluding that age is negatively associated with nutritional knowledge (36), but this differs from Hendrie, Coveney and Cox (75). These differences may be due to the fact that the questionnaire items are according to the latest healthy dietary recommendation guidelines, which differ from the past versions. Access to up-to-date knowledge can be a challenge for the elder community (76). Accordingly, this points to the elder population as a priority group for dietary interventions.

Previous studies have shown that residents with higher incomes have access to health information and services (67, 77, 78). Our study also found significant differences in nutritional knowledge and information understanding capacity between income levels, that is, those with higher incomes generally had more nutritional knowledge, including PNK and DNK, and higher health literacy. While lower income groups are the ones that need more attention in dietary interventions owing to poor performance in terms of knowledge and health literacy.

It has been shown that higher education levels not only help individuals to acquire knowledge and skills, but also enable them to better translate this information into health literacy (79, 80). Our findings also validated this finding and uncovered that those with higher education levels showed better in terms of dietary behavior, which is consistent with the Yang et al. (81). Furthermore, Kristal et al. (82) pointed to a relationship between the effectiveness of the dietary intervention and the years of education of the subjects. The educational level has been confirmed in several studies to have a significant positive effect on health behaviors (83, 84). In light of this study's findings, individuals with lower education levels as a high-risk group deserve priority treatment in dietary intervention.

Marital status would affect the residents' health literacy, mainly in the sense that married individuals have better ability to receive health information than unmarried ones. The reason for this may be that married individuals invest more energy in their family life, including paying attention to their family's health, which leads these individuals to be more willing to obtain health information. This also means that unmarried residents need increased focus in dietary interventions.

4.3 Implications for designing dietary intervention

4.3.1 Implications for designing intervention information

By investigating the nutrition knowledge, FHL, and dietary behavior of rural residents in northeastern China and analyzing the relationships between these factors, this study identifies priority intervention information and populations for health dietary promotion programs. We found that the nutrition knowledge, FHL, and dietary behavior is not well developed and needs to be improved. Among them, PNK and FHL have significant positive effects on dietary variety. In order to more effectively promote healthy dietary behaviors, the intervention information needs to involve knowledge of how to more efficiently and rationally implement healthy dietary and improve individual health literacy. Dietary intervention programs in China now mostly introduce residents to what constitutes a healthy diet, i.e., DNK, which helps improve DNK but has limited effect on behavior improvement. Developing Internet and mobile phone app–based dietary guidelines is also essential to decrease the difficulty of accessing, understanding, and applying information.

4.3.2 Implications for targeting high-risk population groups

Moreover, by understanding the performance of individuals under different demographic characteristics it is also possible to identify priority populations for intervention. Groups that are male, older adult, low-income, unmarried, and low education levels should be given more attention because they perform worse in terms of knowledge, health literacy, and dietary behaviors. The number of mobile Internet users in China is nearly one billion (85), which allows the use of big data technology to push healthy diet information to priority groups.

4.4 Limitations and future studies

Although we have made an in-depth consideration of the research design there are still some limitations in this study. First, we selected only DQI-I as a marker for dietary behavior assessment. Other markers could be added for dietary behavior assessment in future studies, such as the proportion of macro-energy supply and micronutrient intake. Second, this study focused only on nutritional knowledge and FHL as influencing factors of dietary behavior. However, in previous studies it has also been revealed that there are other factors that may have influenced dietary behaviors, such as social network type, self-efficacy, and food availability (86, 87). In coming studies, psychosocial models and environmental factors could be considered to evaluate dietary behavior. Additionally, this study used the FFQ as an instrument to investigate dietary behavior. Although this measurement method is low-cost and valid, its accuracy is slightly lacking. More accurate survey tools, such as logs or real-time images, can be chosen to record dietary behaviors. Finally, we only surveyed the northeastern region of China, and although the northeastern region is quite representative, a national survey could be considered in the future to get a clearer picture of the dietary situation of Chinese residents.

5 Conclusion

This study showed that the dietary behavior, nutrition knowledge, and health literacy of rural residents in China need to be improved. FHL is an important factor affecting dietary behavior, and more attention should be paid to this issue in dietary behavior interventions. As a different type of nutrition knowledge, procedural nutrition knowledge showed a significant positive influence on dietary behavior, whereas declarative nutrition knowledge was not significantly influenced with dietary behavior. The promotion of procedural nutrition knowledge should be reinforced in the promotion of healthy diets going forward. The results of differences analysis demonstrated that demographic variables affect individual nutritional knowledge, health literacy, and dietary behavior and identified males, older adult, unmarried, low-income, and low-education populations as high-risk group. This provides evidence-based guidance for prioritizing information and populations for healthy dietary interventions.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by School of Biological and Agricultural Engineering, Jilin University. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

LB: Conceptualization, Data curation, Formal analysis, Methodology, Validation, Writing – review & editing. HT: Resources, Formal analysis, Investigation, Writing – original draft. MW: Supervision, Conceptualization, Writing – review & editing, Funding acquisition. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2024.1239449/full#supplementary-material

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Gut microbiota, nutrition, and mental health

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The human brain remains one of the greatest challenges for modern medicine, yet it is one of the most integral and sometimes overlooked aspects of medicine. The human brain consists of roughly 100 billion neurons, 100 trillion neuronal connections and consumes about 20–25% of the body's energy. Emerging evidence highlights that insufficient or inadequate nutrition is linked to an increased risk of brain health, mental health, and psychological functioning compromise. A core component of this relationship includes the intricate dynamics of the brain-gut-microbiota (BGM) system, which is a progressively recognized factor in the sphere of mental/brain health. The bidirectional relationship between the brain, gut, and gut microbiota along the BGM system not only affects nutrient absorption and utilization, but also it exerts substantial influence on cognitive processes, mood regulation, neuroplasticity, and other indices of mental/brain health. Neuroplasticity is the brain's capacity for adaptation and neural regeneration in response to stimuli. Understanding neuroplasticity and considering interventions that enhance the remarkable ability of the brain to change through experience constitutes a burgeoning area of research that has substantial potential for improving well-being, resilience, and overall brain health through optimal nutrition and lifestyle interventions. The nexus of lifestyle interventions and both academic and clinical perspectives of nutritional neuroscience emerges as a potent tool to enhance patient outcomes, proactively mitigate mental/brain health challenges, and improve the management and treatment of existing mental/brain health conditions by championing health-promoting dietary patterns, rectifying nutritional deficiencies, and seamlessly integrating nutrition-centered strategies into clinical care.

KEYWORDS
brain-gut-microbiota axis, neuroplasticity, mental health, brain health, nutritional psychiatry, lifestyle psychiatry

1 Introduction

The complex interplay between the foods we eat and how our brains react to nutrition highlights the interconnectedness of daily lifestyle habits and the health of the brain, mind, and body. Understanding the relationship between food and its impact on mental/brain health, in conjunction with the reciprocal influence of mental/brain health on whole-body health, including gut health, and daily lifestyle habits, such as dietary choices, requires a transdisciplinary approach that incorporates the fields of psychiatry, psychology, neuroscience, nutrition, and lifestyle medicine (1–4). This review will explore the significant impact of nutrition on brain health, mental well-being, and cognitive functioning. It will highlight the emerging role of lifestyle interventions and nutritional neuroscience in proactively improving patient outcomes and managing mental/brain health conditions.

The brain has the greatest metabolic demands (approximately 20–25% of the body's total energy consumption) of any human organ (5). Additionally, optimal brain health requires various nutrients, including carbohydrates, essential fatty acids, proteins, vitamins, and minerals (6, 7). Glucose derived from carbohydrates is the primary source of energy for the brain. Essential fatty acids (e.g., omega-3 fatty acids, omega-6 fatty acids) play a critical role in maintaining the integrity of structures in the brain, as well as promoting the synthesis and functioning of neurotransmitters and components of the immune system (8). Finally, amino acids found in protein foods, including tryptophan, tyrosine, histidine, and arginine, are also utilized by the brain to produce neurotransmitters and neuromodulatory compounds (9). Research surrounding the link between nutrition and mental/brain health issues has transitioned from an initial focus on nutrient deficiencies that manifested observable psychiatric and/or neurological symptoms in clinical settings (i.e., the lack of thiamine and the potential development of Wernicke syndrome) to a prioritization of research inquiries aiming to better understand the implications of comprehensive dietary patterns on human well-being in the context of both health and disease (4).

Evidence in the burgeoning fields of lifestyle psychiatry and nutritional neuroscience has made it increasingly evident that diet is not only a matter of physical sustenance but also a fundamental factor influencing cognitive abilities, emotional states, and risk of or protection against mental health issues and/or brain illnesses (4, 10–13). This bidirectional relationship challenges the historical silos of nutrition and neuroscience, emphasizing the need for transdisciplinary collaboration to unravel the intricacies of how the foods we consume shape the functioning of our brains and, in turn, how the state of our brains influences our dietary choices.

2 Intersection of nutrition and mental health

The intersection between nutrition and mental health is an emerging area of research interest. For the purpose of this paper, we will focus on depression since the data is more complete and depression is projected to be one of the top health concerns by 2030 (14). Despite growing medications and therapeutics, the negative impact of depression continues to grow as reflected by the increase in disability-adjusted life-years (DALYs), years lived with disability (YLDs), and years of life lost (YLLs) (15).

2.1 Five theories of neuropathology of depression

In their 2016 review, Loonen and Ivanona postulated five theories regarding the neuropathology of depression (16). First is the well known monoamine theory. The majority of psychotropic medications that have FDA approval for the treatment of depression (e.g., selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, or tricyclic acids) modulate serotonin, as such, the monoamine theory links the origins of depression to deficits of serotonin. Currently, this has been expanded to include norepinephrine and dopamine as well. Second is the biorhythm theory, which centers on sleep disruption and altercations within the REM sleep and deep sleep patterns. A dysfunctional sleep rhythm alters the natural circadian rhythm that is regulated within the nucleus suprachiasmaticus (SCN), It is hypothesized that the altered circadian rhythm within the SCN contributes to mood dysregulation patterns throughout the day.

Third is the neuro-endocrine hypothesis. Thyroid levels, particularly, hypothyroidism has been linked with the onset of depressive symptoms (17). Changes in thyroid hormones have been linked with serotonin insufficiency (18). As will be discussed in more detail, dysregulation within the HPA, particularly higher levels of cortisol have been linked with altercations of the circadian rhythm, hippocampus, and limbic system, which may account for changes of emotions seen in depression. Individuals with depression also as a whole have higher levels of cortisol in the mornings and evenings compared to non-depressed individuals (19). The fourth is the neuro-immune hypothesis, which also will be discussed in more detail. The HPA axis and the immune system are significantly interconnected, and changes with cortisol levels can greatly impact the immune system. Changes within neurohormones or other triggers cause the release of neurotrophic factors, like BDNF, regulatory cytokines, etc., which have been linked with changes in the hippocampus, limbic system, SCN and have been linked with depression. Finally, the fifth is the kindling hypothesis, which states that the actual illness causes cell death and reinforces depressive symptoms with progressive worsening symptoms.

In the 2021 review, Marx et al., show dietary patterns, commonly known as the Western Diet or Standard American Diet, which are high in saturated fats, refined carbohydrates and ultra-processed foods, can create many of the Loonen and Ivanona hypotheses (16, 20). A systematic analysis of the Global Burden of Disease Study assessing the health effects of dietary risks in 195 countries from 1990 to 2017 found that diet-related risk factors were responsible for approximately one-fourth of all deaths among adults and almost one-fifth of all disability-adjusted life years among adults (21). Particularly concerning is the increasing consumption of UPF. Prior to COVID-19 pandemic, the typical U.S. diet consisted of about 60% UPF. The consumption patterns were consistent between gender and race (22), and the global consumption of UPF has increased in the post-pandemic era (23). UPF contains excessively high levels of refined sugars, saturated fat, trans-fat, caffeine, and sodium, with regards to both overall macro- and micronutrient content and energy density, as well as very low levels of dietary fiber.

2.2 Ultra-processed food and neuropathology

In an attempt to categorize food content, the NOVA food classification system was developed, which categorizes food into four subgroups: 1) unprocessed and minimally processed foods, 2) processed culinary ingredients, 3) processed foods, and 4) ultra-processed food (UPF), which are defined as "food substances of no or rare culinary use" (24, 25). A 2021 meta-analysis from Lane et al. of over 345,000 individuals noted that higher rates of UPF predicted an increased risk of subsequent mental health symptoms (26). In a cross-section design of 10,359 participants, Hecht et al. showed that individuals who consumed primarily NOVA4, had an odds ratio for developing depression (OR: 1.81; 95% CI 1.09, 3.02). They had a risk ratio for being more mentally unhealthy (RR: 1.22; 95% CI 1.18, 1.25). Finally, they were also significantly less likely to report zero mentally unhealthy days (OR: 0.60; 95% CI 0.41, 0.88) (27). A potential explanation may be how a diet rich in UPF leads to dysregulated neuroimmune responses (28), increased neuroinflammation (29, 30), and altercations within the neuroendocrine system (29).

2.3 Ultra-processed food and the gut

People suffering from mental illness consume more UPF (30) and people who consume more UPF are prone to develop mental illness (31, 32). Apart from the neuroinflammatory contribution of mental illness on the microbiota, diets high in UPF promote low-grade inflammation, affecting the microbiota (29). In a recent meta-analysis conducted by Nikolova et al. (33), 34 studies comprising more than 1,500 individuals with mental health illness were evaluated and showed a pattern of microbiota among mental illness diagnoses, which were depleted of pyruvate-producing bacteria. It is important to note that this shift in microbial diversity, which affects the absorption of key amino acids and adversely affects brain health (34, 35).

The following sections delve into the current state of understanding regarding these intersections, shedding light on the mechanisms through which nutrition influences mental well-being and offering insights into potential avenues for therapeutic interventions.

3 The brain-gut-microbiota: the developmental origins and a review

3.1 Developmental origins

The BGM system is a bidirectional communication network connecting the gastrointestinal system and the brain that has emerged as a focal point linking nutrition, health, and well-being (36, 37), particularly related to mental/brain health. The gut microbiota is a diverse community of microorganisms inhabiting the digestive tract that influences various aspects of brain function through the production of neurotransmitters, immune signaling molecules, and metabolic substances (38). Dietary patterns alter the microbiota composition of the gut (39). Strengthening the gut microbiota through dietary interventions holds promise as a novel approach to ameliorate mental/brain health symptoms, risk factors, and protective factors as the BGM system is a primary mechanistic channel through which the gut microbiota exert their effects on mental/brain health through nutrition-related pathways (4, 33).

The gut and brain are both derived from neural crest tissue during embryogenesis and influence each other during human developmental processes as they integrate into the enteric nervous system (40, 41). Microbes initially colonize the gastrointestinal tract at the time of birth. A microbiota is a biological community that forms when microorganisms live in a specific habitat and produce genetic material. The human microbiota develops after the first year of life and continues to diversify throughout life. Evidence indicates that microbiota bacteria have undergone a co-evolutionary process alongside humans and engage in bidirectional physiological interactions with our bodily systems (42). It is estimated that the ratio of microbial cells to human cells in the body is approximately one-to-one, which points to the significance of microbiota in facilitating processes that support human flourishing across the lifespan. There are three primary pathways through which the gut microbiota interacts with the brain along the BGM system, including neuroimmune, neuroendocrine, and vagus nerve pathways (37).

3.2 BGM system-neuroimmune pathway

Dietary habits play a huge role in maintaining a healthy gut microbiota (3), which inturn plays a key role in modulating the immune system. Diets rich in dietary fibers, not UPFs, activate microbial enzymes within certain bacteria (*Bifidobacterium, Lactobacillus, Lachnospiraceae, Blautia, Coprococcus, Roseburia, and Faecalibacterium*) are able to break down complex carbohydrates (43), via a fermentation, into short-chain fatty acids (SCFA), namely acetate, propionate, and butyrate (3). These SCFA have a wide range of host activities, including metabolism, cell differentiation, gene regulation (3, 44), and regulating anti-inflammatory and pro-inflammatory cytokines (45). Within the gut, SCFAs strengthen the epithelial barrier functions, which maintains an favorable environment for commensal bacteria and inhibits pathogen's growth (44).

Butyrate is metabolized into acetyl CoA, which is needed in mitochondrial metabolism. It also plays a pivotal role in regulating IL-10 receptors and maintaining the gut epithelial tight junctions (44). Without this, a change of the overall gut microbiota diversity can develop, which may lead to a condition known as dysbiosis. The growth of *Enterobacteriaceae*, especially *Escherichia, Shigella, Proteus,* and *Klebsiella* can increase in enterotoxin levels (46), which leads to dysbiosis. This pro-inflammatory microbial imbalance typically occurs in diets rich in UPFs, sodium, saturated fats, *trans*-fat, and refined sugar (47, 48). It is significant to note that dysbiosis can lead to dysregulated immune responses that can contribute to chronic inflammation and have a wide range of negative health implications, including health challenges such as neuropsychiatric conditions and autoimmune diseases in which neuroinflammation is a key contributing factor (49, 50).

Specifically, chronic inflammation from the *Enterobacteriaceae* can release lipopolysaccharide (LPS) from their own cells. Once released within the gut, they impair gut-associated lymphoid tissue (GALT), which includes the multi-follicular Peyer's patches of the ileum, the numerous isolated lymphoid follicles (ILF) distributed along the length of the intestine, and the vermiform appendix (28). Additionally, the disruption of the immune system within the enteric system will alter system immunity. Additional critical consequences of LPS include: increases blood brain barrier permeability, altering the microglia of the CNS as it promotes gliosis and neuronal damage (51). Due to the breakdown of the blood brain barrier, there is an increase of plasma proteins into the brain, particularly the component proteins, which can adversely affect synaptic pruning (52).

Communication between the gut microbiota and the immune system occurs as part of the broader BGM system, rather than in isolation. Bidirectional crosstalk between these two major biological systems happens in such a way that signals from the gut can affect the brain and vice versa. The immune system may send signals to the brain when it detects inflammation in the gut, which can affect mood, behavior, and cognitive function. There is evidence that this bidirectional communication can contribute to the development or progression of neuropsychiatric conditions such as depression, anxiety, and as well as other mood disorders (47).

3.3 BGM system-neuroendocrine pathway

The neuroendocrine pathway of the BGM system involves a complex network of communication between the brain, the gut, and the endocrine system (37). In addition, the production of LPS has been shown to activate the hypothalamic–pituitary–adrenal axis (HPA) (53). Heightened levels of cortisol can in turn change intestinal permeability by activating interferon gamma, interleukin 6, interleukin 1 beta, and tumor necrosis factor alpha (54), which alter the diversity of the gut microbiota, leading to dysbiosis (55), neuronal damage within microglia and astrocytes, and depletion of neurotrophic factors, like BDNF (56). Heightened levels of cortisol can affect brain function by decreasing prefrontal cortex activity, heightening amygdala fear response and decreasing functional memory due to its negative hippocampal interactions.

Additionally, there is a growing body of literature that a number of neurotransmitters that function as hormones are also mediated within the BGM axis. Serotonin, for example, is derived from the essential amino acid tryptophan, which is absorbed within the kynurenine pathway (34) and regulated through the gut microbiota (46, 55). Serotonin concentration within the brain can contribute to the development and or progression of depression and anxiety (57). *Enterobacteriaceae* have also been shown to be histamine producing bacteria (58). Histamine has been linked with visceral gut hypersensitivity, increased gut permeability and altered gut motility (59), and studies have linked depression to these heightened eosinophilic conditions (60).

3.4 BGM system-vagus nerve

The vagal pathway of the BGM system involves the vagus nerve, the tenth cranial nerve, that plays a significant role in the bidirectional transmission of signals between the brain and the gastrointestinal tract. The vagus nerve extends from the brainstem into the abdomen through the gastrointestinal tract and other organs, including the heart and lungs and transmits both sensory and motor signals throughout the mesenteric organs. The sensory components of the vagus nerve called vagal afferents relay information from numerous organs to the brain, including signals associated with the gut environment such as the presence of inflammation, gut distension, nutrient availability, and gut hormones (i.e., leptin, ghrelin, glucagon-like peptide 1, and insulin), and gut microbial metabolites (29, 61). Bidirectional communication between the brain and gut relies on an axis composed of 80% afferent and 20% efferent neurons (62). These microbial sensory signals can convey information about the composition and activity of the gut microbiota to the brain. The vagus nerve, which is also composed of motor branches known as vagal efferents, sends signals from the brain to the gastrointestinal tract and other organs. Vagal motor signals can influence functions of the gastrointestinal tract like gut motility, the secretion of digestive enzymes, and the modulation of immune responses in GALT (63).

4 Brain health, mental health, and wellness

While mental health is known by both the public and scientific community, it does not capture the importance of the concept of *brain health*. Brain health is defined by the WHO as the fostering of optimal brain development, cognitive health, and well-being throughout the entire lifespan (64). As such, brain health includes what is thought, done, said, and felt. The lifespan continuum of brain health is also in alignment with current evidence regarding neuroplasticity, the ability of the brain to adapt and escape previous genomic restrictions through the formation and reorganization of synaptic connections.

Brain health includes the concepts of wellness, mental health, and brain health (65) (see Figure 1 for a representation of the relationship between wellness, mental health, and brain health). With this framework in mind, it is important to note how dietary choices across the lifespan have the potential to positively alter brain structure and improve brain health or negatively impact it.

5 Nutrition and brain changes across the lifespan

The brain and body are exposed to a wide array of exogenous and endogenous stimuli that can impart various levels of functionality across biopsychosocial spheres of health, which determine both short- and long-term outcomes across the lifespan. A healthy early life development of the BGM system helps prevent later disease development. Nutritional programming is the concept that key cells within the body will be able to absorb nutrients or synthesize them *de novo* in key periods of time to support early life development (66). Multiple nutrients with epigenetic potential that are present in the diet or produced via microbial metabolism in the human gut. The B-complex vitamins, SCFAs, and polyphenols are among nutrients known to exert epigenetic effects on the host (67). Significant synaptogenesis in the brain occurs simultaneous to diversification of gut bacteria during critical windows (68, 69). Critical windows are periods of development during which the phenotypic outcomes (e.g., intelligence quotient) of an individual are remarkably sensitive to interactions between environmental and genetic factors. Environmental factors, such as diet, can significantly alter the developmental course of high-plasticity bodily systems, such as the central nervous system, cardiovascular system, gastrointestinal system, and immune system (70). As such, within the nutritional framework, nutrients need to be available for optimal development (66).

5.1 Fetal period

The fetal period is a key nexus period within the nutritional framework. It is estimated that over half of the maternal energy

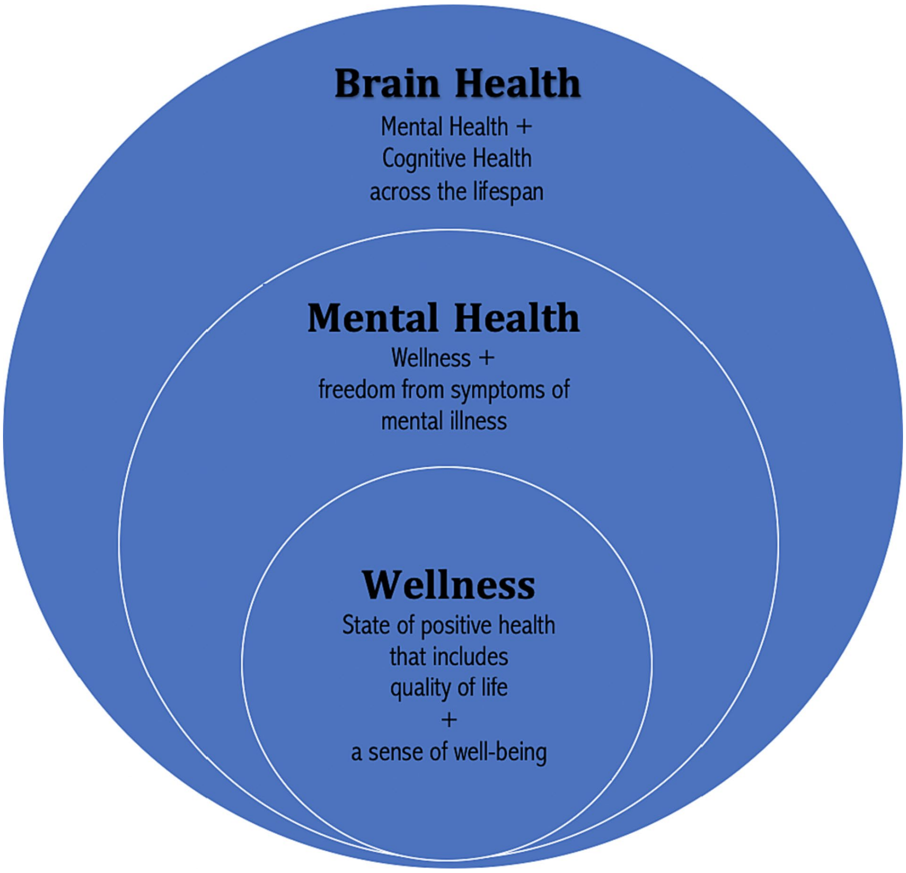

FIGURE 1
Relationship between wellness, mental health, and brain health. Copyright 2023. From Lifestyle Psychiatry by Gia Merlo & Chris Fagundes. Reproduced by permission of Taylor and Francis Group, LLC, a division of Informa plc.

available to the growing fetus during pregnancy is allocated to brain development (71). The brain health, quality of life, and overall well-being of offspring are critically dependent on the trajectory of their neurodevelopment, which begins prenatally (72, 73). An explanation for the relationship between postnatal neurodevelopment and gut microbiota diversity may lie in their influence on each other's maturation processes mediated through the BGM axis (74).

Diet plays a critical role in the development of the gut microbiota in early life (75, 76). Research has demonstrated that the presence of breast- or formula-feeding, as well as the timing of transition to solid foods, are major drivers in shifting the gut microbiota to a more adult-like composition (77). Gut microbiota composition varies between infants fed breast milk versus formula. The microbiota of breast-fed infants primarily consists of *Bifidobacterium*, *Lactobacillus*, and *Staphylococcus* (77, 78). Notably, the microbiota of formula-fed infants is predominantly *Clostridium*, *Anaerostipes*, and *Roseburia*. Moreover, data indicates that the introduction of solid foods around 6 months of age (within the critical neurodevelopmental window) in infants with an immature gut microbiota can fortify their health by stimulating the growth of microbes typically present in the adult gut (79). Adult-like gut microbiota are typically inclusive of *Anaerostipes*, *Bacteroides*, *Bilophila*, *Clostridium*, and *Roseburia* (77).

It has also been noted that breast milk feeding and duration of breastfeeding are positively associated with enhanced structural connectivity of neuronal networks in both white and gray matter, including regions of the brain consistent with improved outcomes related to cognitive and behavioral performance (80–83). Studies have not only revealed that levels of cognitive function of breast-fed children are significantly higher than formula-fed children at six to twenty-three months of age, but also that this distinction in brain performance persists over time as children age (84–86).

5.2 Early life

Early life eating patterns, which modulate and prime the gut microbiota have been found to influence both short- and long-term human health and disease, including brain health and heart disease (87). Codagnone et al. (88) identified the gut microbiota as the fourth most significant element in the programming of brain health and disease during early life, in addition to host genetics and prenatal and postnatal environment. Adolescence is a critical period of neurodevelopment that coincides with maturing socially, cognitively, and improving executive function (89). Typical adolescent diets tend to be high in UPF, high in sugar containing foods and beverages, and low in fiber. Adolescent diets can contribute to mental health symptoms, yet experts are still investigating the crossroads of a healthy gut microbiota, a developing brain, and brain health (90).

5.3 Adult life

Composition of gut microbiota gradually shifts throughout the lifespan and has been shown to play a role in the regulation of age-related changes in cognitive function and immunity (91). It is of significance to note that the current global burden of disease is mainly caused by neuropsychiatric conditions and cardiovascular disease. Poor diet, which can induce dysbiosis, has been established as one of the major contributing factors to the global burden of disease (92). Individuals affected by neuropsychiatric conditions are also more likely to be affected by chronic conditions, such as cardiovascular diseases (93). Daily lifestyle choices, including healthy or unhealthy eating patterns, can serve as protective factors or risk factors for the development and progression of neuropsychiatric conditions and chronic health conditions.

Individual differences in lifestyle-related factors, such as diet, contribute to cognitive reserve and physical reserve. Cognitive reserve is the brain's adaptive capacity to be resilient against neural damage or age-related cognitive decline by efficiently using available brain resources through pre-existing or compensatory processes (94). Physical reserve is the body's capacity to maintain physical functionality in the setting of illness, injury, or age-related physiological changes (95). Robust evidence indicates healthy eating (96). The World Health Organization describes a healthy diet as an eating pattern that is rich in fruits, vegetables, legumes, nuts, and whole grains and restricted in refined sugar, salt, saturated fats, and *trans*-fats (97). A healthy diet has been found to be positively correlated with cognitive reserve and cognitive function (98).

5.4 Elderly life

The gut microbiota composition again changes in this phase of adult life as the bacterial diversity decreases. Opportunistic bacteria, like the *Enterobacteriaceae* family, increase in density (99). Animal models have shown that higher concentrations of LPS in adults can lead to increased blood brain permeability, tau hyperphosphorylation and additional neuroinflammation and may account for cognitive deficits (100). In a cross-sectional study of 127 participants, Saji et al. found a correlation between LPS concentration and mild cognitive impairment (odds ratio: 2.09, 95% confidence interval: 1.14–3.84, $p = 0.007$) (101).

6 BGM system and neuroplasticity

Brain development is a process that occurs throughout the lifespan of the individual. After the initial fetal development, which is driven by the actual genetics of the fetus, subsequent development, also called neuroplasticity, is significantly driven by environmental and epigenetic changes. Changes can provide benefits or maladaptive effects that can lead to a spectrum of neuropsychiatric sequelae (102). In a recent review, Innocenti identifies five potential targets of neuroplastic change: 1) neuronal cell count, 2) neuronal cell migration, 3) differentiation of the somatodendritic and axonal phenotypes, 4) formation of neuronal connections or pathways, and 5) cytoarchitectonic differentiation within the microglia. The intent of this section is not to provide a definitive review of all possible implications but rather show examples within the metabolic, immune, neuronal, and endocrine pathways.

6.1 Neuronal cell count

Neurogenesis is a fundamental component of neuroplasticity, as well as the functional and structural processes related to brain health homeostasis. The formation of new neuronal cells continues in the adult hippocampus throughout the course of the lifespan. The hippocampus is a region in the brain that modulates learning, memory, and mood and is extremely sensitive to environmental stimuli, including diet (103). Evidence suggests that decreased neurogenesis contributes to cognitive impairment and neuropsychological conditions, such as anxiety and depression (104, 105). Zainuddin & Thuret suggest that nutrition can influence adult hippocampal neurogenesis via four primary pathways, including caloric intake, the nutritional content of meals, frequency of meals, and texture of meals (106).

6.2 Neuronal cell migration

Recent literature suggests that neuropsychiatric disorders and cognitive dysfunction are linked to damage induced by oxidative stress on nuclear and mitochondrial DNA (107, 108). Oxidative stress is a key pathway through which dietary factors affect neuronal cell migration. Of note, reactive oxygen species (ROS) involved in pathways related to oxidative stress have been found to induce epigenetic changes in aging processes of the brain (109), as oxidative damage has been recorded as a significant contributor to neurodegeneration (110). Increased production of free radical production and inflammatory responses may occur when long-term exposure to prooxidant and proinflammatory metabolic factors exceeds the capacity of bodily systems to protect against tissue injury and mitochondrial damage (111). Long-standing excess in certain nutritional components can induce a metabolic state of chronic, dysregulated, low-level inflammation often co-occurs with mitochondrial dysfunction (112).

Oxidative stress and damage can be caused by prooxidant foods, which have been found to decrease antioxidant activity and increase the production of ROS (113). The quality and quantity of various macronutrients and micronutrients can interact with prooxidant or antioxidant metabolic pathways (114). Data indicates that oxidative mechanisms inhibit the proliferation of precursor neurons, as well as the migration, differentiation, and viability of new neuronal cells (115, 116).

6.3 Cell phenotypes

The differentiation process of a neuron into somato-dendritic or axonal phenotypes engenders alterations in metabolic needs that vary from those of precursor or stem neuronal cells and are mediated by dietary nutrients (117). Differentiated mature neurons require higher levels of energy. The increased energy needs of the developing or mature brain is bolstered through a metabolic shift from energy primarily sourced from cytoplasmic aerobic glycolysis to neuronal oxidative phosphorylation modulated by the mitochondria (117, 118). It is important to note that the reprogramming of metabolic processes related to the oxidation, glycolysis, and mitochondria supports neurogenesis and the functionality of differentiated neuronal cells by promoting adequate epigenetic modulation of gene expression and increased signaling of neurotransmitters in both the central nervous system and across the BGM system.

6.4 Neuronal connections

Increasing evidence substantiates that the both cognitive and non-cognitive functions of the brain encoded in the human genome are vulnerable to modification via epigenetic and epitranscriptomic mechanisms (119–122). The bidirectional relationship between food and the BGM system can alter neuroplasticity through interactions with these epigenetic and epitranscriptomic pathways. Nutrient intake can regulate gene expression that modulates learning, memory, and adaptive behaviors (123). Alternatively, neuroplastic changes in learning, memory, and adaptive behaviors can alter gene expression to promote different eating patterns. For instance, peptide hormones, such as ghrelin, leptin, and insulin, which are implicated in physiological processes surrounding hunger and satiety, utilize nutrient sensing along the BGM system to modulate signals in the brain related to hunger, satiety, and food-induced reward (124). Reception of these signals then shapes adaptive behaviors and experiential learning and conditioning associated with food intake, which can regulate mechanisms for the activation or repression of certain genes (125).

6.5 Cytoarchitectonic differentiation

Bioactive nutritional compounds may have the potential to restore quiescent capacity of microglia, which are cells that play a vital role in neurodevelopment (e.g., neuronal proliferation, neuronal differentiation), brain health homeostasis, neuroplasticity, and injury response and repair mechanisms in the central nervous system. Dysregulation of microglial cytoarchitectonic differentiation has implications in neuroinflammation, cognitive deficits, neuropsychiatric conditions, and chronic inflammatory diseases (126). Cytoarchitectonic differentiation within the microglia denotes the process of area-specific structural organization of these nervous system-specific macrophage cells. Neuroinflammatory responses can be induced by microglial cells in response to immune signals from the periphery. Evidence has demonstrated that age-related alterations in the brain cause changes in microglial morphology, as well as attenuated microglial functional capability to regulate injury and repair processes through adequate homeostatic shifts between anti-inflammatory and proinflammatory states and migratory and clearance abilities (127). Epigenetic modifications also change microglial functional profiles (128). Data suggests that microglia exposed to different environmental factors early in life, such as certain nutrients, may have implications in microglial diversity in later life through these epigenetic modifications (129).

7 Neuropsychiatric disorders affected by food

As previously discussed, there is a bidirectional link between metabolic aberrations and a diverse array of neuropsychiatric disorders (130–132). Approximately one in three individuals with a chronic health condition are affected by co-occurring neuropsychiatric condition (133, 134). Not surprisingly, the neuropsychiatric conditions most affected by dietary factors, anxiety and depression (135), are also those most prevalent in the general population. Diet-related pathways for therapeutic targets include the BGM system, inflammation, oxidative stress, mitochondrial dysfunction, epigenetics, the HPA axis, and tryptophan-kynurenine metabolism (20), which address many of neural circuits implicated in depression (16).

As noted, depression continues to be one of the world's most debilitating illnesses. World estimates have estimated the lifetime prevalence between 30 and 40% (136). It is not uncommon for symptoms to last at least 1 year in duration (137). Depression is comorbid with other neuropsychiatric illnesses (i.e., anxiety, cognitive impairment, post-traumatic stress disorder, substance use disorders) and chronic physical disorders (i.e., arthritis, asthma, cancer, cardiovascular disease, chronic pain, chronic respiratory disorders, diabetes, hypertension, obesity) (138). Those with these comorbid outcomes tend to have worse outcomes (137). As a result, individuals with depressive disorders commonly develop a pattern of dysbiosis, showing higher concentrations of the *Bacteroides* species, a species that alters the BGM system (139, 140).

Historically, the treatment of choice for depression has been the use of medications that modulate the uptake of serotonin (i.e., selective serotonin reuptake inhibitors). Many individuals, however, have not received symptom relief from these remedies (141). Lessale et al., conducted a meta analysis of 21 cross sectional studies and 20 longitudinal studies. Individuals were either adhering to the Mediterranean diet (MD), the Healthy Eating Index, the Alternative Healthy Eating Index, the Dietary Approaches to Stop Hypertension, or the Dietary Inflammatory Index. Individuals on the MD had an estimated relative risk of developing depression of 0.67 (5% CI 0.55–0.82) (142). Firth et al. examined 16 randomized clinical controlled trials (dietary interventions varied) comprising over 45,000 participants and noted that dietary interventions improved depressive symptoms compared to controls ($g = 0.275$, 95% CI = 0.10 to 0.45, $p = 0.002$) (29). The SMILES study, a randomized control study, had study participants avoid UPF and fast food. The study showed that the number needed to improve depressive symptoms was 4.1 (143). A meta-analysis from 2018 of epidemiological studies showed that every increase in 100 g of whole fruits or vegetables corresponded with a 5% reduction risk of depression (144). Given these findings the Royal Australian and New Zealand College of Psychiatrists recommend lifestyle changes, including diet and exercise, and therapy for mild and moderate forms of depression (145). Similarly, the World Federation of Society for Biological Psychiatry has adopted a WFBP within its treatment recommendations for depression (146).

8 Future directions related to the gut microbiota, nutrition, and mental health

Prior to the COVID-19 pandemic, it was estimated that 50% of the United States experienced loneliness (147). Following the pandemic, the impact of loneliness has increased. More adolescents report loneliness and isolation and chronic illness. Although there is not a direct correlation between isolation, chronic illness and mental health, those who experience isolation report having increasing mental health symptoms (148). Based on world events, social injustice, and worsening socioeconomic factors, it seems unlikely that these trends will reverse. Although it may seem trivial in the wake of these factors to focus on the BGM system and nutrition, this effort may have more of a global impact. In addition to the mental health symptoms as outlined, dietary choices are the largest driver of chronic illness (21). The health industry promotes protein as the optimal food ingredient to reverse these trends and overlooks the importance of fiber (43). As a result, less than 5% of Americans are consuming an adequate dose of fiber (149), which has been key in developing and maintaining a healthy BGM-system (3, 34, 150).

Traditionally, healthcare professionals receive very little evidence-based nutrition didactics during their formal education (151). The reasons vary from nutrition being a "soft science," or there is "too much controversy over the nutrition literature," or there is "only time to teach what is on licensing exams." To ensure that healthcare providers receive this vital training, licensure boards need to incorporate questions regarding plant-based nutrition and the importance of the BGM system. Additionally, we encourage other medical organizations to follow the Royal Australian and New Zealand College of Psychiatrists and World Federation of Society for Biological Psychiatry and adopt lifestyle guidelines within their mental recommendations.

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A remotely accessible plant-based culinary intervention for Latina/o/x adults at risk for diabetes: lessons learned

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Introduction: Little research has examined how community-engaged and -participatory dietary interventions adapted to remotely-accessible settings during the COVID-19 pandemic.

Objectives: To identify lessons learned in design, implementation, and evaluation of a remotely-accessible, community-based, nurse-led approach of a culturally-tailored whole food plant-based culinary intervention for Latina/o/x adults to reduce type 2 diabetes risk, delivered during a pandemic.

Methods: A mixed methods quasi-experimental design consisting of a pre-post evaluation comprised of questionnaires, culinary classes, biometrics, and focus groups.

Lessons learned: Community partnerships are essential for successful recruitment/retention. To optimally deliver a remotely-accessible intervention, community leadership and study volunteers should be included in every decision (e.g., timeframes, goals). Recommendations include managing recruitment and supply chain disruption of intervention supplies.

Conclusion: Future research should focus on increasing accessibility and engagement in minoritized and/or underserved communities, supply chain including quality assurance and delivery of services/goods, study design for sustainable, remotely-accessible interventions, and health promotion.

KEYWORDS

plant-based, diabetes, Hispanic/Latino, health equity, community-engaged, nursing, culinary education, remote interventions

1 Introduction

This study focused on Latina/o/x adults living in the Inland Empire (IE), composed of Riverside and San Bernardino Counties, in Southern California, where 49% of the IE population self-identifies as Latina/o/x with the majority being of Mexican origin (1). A recent report estimated that 46% of California's population has prediabetes with Latina/o/x adults having a 50% chance of developing diabetes during their lifetime (2, 3). In the United States, Hispanic/Latino individuals are 1.4 times more likely to die from diabetes than non-Hispanic whites due to social determinants of health and systemic oppression due to allocation of power and resources (4–9). Every year more than $400 billion are spent on diabetes medication and symptom management (10). While physicians and dieticians often provide guidance on dietary choices and nutrition (11, 12), nurses also receive education and training on providing resources for making informed healthcare decisions (13), including those related to nutrition and diabetes.

Originally intended as a face-to-face culinary intervention, due to the pandemic and need for physical distancing, the redesign of this study shifted to a remotely-accessible format. The redesign included meetings and multiple conversations with community members and leaders, advisors, as well as pretesting study volunteers. These discussions focused on the delivery format of research activities and culminated in implementation of a nurse-led, culturally-tailored, WFPB intervention in a remotely-accessible environment for Latina/o/x adults at risk for developing T2DM. Selection of the WFPB intervention was based on community feedback and previous research showing that a WFPB diet is economical and sustainable for individuals and the planet (e.g., potential to prevent or reverse diabetes, lower blood pressure, promote insulin sensitivity) (14–17).

To maintain accountability to the study volunteers, communities, and other stakeholders involved or potentially impacted, a community advisory board (CAB) group consisting of community members and leaders was consulted during the design, implementation, and data analysis stages. While several of the CAB members worked in healthcare centers, schools, and other local organizations and businesses, some of the individuals were working from home or unemployed. Initially, the CAB members met individually with the primary investigator (PI) on a weekly basis or in groups of up to three individuals. Once the study commenced, meetings occurred every 2 weeks. To enhance trustworthiness, address power in the research process, increase accountability and integrity, community partners from the IE were also engaged as reflexivity partners during the data analysis phase for member-checking.

1.1 Aim

The purpose of this paper was to identify lessons learned in design, implementation, and evaluation of a remotely-accessible, community-based, nurse-led approach of a culturally-tailored whole food plant-based (WFPB) culinary intervention for Latina/o/x adults to reduce type 2 diabetes risk (T2DM), delivered during the COVID-19 pandemic, over a six-week period (January–February 2022).

2 Objectives

The specific aims of the study included (1) to explore the feasibility, safety, and accessibility of a remotely-accessible WFPB culinary and dietary intervention and (2) to assess the WFPB intervention on knowledge and self-efficacy for making healthy WFPB food choices with assessment at baseline and post-intervention. Guided by the PRECEDE-PROCEED Model (18), this remotely-accessible intervention included learning about WFPB food preparation and nutrition while collecting and self-monitoring biometric data.

3 Methods

After receiving approval from the University of Massachusetts Amherst Institutional Review Board, the quasi-experimental study commenced in January 2022. The target population was individuals that self-identify as Latina/o/x adults from the community, ages 18–65 years old, who were determined to be at risk for diabetes or prediabetic as determined by the American Diabetes Association Risk Tool (ADART) (19). Individuals were recruited by word-of-mouth and a flyer. During the design of the study and questionnaires, the researchers, CAB members, and pretesting group discussed the term, "Latinx." This term appeared during the mid-2000s from Latinx lesbian, gay, bisexual, transgender, and queer (LGBTQ) communities in the U.S. as a gender-neutral term (20). Supporters of the term state that it is inclusive of all genders (20). Some critics of the term state that "Latinx" is difficult to pronounce, a colonialist residue, does not follow traditional grammar, and only used by 3% of the population (21). However, it is important to also remember that gender neutrality does not necessarily equal gender inclusivity and a catch-all term may cause unintended marginalization (22). Therefore, in this study, the researchers, CAB members, and pretesting group agreed that the term "Latina/o/x" would be used, with the exception of the manuscript introduction where "Hispanic/Latino" was also used. In addition, Table 1 includes a footnote stating that study volunteers were provided with additional options, on questionnaires, such as non-binary or not listed, including write-in and prefer not to reply, but none of these were selected by respondents. After providing informed consent, study volunteers (Table 1) self-selected to join one of two groups. Study volunteers in the WFPB intervention group ($n = 15$) verbalized an interest in learning more about WFPB nutrition, T2DM prevention, and cooking WFPB recipes. They participated in culturally-tailored WFPB culinary classes, through videoconferencing, adapted and based on the "Culinary Medicine Curriculum" from the American College of Lifestyle Medicine, originally designed by physician and chef, Dr. Michelle Hauser (23). Additional WFPB recipes were adapted from "Decolonize Your Diet," a plant-based Mexican-American cookbook (24) The second group ($n = 6$) also met through videoconferencing, as a comparison group (ADA), and received standard care using the "CDC Prevent T2" curriculum and American Diabetes Association recommendations for diet and meal planning (25, 26).

Previous studies have used the PRECEDE-PROCEED Model to evaluate the effectiveness of community-based health programs, as well as design, implementation, and evaluation of interventions (18, 27, 28). During the PROCEED phases, identification of desired outcomes and program implementation were evaluated based on reflection questions such as, "Are you doing the things you planned to do?" "Is the intervention having the desired impact on the target population?"

Using the Model as a guide, each approach (e.g., WFPB, nurse-led, culturally-tailored) was reviewed and evaluated. This analysis was designed, in part, to help answer questions in the context of collaborating with the Latina/o/x community disproportionately

TABLE 1 Study volunteers' characteristics ($n = 21$).

Characteristic	Description	Whole food plant-based (WFPB; $n = 15$)	Standard care (ADA; $n = 6$)
Age*	18–40	5 (33%)	1 (17%)
	41–65	10 (67%)	5 (83%)
Gender/Gender Identity**	Women	11 (73%)	4 (67%)
	Men	4 (27%)	2 (33%)
Relationship Status*	Never Married	2 (13%)	1 (16.7%)
	Married	11 (73%)	4 (66.7%)
	Domestic Partnership	1 (7%)	–
	Divorced	1 (7%)	1 (16.7%)
Income Level*	$0–49,000/year	5 (33%)	2 (33.3%)
	Above $50,000/year	7 (47%)	2 (33.3%)
	Refused/Unknown	3 (20%)	2 (33.3%)
Level of Education	Less than High School (HS) degree	–	1 (16.7%)
	HS/Gen Ed Development (GED)	4 (26.6%)	2 (33.3%)
	Some College	4 (26.6%)	–
	4-Years of College or Higher	7 (47%)	3 (50%)
Family History of Diabetes	Yes	14 (93%)	4 (67%)
	No	1 (7%)	2 (33%)
Personal History of Hypertension	Yes	5 (33%)	2 (33%)
	No	10 (67%)	4 (67%)

*Study volunteers were provided with options for age, as well as income ranging from $0–100,000+/year. Both categories were dichotomized to protect study volunteers, due to decreased variability in responses. Also, the majority of study volunteers had health insurance, but due to decreased variability in responses, this information was not included in the table. **Study volunteers were provided with additional options such as non-binary or not listed: write-in, prefer not to reply, but none of these were selected by respondents.

impacted both by the pandemic and by systems of oppression and marginalization that place them at higher risk for negative health sequelae such as T2DM.

4 Lessons learned: results and discussion

The overall study was well-received with 71.4% of study volunteers reporting that if given the chance, they would participate in the program again. Study volunteers in both the intervention and comparison groups verbalized that they shared the study materials (e.g., recipes, culinary and T2DM prevention resources) with their family and friends. Lessons learned are listed based on the approaches.

4.1 Community-based approach

Prior to design and implementation of the intervention, a community assessment, as well as dialog with community leaders and members took place. Community leaders were defined as individuals that had leadership roles or strong relationships with the Latina/o/x communities (e.g., community organizers, healthcare professionals, educators), while also self-identifying as Latina/o and working and/or residing in the IE. Community members were individuals that resided in the area, while also expressing an interest in improving the overall health of the community. These individuals made recommendations (e.g., potential need for a translator, time of year to implement the study) to the PI for inclusion. Recommendations were then integrated into the overall design. This provided opportunities to build trust, as well as create an inclusive environment for the community to voice concerns, provide feedback, and be involved in the overall process and design.

The PI's previous work in the IE allowed for long established relationships with community partners that were key for recruitment. Community-and faith-based networks were also utilized for recruitment based on feedback from community leaders and members and previous research (29–35). Although the partnership between the PI, university, and the community had a duration for the length of the study, individuals from the community and the university both expressed interest in potential future collaborations.

4.2 Nurse-led approach

Previous researchers reported that Latina/o/x individuals preferred participating in research activities led by healthcare providers (36). Therefore, the PI and the focus group moderator were masters-level registered nurses, multicultural, multilingual, and had additional training and/or certifications in WFPB nutrition and diabetes education. This nurse-led approach provided opportunities for community members to build connections with nurses from the IE with expertise in WFPB nutrition, T2DM, and health promotion.

4.3 Culturally-tailored approach

Cultural-tailoring occurs when the structure of a program or practice is reviewed and adapted to fit the needs and preferences of a particular cultural group or community (37, 38). Cultural-tailoring may range from the use of bilingual and bicultural staff, social and community support, to curriculum development that embeds values, practices, and traditions (39). In this study, the curriculum was adapted to include discussion of cultural traditions surrounding identity and food, language, group problem solving, discussions regarding beliefs about family, health and illness (e.g., healthy weight, natural remedies, seeking professional advice), and recipes. Although culturally-tailoring can be beneficial, it is important to acknowledge that people are unique individuals, regardless of group-identification. While WFPB nutritional recommendations are often presented in contrast to a standard American diet, this study included cultural-tailoring of the WFPB culinary curriculum. This resulted in a strengthened curriculum that provided additional opportunities (e.g., using familiar recipes, discussion topics, conducive to beliefs and practices) (40) to reach the Latina/o/x communities. One WFPB intervention study volunteer, that attended more than half of the classes stated, "I think it definitely needs to be tailored to culture, because I think that's the best way to increase the chances that the person is going to be 'compliant'" while also stressing the importance of assessing community needs. Study volunteers also verbalized the importance of family and social support, and the impact that support has on lifestyle changes. This feedback reinforced the group format study design that provided a safe space for study volunteers to meet remotely during the COVID-19 pandemic. One study volunteer expressed that the weekly sessions helped them to realize when thinking about health and nutrition, "it is okay to be different from the others" (e.g., lifestyle changes) and five study volunteers shared experiences on making compromises and negotiating with their family members' choice of restaurants, grocery shopping, and meal planning to follow a WFPB diet. While some study volunteers expressed having support systems in place for lifestyle changes, other study volunteers expressed that even after verbalizing intentions to family and friends, they did not always feel supported.

The researchers emphasized the importance of culture (e.g., customs, family, community, ethnicity and ethnic foodways), as it has the potential to impact all aspects of the study, including recruitment and retention, social support for study volunteers, and building trust.

4.4 Remotely-accessible setting

Study volunteers reported that the remotely-accessible setting was feasible, but still posed challenges. Challenges included needing reliable internet access and finding a private workspace that allowed access to both the device screen and cooking area. Some individuals switched from using a desktop computer to a mobile device, but mentioned not always having the ability to view the small screen from a distance and running out of battery.

Although study volunteers selected their preference for class times, it may be beneficial to provide an asynchronous option for future studies. However, some study volunteers reported preferring the weekly synchronous format because it helped with "accountability" and "staying on track." They also reported that the format enabled participation during the COVID-19 pandemic, so they "felt safe," with one individual stating, "From my perspective, I do not think I would have participated if it wasn't online." The synchronous format also provided the benefit of immediately observing and implementing culinary skills within study volunteers' kitchens while using their own cooking utensils and supplies.

Some study volunteers requested copies of the slides and recordings to review due to being hard of hearing and stated that they preferred to use the chat feature in Zoom, rather than speaking. Study volunteers often turned off their cameras and microphones during recorded sessions. For this reason, it was decided not to record at all times, but rather during selected sessions or portions. Previous research regarding technology access and use among low-income immigrant Latino parents revealed that individuals frequently used text messaging (40), which might partially explain the preference for the chat feature.

4.5 Whole food plant-based approach

The PI noted that community members would sometimes receive food assistance, including fresh fruits and vegetables, which they would then request to trade for processed food. When asked, individuals often reported an interest in WFPB nutrition and/or increasing fruit and vegetable intake, but stated were often unsure of preparation of the fresh fruits and vegetables, "so they usually just sit in the back of the refrigerator." Knowledge from these conversations was included in the design.

During the study, study volunteers discussed ways to increase their weekly fruit and vegetable consumption, discovered new foods, reported enjoying "cooking on Thursday evening means that I have food for the weekend," attempted preparing and eating additional WFPB meals during the week, and tried "to learn how to plan ahead." By providing study volunteers with resources on batch cooking and cooking on a budget, individuals gained knowledge on preparing one versatile item, for example, quinoa, and then using the quinoa to create five different main dishes.

In addition, study volunteers shared multiple recipes with individuals outside the study. Recipes were described as meeting the goal of food preparation: "healthy and delicious." Because mealtimes are often communal, one lesson learned was that the recipes must be delectable to those that the person prepares food for, not just the individual.

4.6 Focus groups

Two voluntary remote focus groups were included as part of the WFPB intervention assessment. The 60-min focus groups provided an opportunity for the study volunteers to discuss their lived and study experiences, including challenges. The ADA standard care group had discussion times within their weekly classes. The first focus group ($n = 5$) met in week four and the second one ($n = 2$) met a few days after the intervention concluded in week six. Using a semi-structured interview guide, a registered nurse trained as a diabetes educator and a student nurse research assistant moderated the focus groups.

Two research team members read the transcripts and independently identified common themes using selected comments as examples for each theme. One team member coded the transcripts, line-by-line, with constant comparison with a member of the research team, using descriptive thematic analysis and *in vivo* coding in NVivo, version 12. By using *in vivo* coding, study volunteers' actual spoken words and phrases were used as codes. Codes were grouped and clustered into categories. From these categories, themes and concepts were identified as those repeatedly or consistently discussed in relation to the study objectives and indicated in the codebook. Memoing, constant comparison, and close member check-in resulted in the finalizing of the categories and main themes.

Topics covered perceptions of health/illness, current dietary habits, experiences of Latina/o/x individuals, intervention and accessibility, and personal vision and goals related to their health. The focus groups were conducted in English with a trilingual (English, Spanish, and Portuguese) focus group moderator, not the PI. Future focus group study volunteers may benefit from a printed list of the discussion questions beforehand, as well as incorporating elements of photovoice to increase engagement. Study volunteers expressed enjoying sharing photographs of prepared food as a way of promoting conversation and receiving recognition for the creativity they used to engage in the intervention.

4.7 Budget

This research was conducted as part of a dissertation research project with study volunteers' biometric equipment funded by Beta Zeta at-Large Chapter of Sigma Theta Tau International Honor Society of Nursing. The disruption of the supply chain during the implementation of the study impacted the price of the study volunteers' equipment as prices increased from the time the grant was submitted and obtained. Study volunteers were responsible for costs associated with purchasing their own food items and cooking supplies for the culinary classes. For future studies, it is recommended to proactively create a detailed budget that takes into consideration food cost inflation. Food items that study volunteers and the PI purchased for the culinary sessions (~$25-30/week, depending on items already available at home and where the items were purchased), as well as the cost of equipment and time spent shopping for items also increased. For future studies, it might be more convenient if food items and/or use of a home-based delivery service were provided to reduce participant burden.

4.8 Equipment

All study volunteers received glucometer kits, automatic blood pressure cuffs, bathroom scales, and tape measures through the mail. The PI conducted videoconferencing training to teach and/or review use of the equipment with study volunteers prior to biometric data collection. Several study volunteers reported that they had "never paid attention to the numbers at the doctor's office." During the WFPB culinary classes and also the ADA standard care sessions, study volunteers were provided with resources and training on parameters for blood pressure and fasting blood glucose, including when to follow up with a healthcare provider.

In some cases, even when using expedited one-or two-day shipping, study equipment was delayed. The U.S. Postal Service reported delays due to a worker shortage and employees in quarantine due to the pandemic. However, there have been previous reports of longstanding issues (e.g., financial and operational), as well as infrastructure underinvestment (41). Based on this information, future remotely-accessible studies should include options to accommodate a variety of study volunteer requests (e.g., asynchronous, additional ways of obtaining biometrics) and/or supply chain disruptions.

While 71.4% of study volunteers completed return demonstrations on equipment use without challenges, 28.6% of individuals reported challenges with the lancing devices (e.g., setup, fear of needles). Post-intervention, 28.6% of study volunteers did not want to use the glucometer, specifically the lancet devices, and did not submit all of their final biometric data. When asked about the lancet devices, one study volunteer stated, "I do not want to poke myself again. I do not know how people with diabetes do this every day." Previous studies have shown that when providing individuals with training involving needles, it may be beneficial, as was conducted in this study, to provide training at a time that is separate from other activities, using the smallest gauge available, while raising awareness of prevention and treatment options, and discussing any potential barriers (42, 43). Community partners suggested in the future, it might be beneficial to offer the option of a serum lab draw or allowing family members to assist with biometric data collection.

4.9 Strength and limitations

The strengths of this study included assessing and evaluating the needs of Latina/o/x adults in the IE with community leaders and members prior to the design. At the time design, consultants with expertise in nursing, community-based participatory approaches, interventions including Latina/o/x individuals, and T2DM provided their invaluable feedback. In addition, prior to the six-week study, all questionnaires were reviewed and completed by the pretesting group. At the close of the study, interested study volunteers were also able to review the findings and results prior to submission for publication. Although the results are potentially transferrable to other contexts and/or settings, this study was specifically designed for Latina/o/x adults residing in the IE.

Limitations of this study include self-reported data, missing data, and time constraints. In addition, community partners and members were not involved in shaping the research instruments. While multiple attempts were made to recover missing data, results may also reflect systematic biases in terms of who was able to complete the study. Based on feedback and patterns in the data collected, there is the potential to expand this study in the future. While qualitative data and use of questionnaires are self-reported, multiple strategies including an audit trail and member-checking activities were used to increase trustworthiness and rigor (44, 45).

5 Conclusion

Through this study, the researchers identified lessons learned and found ways to improve implementation of future WFPB remote interventions for Latina/o/x populations. Findings from this research indicate that a remotely-accessible, nurse-led, culturally-tailored WFPB culinary intervention designed to reduce T2DM risk and increase self-efficacy in Latina/o/x individuals is feasible, safe, and enhanced accessibility. Knowledge generated revealed that this type of intervention may not only increase awareness and potentially promote health, but also has potential to increase fruit and vegetable intake among Latina/o/x adults, as long as "healthy and delicious" recipes are provided.

Nurse-led interventions can provide opportunities to explore and gain a better understanding of individual's beliefs about dietary and lifestyle practices leading to improving future design of nutrition studies. Through identification of risk factors and education, Latina/o/x adults can access additional options and resources for improving their overall health outcomes and making informed healthcare decisions.

Data availability statement

The datasets for this article are not publicly available due to concerns regarding participant anonymity. Requests regarding datasets should be directed to the corresponding author. The full dissertation with data to support this study will be available through Scholarworks@UMass from May 13, 2027 (see Acknowledgements).

Ethics statement

The studies involving humans were approved by University of Massachusetts Amherst Institutional Review Board. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

LK: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Writing – original draft, Writing – review & editing. FI: Conceptualization, Methodology, Resources, Writing – review & editing. AM: Conceptualization, Formal analysis, Methodology, Resources, Validation, Writing – review & editing. KC: Conceptualization, Resources, Writing – review & editing. IB: Conceptualization, Resources, Writing – review & editing. RW: Conceptualization, Formal analysis, Funding acquisition, Methodology, Resources, Software, Supervision, Validation, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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Case series: raw, whole, plant-based nutrition protocol rapidly reverses symptoms in three women with systemic lupus erythematosus and Sjögren's syndrome

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Systemic lupus erythematosus (SLE) and Sjögren's syndrome (SS) are chronic autoimmune diseases. Symptoms of SLE can vary widely but often include fatigue, pain, photosensitivity, and, in some cases, nephritis. SS is frequently characterized by extreme dry eye and mouth, resulting from damage to moisture-producing glands, and is often present in combination with SLE. While the health benefits of plant-based diets have been well-established with respect to weight and cardiometabolic outcomes, less research is available to support the role of diet in treatment and management of autoimmune disease. This case series presents three women with SLE and SS who adopted a nutrition protocol to reverse symptoms of autoimmune disease. The protocol emphasizes leafy greens, cruciferous vegetables, omega-3 polyunsaturated fatty acids, and water, and includes predominately raw foods. The three patients reported dramatic improvements in physical symptoms, with nearly all symptoms of SLE and SS resolving after 4 weeks or less of adhering to the protocol. All three patients have remained symptom-free, two of whom have remained symptom-free for 6+ years with no recent medication use. Patients and practitioners should be made aware of the promising possibility of food as medicine in the treatment of SLE and SS. Future research should explore whether dietary changes may be a potential treatment strategy for individuals suffering from severe symptoms and poor quality of life due to SLE and SS.

KEYWORDS

systemic lupus erythematosus, Sjögren's syndrome, raw foods, whole-food, plant-based (WFPB), vegan, disease reversal, autoimmune, lifestyle medicine

Introduction

Sjögren's Syndrome (SS) is a chronic, autoimmune disorder characterized by damage to moisture-producing glands, resulting in dry eyes (xerophthalmia) and mouth (xerostomia). It can also encompass other symptoms including joint pain, swelling, rashes, and fatigue. SS may be present in combination with other autoimmune diseases, such as systemic lupus erythematosus (SLE). SLE is also a chronic, autoimmune disease, but symptoms can vary widely in both scope and severity. Common symptoms include extreme fatigue, joint pain and swelling, hair loss, photosensitivity, and a butterfly-shaped rash across the cheeks and nose. More serious damage such as nephritis and pleuritis can also occur. The prevalence of SLE is estimated to be 43.7 (range 15.87 to 108.92) per 100,0000 persons globally, with a prevalence of 78.73 (28.61 to 196.33) per

100,000 in women and 9.26 (3.36 to 22.97) per 100,000 in men (1). Estimates of the prevalence of SS in SLE patients in the literature vary from 6–19%, likely due to the use of different criteria to define SS (2–4).

There is an extensive amount of research documenting the health benefits of plant-based diets with respect to weight and cardiometabolic outcomes (5–11). A growing body of research has shown that lifestyle change, specifically adherence to more plant-based diets, may both protect against autoimmune disease as well as improve symptoms of autoimmune dysfunction (12, 13). A 2022 study suggested that individuals adhering to a vegetarian diet had lower odds of being diagnosed with SLE compared to non-vegetarians (14). This case series details three women with SLE and SS who reported remission of symptoms after following a strict, customized, plant-based nutrition protocol for recovery (recovery protocol) that eliminates all processed foods and was developed by the author, Dr. Goldner (BG). The three cases presented completed the author's Rapid Recovery Program (RRP), in which they work with the author (BG) on a daily basis for personalized recommendations and maximum support with respect to adhering to the recovery protocol. The RRP is offered as either a 4-week, one-on-one program or a 6-week group program.

Whole-food, plant-based (WFPB) diets eliminate processed foods, added oils, sugars, and animal products, and the recovery protocol shares similarities with a WFPB diet; however, it is further refined to focus on predominately raw foods and high intakes of leafy greens and cruciferous vegetables, omega-3 polyunsaturated fatty acids (whole, ground flax or chia seeds; cold pressed flaxseed oil), and water. On the recovery protocol, while raw vegetable intake is allowed *ad libitum*, minimum daily intakes are set as follows: 16 oz. leafy greens (i.e. spinach, kale) and cruciferous vegetables; ½ cup flax or chia seed or 3 tablespoons cold pressed flaxseed oil; and 96–128 oz. of water. Fruit is recommended at no greater than 25% of total dietary intake to ensure that patients are able to consume the recommended amount of raw vegetables before reaching satiety. Vitamin B12 and vitamin D supplementation is recommended. If remission of symptoms is achieved, patients are allowed to step down to a maintenance phase which allows for the incorporation of some cooked whole, plant foods as well as more fruits, and the addition of nuts and seeds. Patients are advised to try one new change at a time, waiting 3–5 days in between to ensure there is no re-emergence of symptoms. If symptoms emerge, patients return to the recovery protocol. The maintenance phase remains 100% plant foods with 75% of intake recommended to be raw, continuing with daily smoothies or salads, and incorporating 64 oz. of water or more unless otherwise recommended by the patient's physician. Fruit is not restricted, and other whole, plant foods such as legumes and whole grains may be incorporated during maintenance. After 6 months of remission, processed vegan foods, foods with sugar or oil, and alcohol are allowed 1–2 times/week (termed 'recreational eating'), while otherwise continuing the maintenance protocol, if patients remain asymptomatic (Table 1).

Case descriptions

Case 1

Case 1, a 40-year-old female, was approximately 9 months pregnant when diagnosed with SLE and SS in 2013 and reported experiencing symptoms since at least 2010. She was taking hydroxychloroquine for

TABLE 1 Summary of dietary recommendations during rapid recovery and maintenance phases.

	Initial rapid recovery/reversal phase	Maintenance[5]
Include	• Raw vegetables (unlimited); focus on high intake of leafy greens and cruciferous vegetables, minimum recommended 16 oz. per day[1] • Fruits (recommended ≤25% total dietary intake/day) • Whole, ground flax and chia seeds (minimum 1/2 cup recommended per day initially and increase as tolerated)[2] or 3 tbsp. cold pressed flaxseed oil • Water[3] • Vitamin B12 and D supplementation • 1 tsp. salt/day • *Ezekiel bread (not typically included) allowed for Case 1, due to increased hunger during pregnancy*	• Vegetables (focus on high intake of cruciferous vegetables); recommended 75% raw • Fruits (no recommended restriction) • Seeds and nuts • Whole, ground flax and chia seeds (minimum 1/4 cup/day) • Water, recommended 64 oz. or more • Intact, whole grains • Legumes • Vitamin B12 and D supplementation • 1 tsp. salt/day
Eliminate	• All animal products (i.e., meat, dairy, seafood) • Added oils[4] • Processed foods • Added sugars • Cooked foods • Grains • Legumes	• All animal products (i.e., meat, dairy, seafood) • Added oils[4] • Processed foods, added sugars, alcohol (exception noted below) – After 6 months of remission, processed vegan foods, foods with sugar or oil, and alcohol are allowed 1-2 times/week (termed 'recreational eating'), while otherwise continuing the step-down[5] or maintenance protocol. This is only allowed when individuals remain asymptomatic.

[1]Recommend at least 64 oz green smoothie per day as a way to more easily consume the recommended vegetables.
[2]Assess gastrointestinal discomfort; recommended to spread intake throughout the day.
[3]If body weight ≥ 120 lbs., recommended 96–128 oz. per day (approx. 1 gallon); if body weight < 120 lbs., recommended water is oz. of body weight (i.e., 80 lbs. = 80 oz. water/day); some patients (i.e., Case 3) may need to individually adjust requirements with their physician.
[4]Exception for cold pressed flaxseed oil.
[5]When moving from initial rapid recovery phase to maintenance phase, patients are advised to try one new change at a time, waiting 3–5 days in between to ensure there is no re-emergence of symptoms. If symptoms emerge, patients return to the recovery protocol.

TABLE 2 Case 1: summary of laboratory testing from 2014 to 2018.

	Date of laboratory testing						
	6/23/14	8/4/16	10/20/16	1/6/17	6/19/17	10/19/17	3/8/18
DNA (DS) antibody, IU/ml[a]	3 (negative)	5 (indeterminate)	5 (indeterminate)	6 (indeterminate)	–	–	–
Sjögren's antibody: SS-A	>8 (positive)	–	–	–	>8 (positive)	–	>8 (positive)
Sjögren's antibody: SS-B	3.3 (positive)	–	–	–	<1 (negative)	–	<1 (negative)
ANA[b]	positive	–	–	–	–	positive	–
Lupus Anticoagulant (LAC)[c]	–	–	–	–	–	not detected	–
Cardiolipin antibody-IgM[d]	25 (high)	24 (high)	–	–	–	–	–
Cardiolipin antibody-IgG[d]	<14 (negative)	<14 (negative)	–	–	–	–	–
Cardiolipin antibody-IgA[d]	–	<11 (negative)	–	–	–	–	–
PTT screen (LAC)[e]	43 (high)	–	–	–	–	37 (normal)	–
CRP (mg/dL)[f]	0.1 (in range)	–	–	–	–	–	–
C3 (mg/dL)[g]	96 (in range)	–	–	–	–	91.6 (in range)	–
C4 (mg/dL)[g]	38 (in range)	33 (in range)	–	–	–	28.5 (in range)	–

[a]Antinuclear antibody frequently present in individuals with SLE; may suggest more serious SLE.
[b]identifies autoantibodies characteristic of autoimmune disorders; most individuals with SLE have positive ANA.
[c]Lupus anticoagulants (LA) are antiphospholipid antibodies that specifically target phospholipids and associated proteins and can interfere with blood clotting.
[d]Cardiolipin is another antiphospholipid antibody. The presence of LA and cardiolipin do not indicate a diagnosis of SLE; however, these tests can indicate potential risk of complications from antiphospholipid antibodies in SLE patients, such as miscarriage, blood clot, or stroke.
[e]Partial thromboplastin time (PTT) measures time it takes for blood to clot and can identify if blood contains anticoagulant antibodies.
[f]Blood marker for inflammation.
[g]Low levels of complement C3 and C4 reflect inflammation.
– indicates test not performed.

management of SLE and SS and aspirin to reduce risk of blood clot and miscarriage. She experienced extreme photosensitivity, fatigue, and pain in the legs that required her to spend much of the day lying down. She also experienced extreme dry skin, including cracks that would not heal, dry eye, and dry mouth. Other symptoms included stomach cramping, diarrhea, and severe pelvic pain. Interested in natural treatments, she contacted the author (BG) in April 2017 and immediately began her 4-week, one-on-one RRP to which she reports being 100% adherent. She notes that while she did consult with her rheumatologist prior to beginning the RRP, she did not consult with her obstetrician because, in her words "I was desperate to get healthy and scared of a flare-up after delivery, which is what happened with my first pregnancy." She consumed one 64 oz. green smoothie daily, composed predominately of raw leafy greens such as kale or spinach, water, and fruit added for flavor. She also incorporated flaxseed, first starting with ½ cup and working her way to a full cup. Her other meals throughout the day included foods such as salads and raw vegetables, in addition to drinking a gallon of water. The only non-raw food that she consumed was Ezekiel bread, a sprouted whole grain bread, at the recommendation of the author, which is not typically included with the recovery protocol but was allowed due to increased hunger during pregnancy.

Two days into the RRP, she reported that her pelvic pain had stopped. Most other symptoms completely resolved over the 4 weeks, including the dryness, pain, and fatigue. The cracks in her skin were actively healing, and completely resolved within 3 months of beginning the RRP. She remained active during pregnancy, gave birth to a healthy child, recovered quickly from her C-section, and continued with no pain and increased energy post-birth.

Two months after completing the RRP she went outside for the first time and experienced no photosensitivity. By approximately 6 months after completing the RRP, she had discontinued both hydroxychloroquine and aspirin. Post RRP, her lab results showed a decrease in SS-B, a marker antibody for SS, as well as a decrease in partial thromboplastin time (PTT), for which a prolonged PTT (>40) may suggest SLE (Table 2). She transitioned to a maintenance diet, still including no processed foods, 40 oz. per day of green smoothie, a gallon of water, and approximately 90% raw, whole plant foods during the day with a cooked plant-based meal for dinner. As of last contact (December 2023), she remained off all medications, had an additional healthy pregnancy and delivery in 2020, and reported no recurrence of symptoms. She reports feeling that the protocol "was such an easy fix for my illnesses." Please see Figure 1 for a timeline of symptoms and treatment. The Supplementary File includes a personal testimony from the case.

Case 2

Case 2, a 54-year-old female, experienced photosensitivity, butterfly rash, itchy scalp, and constant fatigue since approximately 2006. In subsequent years, she was in and out of the hospital with pleurisy, as well as joint stiffness in the fingers, elbows, and knees. She experienced severe dry mouth, which interfered with eating, as well as severe dry eye that began around May 2015. She had been diagnosed with SLE based on bloodwork on July 5, 2015 and was prescribed hydroxychloroquine which she reports did not improve symptoms. Months later, she was diagnosed with SS. In February 2016, she saw a neurologist due to neuropathy (fingers, arm) who recommended she reach out to the author (BG) which she did on February 14, 2016.

Case 2 read the author's book (BG) detailing the recovery protocol (15) and eliminated all meats, sugars, processed foods, and added oils except for cold pressed flaxseed oil from her diet and began to incorporate more greens. She had an initial consultation with the

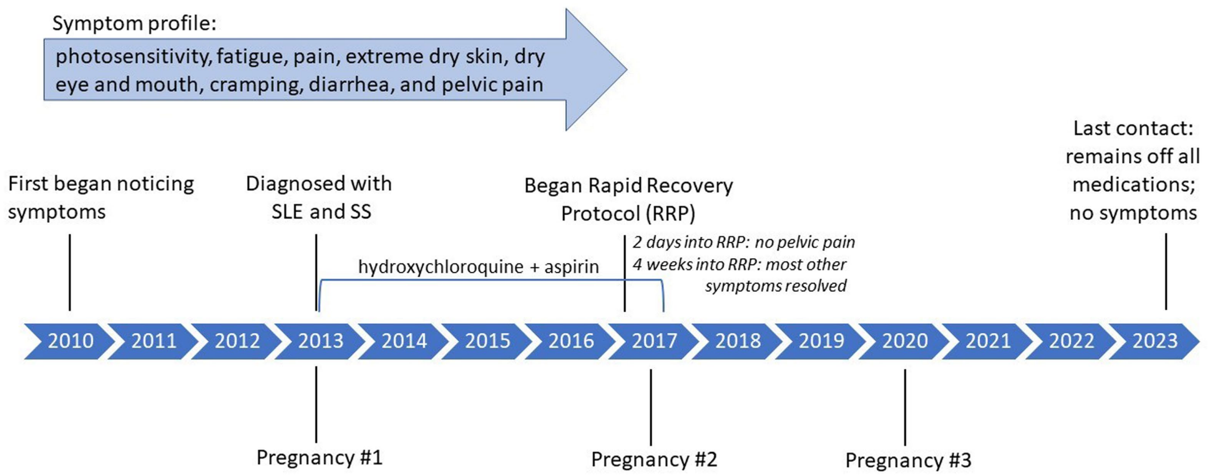

FIGURE 1
Case 1: timeline of symptoms and medication use.

author (BG) about 2 weeks later and further refined her diet to incorporate a higher amount of greens, such as kale and spinach, which she estimates at approximately 11 cups per day (range 2.5–16), as well as raw fruits and omega 3 (chia seeds/flaxseed oil). She enrolled in the 4-week RRP and, after further consultation, her diet included two 32 oz. green smoothies per day, a salad at lunch, and dinner consisting of foods such as kale, cabbage, and Brussels sprouts.

Her symptoms, including neuropathy, joint stiffness, pain, fatigue, itchy scalp, and photosensitivity, resolved within 14 days, and dry eye improved over several months. After 6 months, her ophthalmologist confirmed in an exam that she no longer had any visible eye inflammation and showed no physical symptoms of dry eye. Her anti-double stranded DNA (anti-dsDNA) test results, for which higher numbers suggest higher presence of SLE antibodies, decreased from 20 IU/mL in January 2016 to 16 IU/mL in January 2017. Although 16 is still above normal, it should be noted that dsDNA can remain positive even when clinical symptoms are not present.

She maintained the diet as prescribed by the author (BG) for a year, at which point she started to replace one salad with a cooked plant-based meal, still eliminating all processed foods. She discontinued hydroxychloroquine in January 2017. She reports eating a vegan cake at her wedding made with processed sugar and experiencing joint stiffness after. However, when she went on a cruise and ate unprocessed, whole plant-based foods, she did not experience any symptom flare-ups. After approximately 2 years, she significantly reduced the amount of omega 3 consumed but has not experienced any flares in symptoms or changes in blood work. As of last contact in July 2023, she remains symptom free and continues to eat a whole-food, plant-based diet that incorporates both daily green smoothies as well as cooked foods. She stated "I am doing so well….I'm convinced that it [the recovery protocol] saved my life." Please see Figure 2 for a timeline of symptoms and treatment. The Supplementary File includes a personal testimony from the case.

Case 3

Case 3, a 45-year-old female, reports that from approximately 2003–2008, she often felt sick and achy with flu-like symptoms, migraines, intermittent dizziness, weakness, and increased feelings of dry mouth. She reports having visited her primary care physician (PCP) on multiple occasions, who was unable to determine a cause of her symptoms, although she was never tested for autoimmune disease. In 2008, after the birth of her fourth child, she was referred to a rheumatologist who was also unable to determine a diagnosis. She continued seeing her PCP for her symptoms until he later, still unable to diagnose her, referred her to a psychiatrist. At this time, blood work detected anticardiolipin antibodies, which remained present for the next 7–10 years. Her child was then diagnosed with neonatal lupus at around 10 weeks old. This prompted testing of Case 3 and a subsequent diagnosis of SS based on the presence of antibodies (anti-SS-A and anti-SS-B) and dry eye symptoms. Antinuclear antibodies (ANA) were also detected; however, SLE was not officially diagnosed due to lack of typical clinical symptoms. Of note, the child no longer tested positive for antibodies after around 1 year of age and currently remains antibody free at 15 years of age. Around 2010, Case 3 began taking levothyroxine (100 mg/day) as she was found to have high antibodies for Hashimoto's disease, and her parents both had experienced thyroid disease. She was also prescribed an immunosuppressant (azathioprine) in 2010 that did not improve symptoms and she eventually stopped, and was then prescribed methotrexate. In 2012, she began hydroxychloroquine which did help to manage symptoms.

For the next decade, she continued to experience the symptoms previously described. Around 2014, she sought care with a rheumatologist and was diagnosed with a 'non-specific' autoimmune condition because she did not have typical SLE symptoms. In 2017, she was officially diagnosed with SLE based on the presence of antibodies and increasing symptoms such as constantly feeling sick and revolving nerve pain in 6–8 inch wide areas of her skin.

In September 2020, due to extreme stress related to Covid-19, her symptoms exacerbated significantly, including extreme fatigue, pain, a migraine that lasted for 4 months, a diagnosis of hyponatremia with hospitalization, and extreme light sensitivity and eye pain, described as varying from a feeling of "someone squeezing my eyes" to a feeling of grittiness or sand in the eyes that prevented her from being able to open both eyes at the same time. Please see Figure 3 for detailed timeline of symptoms and treatment.

She reports having followed a keto diet 'off and on' from 2007 to 2020 but had not experienced any improvements in symptoms. After

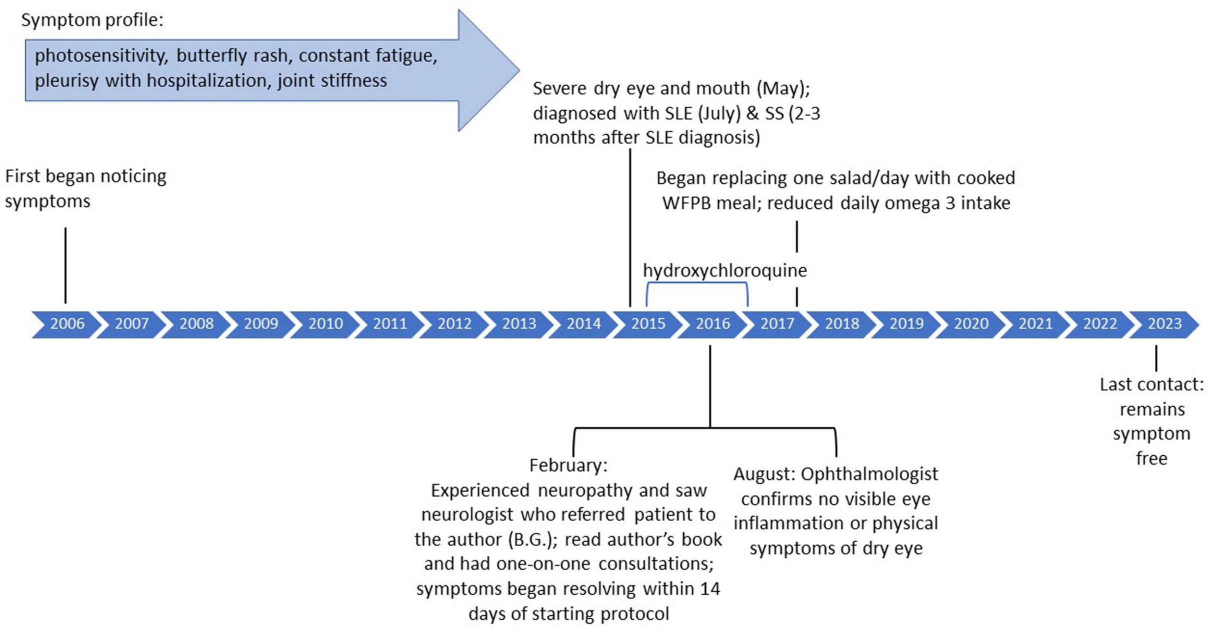

FIGURE 2
Case 2: timeline of symptoms and medication use.

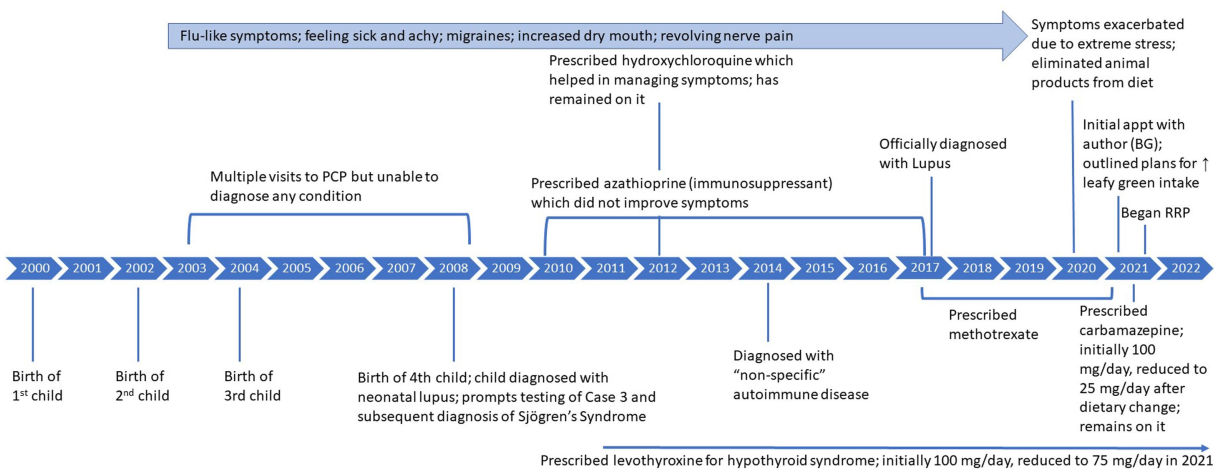

FIGURE 3
Case 3: timeline of symptoms and medication use.

the extreme exacerbation of symptoms in 2020, she read the author's (BG) book detailing the recovery protocol (15) and started to follow a plant-based diet with no animal products, specifically incorporating spinach (approximately 10 oz./day) but not restricting sugar. She noticed small improvements in symptoms. She began working with the author (BG) in February 2021, at which point it was emphasized that she needed to greatly increase intake of greens and cruciferous vegetables and eliminate added sugar. Initially, although "not super strict" about adhering to the plan outlined by the author (BG), she saw fatigue and energy improve in just 2 weeks, migraines improved in about 1 month, and dizziness subsided later. At this time (2021), her physician also prescribed carbamazepine to help with trigeminal neuralgia. When she was diagnosed with Covid-19 in 2021, her doctor suggested temporarily stopping methotrexate, and she never restarted as symptoms were significantly improving.

In June 2021, motivated to further improve symptoms, she completed the author's (BG) 6-week RRP. Within 3 weeks of strict adherence to the RRP, her migraines and revolving pain on her skin resolved, and her dry mouth and dry eye significantly improved and continued to improve with continued adherence to the protocol. Her recovery diet was comprised predominately of large salads, and she estimates that she consumed approximately 1.5–2 lbs. of raw, cruciferous

TABLE 3 Case 3: key laboratory results pre- and post-rapid recovery protocol.

	September 2020 *Pre RRP*	May 2022 *Post RRP*	March 2023
C3 (mg/dL)[1] *Normal range 83–180*	53	84	104
C4 (mg/dL)[1] *Normal range ≥ 10.0*	<8.0	15.2	20.2
White blood cell count (K/uL) *Normal range 3.7–11.1*	1.9	3.7	4.9
Red blood cell count (M/uL) *Normal range 3.60–5.70*	3.50	3.23	4.16
ANA *Normal reading: Negative*	Positive	Positive	Positive

[1]Low levels of complement C3 and C4 reflect inflammation.

vegetables and/or spinach, approximately 1 pound of other vegetables, microgreens, 6 tbsp of flaxseed oil and, initially, approximately 128 ounces of water per day. In November 2022, she was diagnosed with hyponatremia by her regular physician, although was not hospitalized as she was in 2020. It should be noted that her endocrinologist previously diagnosed her with a pituitary tumor that may be contributing to syndrome of inappropriate antidiuretic hormone secretion (SIADH), thus resulting in hyponatremia. Under the care of her medical team, she slowly reduced her water intake to 96 oz. and, finally, 60–80 oz.

The key laboratory results of interest to her physician post-recovery were complement protein 3 (C3), complement protein 4 (C4), white blood cell count, red blood cell count, and ANA (Table 3). While ANA remained positive pre- and post-recovery, C3, C4, and white blood cell counts improved, moving into normal ranges. A few months after symptoms resolved, she tried to introduce additional plant-based foods such as beans, more fruit, and almond flour into her diet but reports not feeling as well and returning back to strict adherence to the recovery protocol. After 8–12 months adhering to the protocol and eating mostly raw foods, all symptoms had resolved. She has felt symptom free since early spring 2022.

As of last contact (December 2023), she has remained adherent to a predominately raw, plant-based diet with no processed foods, incorporating a small amount of cooked vegetables (approximately 6% of her diet), some fruit and beans, and consuming 2 tbsp/day of cold pressed flaxseed oil or chia seed oil. She is currently on hydroxychloroquine, levothyroxine, and carbamazepine, although her doses of the latter two have been decreased since beginning the recovery protocol. She remains under the care of her medical team, monitoring for hyponatremia, and currently consumes no more than 25–35 oz. of water daily. She reports feeling healthy, being active, and having dramatically improved quality of life.

Please see Figure 3 for a summary of initial symptoms and resolution across all three cases. The Supplementary File includes a personal testimony from the case. Please see Table 4 for a summary of improvement in symptoms for all 3 cases following the recovery diet.

Discussion

This case series details three women, 40, 54, and 45 years of age, with SLE and SS who reported debilitating symptoms that severely compromised both physical health and quality of life. They self-reported remission of symptoms beginning a month after adhering to a customized nutrition protocol for recovery, consisting of whole, predominately raw, plant foods. While a case series cannot establish causality, these results show dietary change as a potentially promising approach for treatment of SLE and SS. At the time of writing, Cases 1 and 2 reported having remained adherent to the maintenance protocol and have remained symptom free with no medication use for 6 and 7 years, respectively, showing the potential for long-term symptom remission. Other case reports in the literature similarly support the use of plant-based diets in reversing diseases such as chronic kidney disease and outcomes related to cardiovascular disease (16–18), suggesting that the recovery protocol may be successful for a number of other chronic diseases.

While this case series details a specific nutrition protocol for recovery, previous research has supported the potential for diet to improve SLE-related symptoms (19–22). Constantin et al. discusses the importance of personalized diet in maintaining homeostasis, remission, and physical well-being for SLE patients (21). A 2020 review by Islam et al. suggests that low-calorie, low-protein diets high in fiber, PUFA, vitamins, minerals, and polyphenols may provide a macronutrient and micronutrient profile that benefits SLE patients (23). SLE and SS are chronic inflammatory diseases (2, 24), and it is well-established that diets high in fruits and vegetables can reduce both inflammation and oxidative stress. The recovery protocol documented in this case series is high in antioxidant-rich fruits and vegetables which may help to reduce the oxidative stress that is characteristic of SLE and can contribute to more severe SLE symptoms (20, 24–26), and diets higher in fruits and vegetables may reduce proinflammatory mediators (27).

The recovery protocol documented in this case series is high in omega 3, a polyunsaturated fatty acid (PUFA) shown to reduce inflammation. One study in autoimmune, Lupus-prone mice suggested that fish oil (omega 3) inhibited production of pro-inflammatory cytokines and improved kidney injury (28), and omega-3 intake has been linked to improved outcomes in SLE patients, including reduced inflammation, disease activity, and oxidative stress (22). Other published work has shown that supplementation, such as with omega-3, can help reduce SLE-related sequelae (22, 29) and disease activity (30, 31) and that omega 3 may reduce the production of inflammatory markers, cytokines and CRP to improve inflammation (32–34). Finally, PUFA supplements, in particular omega-3, may be an effective treatment for non-specific dry

TABLE 4 Summary of symptom improvement among three cases.

	Symptoms prior to recovery protocol	Symptoms resolved immediately (≤1 month) after start of RRP	Symptoms resolved later (>1 month)
Case 1	Extreme photosensitivity, fatigue, pain in the legs, extreme dry skin, dry eye, dry mouth, stomach cramping, diarrhea, severe pelvic pain	Pelvic pain resolved (2 days); dry eye, dry mouth, pain in the legs, stomach cramping, diarrhea, fatigue (4 weeks)	Cracks in skin (3 months); photosensitivity (2 months)
Case 2	Photosensitivity; butterfly rash; constant fatigue; joint stiffness in the fingers, elbows, and knees; severe dry mouth and dry eye; eye inflammation; neuropathy	Neuropathy, joint stiffness, fatigue, and photosensitivity; butterfly rash; dry mouth (2 weeks)	Eye inflammation and dry eye (6 months)
Case 3	Flu-like symptoms; migraines; intermittent dizziness; weakness; dry mouth; revolving nerve pain in skin; extreme fatigue; extreme light sensitivity; eye pain; trigeminal neuralgia.	Migraines, revolving pain on skin, dry mouth, dry eye (3 weeks)	Flu-like symptoms; dizziness; weakness; dry mouth, dry eye, fatigue, light sensitivity, eye pain, trigeminal neuralgia (8–12 months)

eye disease (35, 36). Various mechanisms have been hypothesized to theorize why omega 3 fatty acids may improve outcomes associated with SLE, including by reducing disease activity, reducing inflammation, regulating adipokine production, and improving endothelial function (37). The use of high doses of omega-3 rich foods and oils as part of the recovery protocol is a novel test of this previous research in a clinical setting. However, further research is needed to improve understanding of mechanisms and also to further explore whether different types of omega 3 fatty acids may exert different effects (ALA vs. EPA/DHA) and the relative contributions of the omega-3 fats vs. other aspects of the recovery diet.

SLE is a heterogenous, multi-system disease that is often difficult to diagnose and complex to treat (38), as evidenced by the extensive period that Case 3 experienced illness before a formal diagnosis of SLE was made. SLE disease activity is associated with negative physical and mental health outcomes, including organ damage and poor quality of life (39, 40). Despite the fact that life expectancy is generally favorable (41, 42), racial and ethnic minority groups experience more severe outcomes (43), and SLE can dramatically affect all areas of a patient's life, including physical health, mental health, and social relationships (44). Recent research has highlighted poor physical and mental health related quality of life in patients with SLE, with literature indicating that SLE can cause pain and fatigue (45, 46), poor sleep quality (47), feelings of fear, anguish, and social exclusion (48), decreased sexual function (49), concerns around fertility and reproductive health in women (50), and challenges around economic costs, status, and employment (51). In addition, quality of life may be affected differently at different phases of disease (52). Severe SLE flares were found to be associated with reduced health-related quality of life (53). As described, all three cases experienced a wide array of symptoms and significant negative impacts on physical health, mental health, and quality of life; significant improvements in all symptoms were observed after following the prescribed recovery protocol. It is notable that significant improvement in all symptoms, improvements that were superior to that achieved with medication, were observed.

Although many pharmacological therapies for SLE exist, there is potential for both short- and long-term side effects (54–56), and a recent observational study showed that some pharmacological treatments yield better improvements in quality of life than others (57). Pharmacological therapies are typically targeted at reducing disease activity and preventing mortality; remission is not always possible (58). The 2021 Definitions of Remission in SLE (DORIS) International Task Force highlighted remission as an "aspirational goal in clinical care" and defined remission as minimal to no disease activity based on two indices [Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) and Physician Global Assessment], irrespective of serology, and allowing for use of some pharmaceuticals including antimalarials (59). Although this case series was not able to utilize a disease index such as SLEDAI to assess symptoms, the three cases self-reported no symptomatic disease activity in the period following the adoption of the recovery protocol. Two of the cases were able to stop use of all pharmacological treatment, and all three cases had medications deprescribed under the care of and with monitoring by their physician, not the authors. Despite the experience of these three patients, it is important to note that pharmacological treatment, particularly with hydroxychloroquine (HCQ), remains the current standard of care for SLE (60), and adequately dosed HCQ has been shown to be largely well tolerated, is associated with lower risk of disease activity, and has a protective effect on survival (61, 62). Thus, while this case series is promising, further research such as randomized controlled trials would be needed to examine the role of diet and improved outcomes before broad recommendations for deprescribing of SLE medications could be considered. Although not examined in this case series, remission of symptoms would likely also result in reduced healthcare costs to both patients and payors.

It is important to note the limitations of this work. Case series are observational, descriptive studies and do not utilize a control group. In the hierarchy of evidence, case series provide weak evidence for causality on their own and best serve to provoke consideration for future research. Case series are, however, important for sharing experiences between clinicians and generating hypotheses that may lead to future research (63). As this is a case series, we cannot conclude whether the dietary change alone was responsible for the observed improvement in symptoms; it is not possible to assess confounding factors that may be responsible for the improvement. While causation cannot be established, improvements were temporally related to the adoption of the recovery protocol, as the improvements in symptoms occurred rapidly after the dietary change and have been sustained, up to 7 years in one case, with adherence to the diet. Cases were not counseled with the goal of participating in scientific research, thus food diaries were not collected, and a nutrient analysis of intake was not conducted, nor has a nutrient analysis been conducted with respect to the protocol overall. Adherence was assessed via self-report only. In addition, dietary intake was self-reported by patients after completing the protocol and experiencing symptom remission. Future research should assess dietary change and changes in symptoms prospectively. Finally, the three cases presented reported that the dietary change was low burden relative to their debilitating symptoms and poor quality of life and, as such, they were highly motivated to adhere to the recovery protocol. This may not be the case for all patients, and adherence may be difficult for others attempting this diet. It should be noted that while Case 1 experienced great success with the protocol, pregnant individuals should be encouraged to consult with their obstetrician and medical team before implementing significant dietary changes.

In the United States, poor diet quality, including added sugar intake above recommendations, is a concern (64–67). The recovery protocol described shares similarities with a WFPB diet, particularly in its elimination of all animal products and processed foods. Theoretically, WFPB diets are more nutrient dense than the standard American diet (68), and although a WFPB diet may require supplementation of select nutrients, such as calcium, vitamin D, and vitamin B12 (68–70), a supplemented WFPB diet can be nutritionally sufficient and is less likely to be deficient in underconsumed nutrients such as fiber, potassium, Vitamins A, E, and C, and magnesium (71). Additionally, a WFPB diet does not provide an excess of the nutrients consumed in excess in the US, including saturated fat, sodium, and added sugar. With respect to calcium, plant foods such as leafy greens and broccoli are rich sources (72). The three cases described were advised to take vitamin B12 and D supplements; however, blood work was not conducted to examine nutritional deficiencies. With respect to the high amount of water consumption, it should be noted that all patients on the recovery protocol, including the three documented in this case series, are advised to consume at least 1 tsp. of sodium per day and remain under the care and monitoring of their own physician. Case 3 struggled with hyponatremia both before and over a year after completing the recovery protocol, for which she was carefully monitored and treated by her physician and still reported remarkable improvements in symptoms and quality of life following the dietary change.

In conclusion, three women reported remission of SLE and SS symptoms following adherence to a predominately raw, plant-based recovery protocol diet rich in leafy greens, cruciferous vegetables, and omega-3 fatty acids and eliminating all processed foods. Future research should examine the potential of the recovery protocol to reverse symptoms of SS and SLE in other patient populations. In addition, while this case series focuses on SLE and SS, it is possible that the recovery protocol may be successful in improving symptoms of other chronic diseases, and future research should eventually explore this possibility. A previous case series has documented similar results among patients with SLE-related nephritis (18), and clinicians may consider recommending dietary changes, in combination with pharmacological treatment, as a low-risk strategy with positive side effects for further ameliorating symptoms of autoimmune disease. It would be beneficial for fellow clinicians to document their successes managing autoimmune disease with dietary interventions as case reports. In light of the limited research on diet as a treatment for autoimmune disease, documented cases showing the possibility of lifestyle change as an avenue for treatment could eventually lead to larger-scale studies and, in the longer term, randomized controlled trials. Most importantly, practitioners and patients deserve to be made aware of the promising potential of using food as medicine in the treatment of SLE and SS.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

Ethical approval was not required for the studies involving humans because this was a case series of 3 cases. Written informed consent was obtained. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article. Written informed consent was obtained from the participant/patient(s) for the publication of this case report.

Author contributions

BG is responsible for the conception and design of this work, developed the nutrition recovery protocol, directly oversaw the 3 patients described, and critically reviewed the manuscript. KS interviewed the patients and authored the manuscript. All authors contributed to the article and approved the submitted version.

Conflict of interest

BG is the founder of Plant-Based Health Group LLC, and through this organization, provides services guiding clients through the nutrition protocol described in this manuscript. She offers free classes as well as one-on-one counseling for which she receives payment. KS is employed by the American College of Lifestyle Medicine.

Publisher's note

Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fnut.2024.1208074/full#supplementary-material

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Evaluation of the reach and utilization of the American College of Lifestyle Medicine's Culinary Medicine Curriculum

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Introduction: Despite the growing interest in "food as medicine," healthcare professionals have very limited exposure to nutrition as part of their training. Culinary medicine (CM), an evidence-based field integrating nutrition education with culinary knowledge and skills, offers one approach to fill this training gap. The American College of Lifestyle Medicine published a complimentary Culinary Medicine Curriculum (CMC) in 2019, and the objective of this study is to evaluate its reach and utilization, as well as to collect feedback from users.

Methods: Individuals who downloaded the CMC prior to March 1, 2022 ($N = 6{,}162$) were emailed an invitation to participate in an online, cross-sectional survey. The survey included both multiple choice and free-text questions about whether CM sessions were conducted, if and how the CMC was used, if and how it was modified for use, and additional requested resources. Free-text responses were inductively coded, and quantitative data was summarized using descriptive statistics.

Results: A total of 522 respondents provided consent, indicated that they had downloaded the curriculum, and completed the survey. Of the 522, 366 (70%) reported that they had not led or created any CM sessions. The top-reported reason for not leading a session was lack of time (29%). The remaining respondents who did create a CM session did so across various settings, including academic, clinical, coaching, and other settings, and a variety of professionals delivered the CMC sessions, including physicians (50%), registered dietitian nutritionists (30%), and chefs (25%). The majority of respondents (81%) modified the CMC in some way, with many using the curriculum for guidance or ideas only. Patient education materials (66%) and cooking technique instruction videos (59%) were among top requested resources.

Discussion: The CMC is a versatile resource that can be successfully adapted for use across various settings and by various types of health professionals and practitioners. Future research should investigate whether training in CM results in improved health outcomes for patients/clients. The curriculum will continue to grow to address the needs of users by expanding to include more digital content such as curriculum videos and cooking technique videos.

KEYWORDS
culinary medicine, food as medicine, physician training, practitioner training, lifestyle medicine

Introduction

Diet has been identified as the single most important risk factor for morbidity and mortality in the United States, yet most healthcare professionals spend relatively few hours learning about nutrition during their training (1, 2). Historically, nutrition education has been limited to fewer than 20 hours in the preclinical years of undergraduate medical education, focused on nutrients rather than food, and largely separated from the clinical experience (1, 2). Medical students report not feeling equipped to provide adequate nutrition care to patients, despite their acknowledgment that nutrition is a useful and necessary part of patient care (3).

To fill this void in nutrition training, the American College of Lifestyle Medicine (ACLM) made available the Culinary Medicine Curriculum (CMC) (4), in English, based on the Stanford University course developed by Dr. Michelle Hauser, to healthcare professionals via complimentary download in December 2019 (5, 6). Between December 2019 and March 2022, over 6,000 individuals from across the globe had downloaded the CMC. As of March 2024, the number of unique downloads had grown to over 10,000. The CMC was published for medical schools, health professional training programs, and residency programs with flexibility to be tailored to a variety of settings and audiences. The curriculum includes an instructor's guide, recipes, shopping guides, and equipment lists for creating pop-up teaching kitchens. The beginning of the curriculum includes a section on nutrition not typically covered in medical and health professional schools that is critical for patient education and dietary behavior change.

Culinary medicine (CM) is an evidence-based field that integrates nutrition education with culinary knowledge and skills. The goal is to assist individuals in maintaining health and preventing and treating food-related diseases by choosing high-quality, healthy food in conjunction with appropriate medical care (6, 7). Foundational CM knowledge is characterized by understanding what constitutes a healthy diet and how to find, obtain, and prepare nutritious and delicious food to support improved health outcomes (6).

The recent growth of "food as medicine" (FAM), also called "food is medicine" (FIM), in research, public health, and clinical care has expanded the practitioner's awareness of these concepts. While historically, FAM primarily referred to interventions providing food to patients, such as produce prescription programs and medically tailored meals (MTM), these types of programs may have limited sustainability without supporting education on food preparation (8). The field of lifestyle medicine (LM) focuses on treatment that employs behavior change education to help patients working to improve their health habits, and CM is a natural fit for this approach (9). FAM, as practiced by LM providers, is a key element of LM in the nutrition domain, and can serve to bridge LM and CM (10).

Programs at all levels of medical training are introducing CM educational opportunities to fill the void of practical nutrition skills and to better prepare health professionals to support patients in sustained, healthy dietary changes (2). The first culinary medicine course in the U.S. was Dr. John La Puma's at the State University of New York-Upstate campus in 2003. The first CM continuing medical education conference (Healthy Kitchens, Healthy Lives [HKHL]) was held in 2007, co-sponsored by Harvard Medical School and the Culinary Institute of America in St. Helena, California. In 2012, the first permanent teaching kitchen was established in a medical school at the Goldring Center for Culinary Medicine (GCCM) at Tulane University School of Medicine, led by physician-chef Timothy Harlan (11). This program has grown dramatically and since then, over 30 U.S. medical schools throughout the country have implemented programs (12–14). In addition, other CM programs have been implemented in health systems (15) or community or patient care settings (16–19).

The CMC continues to be offered and has been utilized in the form of a teaching kitchen elective course for medical and physician assistant students at Stanford University School of Medicine and showed significant improvements in attitudes, knowledge, and behaviors around healthy cooking and meal planning (4). Other studies on CM educational programs for health care professionals in training have demonstrated significant and positive impacts on medical students' attitudes, knowledge, and competencies with practical, hands-on culinary skills and nutrition knowledge (12, 20–27).

The objective of this study was to evaluate the use of the ACLM's CMC, as follows: (1) characterize respondents who have utilized the CMC, (2) understand how they have used the CMC, (3) identify modifications that have been made to the curriculum during implementation in academic and clinical settings, and (4) gather information on the challenges and needs of curriculum implementers for the purpose of informing further resource development efforts.

Methods

Individuals who downloaded the CMC from its inception in December 2019 to March 1, 2022 were emailed an invitation to participate in a cross-sectional survey ($n = 6{,}162$). The survey was administered in English, using QuestionPro, a secure, online survey platform and open from March 2–April 22, 2022. This study was administered by ACLM and reviewed by the University of New England Institutional Review Board. All respondents provided informed consent, and all research team members completed training in human subjects research by the Collaborative Institutional Training Initiative (CITI).

The survey was developed by members of the research team (SH, PS, MEH) based on interest in learning about the CMC for the main purpose of quality improvement. The survey was not pilot-tested or validated, and no scoring or classification procedure was applied. The first three questions were used to screen that respondents were at least 18 years of age, understood the study as described in the consent, and agreed to participate. Individuals answering "yes" to these questions were eligible to participate. The remainder of the survey consisted of a maximum of 18 questions, using programmed logic to display only relevant questions. The survey included questions on clinical degree, certification and/or training when the curriculum was downloaded, and whether respondents had created any CM sessions. For those who created one or more CM session(s), follow-up questions were asked on the primary way in which the CMC was used, approximate number of students/patients in each session, number of sessions conducted, primary setting in which the curriculum was used, and who led and/or taught the sessions (i.e., MD, RDN, health coach, etc). Respondents were also asked for details about if and how they used the CMC in creating their sessions, including if and how they modified the curriculum and whether they would have liked additional resources or materials available with the curriculum. Both multiple-choice and free-text questions were used. Respondents who reported not using the CMC were asked to explain why. Supplementary Table 1 contains a summary of the survey questions. The survey was set to only allow it to be completed one time, which is achieved through cookies saved on the browser. The data was additionally reviewed to ensure that two responses with the same email address were not recorded. If so, only the most complete response was retained. Survey responses were confidential, with datasets being stored on a secured server with access restricted to only study team members. In addition, identifying information (name, email) was removed prior to analysis.

Quantitative data were summarized using descriptive statistics. Missing data were not imputed. As this was a descriptive analysis aimed at capturing feedback from individuals who downloaded the curriculum for the purpose of quality improvement and programmatic development, sample size and power calculations were not performed. Two researchers independently inductively coded free-text data to identify emergent categories of responses, and discrepant coding was resolved through discussion with a third member of the research team to modify codes as needed and achieve consensus. Categories of free-text responses were descriptively summarized. Analyses were conducted using SAS version 9.4.

Results

The online survey was accessed 894 times, and 83% ($n=740$) of respondents were at least 18 years old and provided informed consent to participate. Of those providing consent, 71% ($n=522$) completed the survey after removing duplicate responses ($n=2$) and individuals ($n=2$) stating in free-text responses that they had never downloaded the curriculum (Figure 1).

The majority of respondents (47%) reported having a medical degree (MD or DO); 13% reported a nursing credential, 48% of which were advanced practice registered nurses; 30% percent reported credentials in another health professional field (non-MD/DO, non-nursing); and 29% reported a non-clinical credential. Non-clinical credentials reported included chefs, public health degrees, academic doctoral degrees, and degrees in business and education. Twenty-three percent of respondents were certified in LM (DipABLM, DipIBLM, or DipACLM). Eighty-two percent ($n=430$) were from the United States with respondents from 38 other countries represented.

Twenty-three percent had downloaded the curriculum within the past 3 months at the time they were surveyed; however, 35% had downloaded the curriculum more than 1 year prior. Of the 522 respondents in the final sample, a total of 366 (70%) reported that they had not created any CM sessions at their institution or practice. The top reasons reported included lack of time (29%), the program at their organization for which the CMC could be used was still in development (13%), the Covid-19 pandemic (12%), no opportunity (12%), and lack of funding or resources (10%). Lack of interest by patients or clients was reported by only 3% of respondents (Table 1). The remaining 149 (29%) respondents reported that they created a CM session.

Among the 149 respondents that created a session, 113 reported on number of CM sessions run and number of participants in a session. These numbers varied widely among respondents, ranging from 0 to 186 total sessions run [median (IQR) = 4.0 (7.0)] and 0–800 participants in each session [median (IQR) = 10.0 (16.5)]. When asked to identify the primary way in which the curriculum was used, 48% reported using it as inspiration or support for materials that the respondent created, while 14% used the CMC and substantially modified materials. Approximately 3% used all sessions with few or no modifications, and 23% did not use the CMC when leading or creating a session. These respondents reporting that they did not use the CMC ($n=34$) identified the following reasons for non-use: used a different curriculum (50%) or did not yet review the curriculum as a resource (24%), the CMC was not relevant (9%), or the respondent did not have decision-making authority over the curriculum (6%).

One-hundred-thirteen respondents who created a session and used the CMC in some capacity reported further detail on the curriculum setting. Specifically, 39 (35%) used the curriculum in an academic setting, 31 (27%) in a clinician-patient care setting, and 26 (23%) in a client coaching setting (Table 2). Among 39 academic setting users, the curriculum was most frequently implemented in medical school (56%) and graduate medical education such as residency and fellowship (23%) settings. The academic learning environment was 39% hybrid (combined in-person and online), 39% online (36% synchronous, 3% asynchronous), and 23% in-person sessions. Among 31 clinical setting users, the curriculum was most frequently implemented in LM (42%) practices, followed by family medicine (16%), internal medicine (13%), and preventive medicine practices (10%). Another 19% of respondents reported using the curriculum in a combination of 'other' practice types including pediatrics, cardiology, and oncology. The clinical environment was 48% private practice, 45% health system setting, 16% academic practice, and 7% other settings, including one federally qualified health center (3%) (Table 2).

Sessions were most frequently led by physicians (MD/DO, 50%), followed by registered dietitian nutritionists (RDNs, 30%), chefs (25%), and health coaches/health educators (30%). The majority of respondents who led a session reported that additional materials or resources would be helpful to support the curriculum. This included patient education materials (66%), including videos, recipes, handouts or infographics, followed by cooking technique instruction videos (59%), and additional nutrition education curriculum (54%).

Eighty-one percent of respondents ($n=113$) who used the CMC in some way modified the curriculum. The following modifications were reported: reducing the number of sessions (37%), adding content to the curriculum (34%), removing content from the curriculum

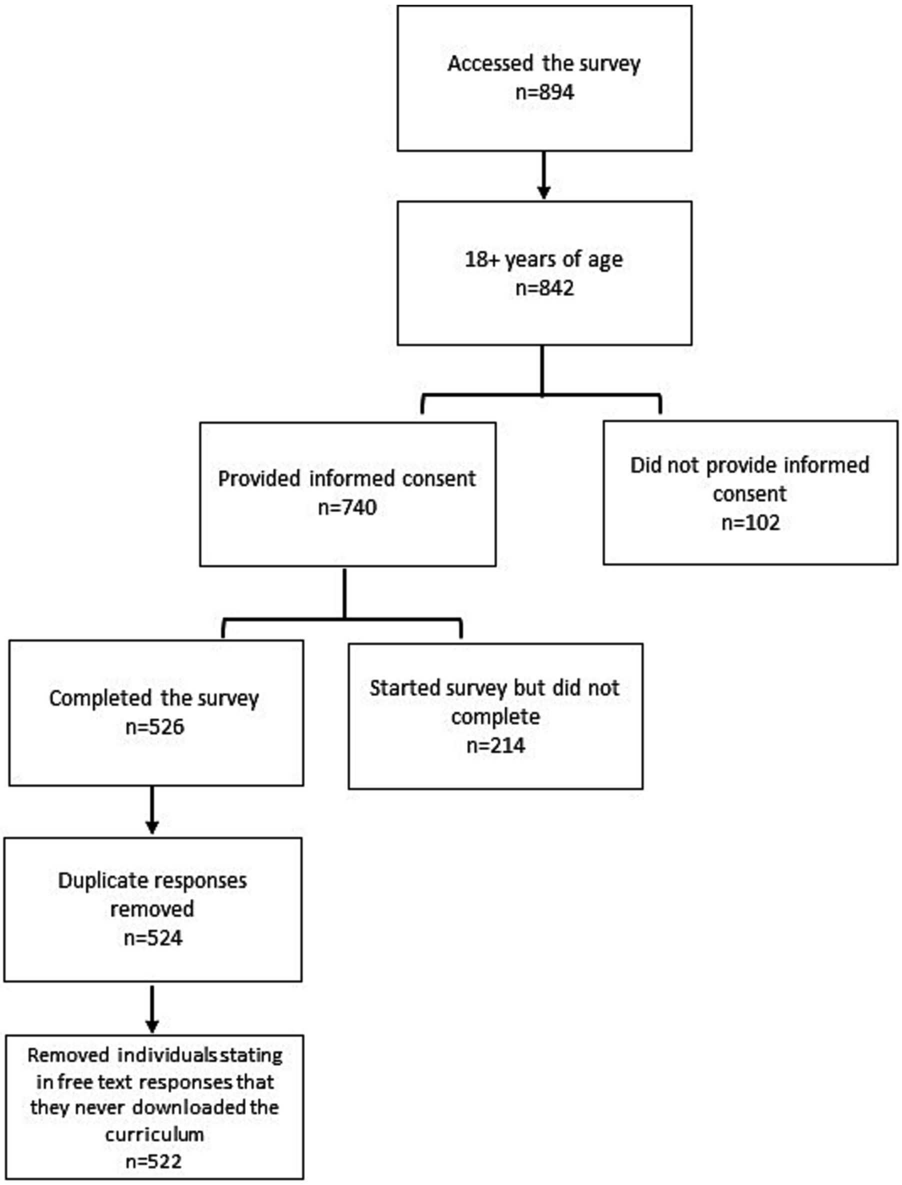

FIGURE 1
Participant enrollment and completion.

(22%), and creating more than 9 sessions either by dividing course material into smaller sessions and/or adding additional content of their own (7%) (Table 3). Respondents were additionally asked to explain their curriculum modifications in greater detail using free text, and answers were inductively coded. Forty-three percent reported using the CMC for guidance/ideas only, 25% changed the CMC to fit the needs of a specific community, culture, or population, 9% shortened or reduced sessions or materials, 9% included additional information or materials, and 7% adapted the CMC to a virtual format.

Discussion

The CMC has emerged as a valuable and flexible resource in the fields of CM and LM. This evidence-based curriculum has seen a substantial increase in number of downloads since its launch reflecting the importance of CM in bridging the knowledge gap for nutrition and LM education among healthcare professionals, students, and non-practitioners alike. A growing body of research indicates that CM programs increase practitioner confidence in nutrition knowledge and skills (13, 24, 28, 29), as well as ability to counsel patients (30) and help patients overcome barriers to healthy eating (13). In addition, CM programs can improve cardiometabolic outcomes in patients (31), as well as improve personal culinary skills (32). The importance of practitioners-in-training improving their personal culinary skills is emphasized in research that suggests medical students and residents with personal experiences following a plant-based diet expressed greater willingness to recommend it to patients (33). The current study is unique, however, in that no other study to our knowledge details how a CM program is utilized and modified in a real-world setting.

TABLE 1 Participant characteristics and creation of culinary medicine sessions.

Licensure/credentials (n = 522)[a]	
Physician (MD/DO)	247 (47.3)
Nursing[b]	65 (12.5)
Other patient care field (excludes MD/DO and nursing)	158 (30.3)
Non-clinical	152 (29.1)
Social work	8 (1.5)
Certified in lifestyle medicine (n = 522)	120 (23.0)
Country (% from United States) (n = 522)[c]	430 (82.4)
How many months ago downloaded the CMC (n = 522)[d]	
0–3	119 (22.8)
3–6	85 (16.3)
6–12	102 (19.5)
12–24	121 (23.2)
>24	63 (12.1)
Not reported	32 (6.1)
Created a CM session at their institution or in their practice (n = 522)[e]	
Yes	149 (28.5%)
No	366 (70.1%)
Why have you not led or created any culinary medicine sessions? (n = 362)[f]	
Lack of time	104 (28.7%)
Program is in progress but not completed/in development	46 (12.7%)
Covid-19 pandemic	45 (12.4%)
No opportunity	44 (12.2%)
Lack of funding/resources	37 (10.2%)
Do not yet feel qualified/prepared to lead a session	28 (7.7%)
Lack of institutional support/organizational issues	28 (7.7%)
Did not answer question (not codable)	28 (7.7%)
Not relevant/unsure of relevancy to current institution/clinic/course/job	18 (5.0%)
Lack of interest by patients or clients	11 (3.0%)
Using a different curriculum/curriculum being developed by someone else	8 (2.2%)
Using curriculum for other use: clinical purposes, personal use, etc.	7 (1.9%)

[a]n = 117 (22.4%) respondents overall reported multiple licensures/credentials, and n = 51 (20.6%) of physicians reported multiple licensures/credentials; [b]n = 31 (47.7%) were advanced practice registered nurses; [c]Other top countries reported by respondents were as follows n (%): Canada 14 (2.7%), Philippines 9 (1.7%), United Kingdom 8 (1.5%), and Brazil 6 (1.2%); [d]At the time of data collection: 3/2/2022 to 4/22/2022; [e]n = 7 missing/prefer not to answer; [f]Responses coded into multiple categories where applicable.

The results of this survey suggest that a major strength of the CMC is its adaptability and flexibility to be used across diverse settings and be led by different individuals, making it a versatile tool to integrate FAM into practice for educators, healthcare providers, and community leaders. Its adaptability enables customization to meet the specific needs and goals of users, further enhancing its utility. Respondents used the curriculum across academic, clinical care, and client/coaching settings and in a variety of forms, specifically online, in-person, and hybrid settings. This flexibility was

TABLE 2 Use of the Culinary Medicine Curriculum among respondents who created a session.

What was the primary way in which you used the Culinary Medicine Curriculum in your sessions? (n = 149)[a]	
I used the CMC as inspiration or for support of materials that I created	72 (48.3)
I did not use the CMC in any way when leading or creating my CM session(s)	34 (22.8)
I used the CMC but modified the materials substantially for my purposes	21 (14.1)
I used 1 or more sessions from the CMC with few or no modifications	16 (10.7)
I used all nine sessions from the CMC with few or no modifications	4 (2.7)
If did not use, why did you not use the CMC? (n = 34)	
Used a different curriculum that was already designed	17 (50.0)
Haven't yet reviewed the curriculum or did not think to review/use it	8 (23.5)
Other[b]	4 (11.8)
CMC was not relevant to the course	3 (8.8)
Curriculum content was not my decision	2 (5.9)
In what primary setting did you use the curriculum (n = 113)[c]	
Academic: teaching students and trainees	39 (34.5)
Primary setting curriculum used in (n = 39)[d]	
Medical school	22 (56.4)
Graduate medical education (residency, fellowship)	9 (23.1)
Continuing education/continuing medical education	4 (10.3)
Pre-professional (bachelor's, associate's, trade program)	4 (10.3)
Culinary	3 (7.7)
Dietetics	2 (5.1)
Master's program	2 (5.1)
Nurse practitioner or physician associate/assistant	3 (7.7)
Nursing (LVN, RN)	1 (2.6)
Psychology or PhD	1 (2.6)
Type of learning environment (n = 39)	
Hybrid (part in-person and online)	15 (38.5)
Online, scheduled sessions	14 (35.9)
In-person sessions	9 (23.1)
Online, on-demand sessions	1 (2.6)
Clinical: patient care	31 (27.4)
Type of practice (n = 31)	
Lifestyle medicine	13 (41.9)
Other[e]	6 (19.4)
Family medicine	5 (16.1)
Internal medicine	4 (12.9)
Preventive medicine	3 (9.7)
Practice environment (n = 31)[d]	
Private practice	15 (48.4)
Health system	14 (45.2)

(Continued)

TABLE 2 (Continued)

What was the primary way in which you used the Culinary Medicine Curriculum in your sessions? (*n* = 149)[a]	
Academic practice	5 (16.1)
Other[f]	2 (6.5)
Clients/coaching	26 (23.0)
Other	16 (14.2)
Prefer not to answer	1 (0.9)
Who leads and/or teaches the culinary medicine sessions (*n* = 113)[c,d]	
Physician (MD/DO)	57 (50.4)
Registered dietitian nutritionist (RDN)	34 (30.1)
Chef	28 (24.8)
Health coach	22 (19.5)
Health educator	12 (10.6)
Other	12 (10.6)
Advanced practice provider (NP, PA)	9 (8.0)
Nurse (RN, LVN)	8 (7.1)
What additional materials or resources would be helpful to have as part of the curriculum or to support the curriculum? (*n* = 113)[c,d]	
Patient education materials	75 (66.4)
Cooking technique instruction videos	67 (59.3)
Nutrition education curriculum	61 (54.0)
Online culinary medicine course for continuing education	50 (44.2)
In-person culinary facilitator training	30 (26.6)
More detailed case studies	28 (24.8)
Other	12 (10.6)

[a]*n* = 2 selected prefer not to answer; [b]includes not enough interest, not enough training, missing response; [c]*n* = 2 who selected "prefer not to answer" regarding the primary way that they used the curriculum and *n* = 34 indicating "I did not use the CMC in any way when leading or creating my CM session(s)" excluded from denominator; [d]Responses coded into multiple categories where applicable; [e]Pediatrics, cardiology, oncology, other unspecified; [f]Federally qualified health center or other (unspecified).

TABLE 3 Modification of the Culinary Medicine Curriculum.

Did you modify the CMC?[a] (*n* = 113)	
Yes	91 (80.5)
How did you modify the curriculum? (*n* = 91)	
Number of sessions was altered from 9 to fewer	34 (37.4)
Content was added to the curriculum	31 (34.1)
Content was removed from the curriculum	20 (22.0)
Number of sessions was altered from 9 to greater	6 (6.6)
Please explain your modifications in detail (*n* = 91)[c]	
Used the curriculum for guidance or ideas only	39 (42.9)
Changed curriculum to fit community, cultural, or local needs	23 (25.3)
Other[b]	10 (11.0)
Changed format- shortened	8 (8.8)
Included additional information/materials	8 (8.8)
Changed format to virtual	6 (6.6)
No	15 (13.3)
Prefer not to answer	7 (6.2)

[a]*n* = 2 who selected "prefer not to answer" regarding the primary way that they used the curriculum and *n* = 34 indicating "I did not use the CMC in any way when leading or creating my CM session(s)" excluded from denominator; [b]Other (unspecified), not codable; [c]Responses coded into multiple categories where applicable.

important given that the curriculum was made available in December 2019, and many of the respondents surveyed were accessing the curriculum during the COVID-19 pandemic. Other published research has shown positive outcomes across both in-person and virtual CM teaching platforms (13, 17, 34). Within clinical settings, use was not just restricted to LM practice (42%) but extended into other medical specialties such as family medicine (16%), internal medicine (13%), and preventive medicine (10%). The integration of lifestyle approaches across these clinical fields through the use of CM is encouraging and consistent with other published literature highlighting the utility of CM across different fields such as women's health (34), pediatrics (19), oncology (16), and in the care of patients with diabetes (17, 31).

Approximately one-quarter of respondents who had created a session adapted the curriculum to fit the unique needs of their community, such as modifying the curriculum to a specific culture, population, or dietary pattern. Tailoring curricula to specific cultural needs is of critical importance, as racial and ethnic minorities in the United States suffer disproportionately from diet-related chronic disease (35). In addition, chronic disease burden is higher and multimorbidity, defined as having two or more coexisting chronic conditions, starts at an earlier age in Hispanic/Latino and African American populations compared to their white counterparts (36). Incorporating culture into nutritional counseling may incite greater adherence to dietary changes (37) and, consequently, promote better health. For example, a recent study showed that a cookbook tailored to a Filipino-American population may potentially motivate individuals to make healthier dietary choices (38).

LM practitioners utilize a team approach, incorporating non-physicians such as nurses, registered dietitians, and wellness coaches (39, 40). The importance of a team approach and the potential for expanded patient reach is further highlighted by the broad array of expertise among those leading/teaching the sessions. While half of those reported to be leading and/or teaching sessions were physicians (50%), registered dietitian nutritionists (30%), health coaches/health educators (30%), and chefs (25%) were frequently reported. Similarly, a 2021 review of nutrition education interventions noted the importance of interprofessional learning (41). This broad reach among health professionals represents the CMC as useful for various professional and clinical backgrounds.

Lack of knowledge and time have been reported as reasons for not providing nutrition education to patients (42). This curriculum is a free, publicly available resource that was created in response to interest in creating CM sessions among individuals who do not have the training and skills to develop their own curriculum from scratch. The CMC is intended to promote greater confidence in creating sessions and, thus, empower interested individuals to lead CM sessions addressing barriers of skills and time. Despite this, the survey results indicate that time constraints remain a significant barrier to implementation, with time overwhelmingly identified as the top reason for not leading a session. This highlights the need for continued support and resources to assist healthcare professionals and educators in finding not just time, but implementing strategies for successful reimbursement allowing for compensated time that could be devoted to fully integrating CM into their practice and setting.

While other reasons for not leading a session varied widely, several reasons cited were related to the infrastructure, specifically lack of funding/resources and lack of institutional support/organizational issues. As Mauriello and Artz discuss, CM can only improve health and reduce healthcare costs when it is fully integrated into the healthcare model. Medical student training alone is not enough (43). There is a need for more documented examples of successful integration of CM programs into a variety of practice settings. Such implementation models could support the documentation of best practices for allocating time and resources for CM curricula in general.

Not surprisingly, the additional materials and resources that were identified as being potentially beneficial to have as part of the curriculum varied, with patient resources and additional information emerging as top themes. Examples of additional requested patient resources included videos (cooking techniques, nutrition), recipes, handouts and infographics. Requests for additional information included clinical cases/case studies and evidence-based nutrition education. To a smaller extent, additional education was requested including on-site facilitator training, and cooking technique instruction videos. The CMC is in the process of being modified to meet the expanding needs of those currently utilizing it as expressed in this survey. Course videos including cooking technique videos and recipe instruction videos for all recipes presented in the curriculum have been filmed. Eight faculty interviews covering the topics of nutrition education and dietary behavior change counseling have also been filmed, as well as eight or more patient case examples with expert faculty counseling and recommendations on dietary behavior change incorporated. All videos are currently in the post-production phase. Finally, even with these additions, it is likely that modification of nutrition education resources like the CMC will still be needed to tailor the curriculum to the patient population. This is a strength of providing a free resource with the potential to be altered for the situation.

A limitation of this analysis is that the recruited sample only represents a proportion of the population that accessed ACLM's CMC; the sample that completed the survey is a small proportion of that group and an even smaller number reported creating a CM session. In addition, the CMC assessed in this study highlights a whole-food, plant-predominant diet, as recommended by ACLM. Thus, results may not be generalizable to the overall population accessing this specific curriculum or utilizing other CM programs. However, since ACLM is a medical professional organization that uniquely serves not only physicians but all healthcare professionals, the CMC is available to a diverse audience including nurses, dietitians, health coaches, and other health professionals, all of which were reflected in the survey respondent base. Additionally, the environments available to utilize the curriculum may have been affected by the COVID-19 pandemic. While the pandemic may have created time barriers and disrupted the implementation of certain programs, it may have also facilitated the transition to successful virtual programs. However, the survey's design and scope do not allow for a comprehensive assessment of these specific effects. Finally, nonresponse bias at the survey level cannot be addressed within the scope of the approved study protocol, which allowed for use of data collected in the survey, as opposed to the other, limited demographic data originally collected upon download. We do have limited data on the credentials/training of survey completers v non-completers (Supplementary Table 2); however, the majority of non-completers did not provide data, making it difficult to assess differences between the groups. Despite these limitations, it is crucial to recognize the pioneering nature of this study, assessing real-world use of the first and only open-source CM curriculum made widely available.

Significant room for improvement exists for better equipping practitioners to address diet and lifestyle with their patients. The CMC has proven to be an asset in the promotion of CM, FAM, and LM. Its broad reach, adaptability, and flexibility position it as a pivotal tool in the quest to improve nutrition education and, subsequently, the overall health and well-being of patients. Future research should assess practitioner confidence and knowledge after completing the CMC. Additionally, since the survey did not assess SMAs or reimbursement approaches, the use of shared medical appointments (SMAs) should be explored as a strategy for creating the compensated time required to deliver the curriculum. Additional research is needed to determine the ability of this particular curriculum to impact health behaviors and outcomes, specifically whether CM training results in improved health outcomes for patients/clients. Continued efforts to address the identified barriers to running CM sessions will be essential in realizing the full potential of this valuable resource.

Data availability statement

The datasets presented in this article are not readily available because the IRB has not approved the release and/or use of this data for individuals not on the research team. Requests to access the datasets should be directed to MK, mkarlsen@lifestylemedicine.org.

Ethics statement

The studies involving humans were approved by University of New England Institutional Review Board. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

KS: Data curation, Formal analysis, Writing – original draft. SH: Writing – original draft. MK: Conceptualization, Supervision, Writing – review & editing. AK: Writing – review & editing. PS: Conceptualization, Supervision, Writing – review & editing. MH: Conceptualization, Supervision, Writing – review & editing.

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Conflict of interest

KS, SH, MK, AK, and PS are staff at the American College of Lifestyle Medicine. MH is a member of the American College of Lifestyle Medicine and developed the Culinary Medicine Curriculum described in this manuscript.

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Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fnut.2024.1338620/full#supplementary-material

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Changes in the consumption of isoflavones, omega-6, and omega-3 fatty acids in women with metastatic breast cancer adopting a whole-food, plant-based diet: post-hoc analysis of nutrient intake data from an 8-week randomized controlled trial

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Background: Diets rich in minimally processed plant-based foods are recommended to breast cancer patients, and some may have an interest in whole-food, plant-based (WFPB) diets that avoid animal-based foods, added fats, and refined sugars. Within WFPB diets, the intakes of isoflavones, omega-6 polyunsaturated fatty acids (n-6 PUFAs), and omega-3 polyunsaturated FAs (n-3 PUFAs), which have been discussed in reference to breast cancer outcomes, have not been well characterized.

Methods: Women with stage IV breast cancer on stable therapy were randomized 2:1 into (1) a WFPB intervention ($N = 21$) or (2) usual care ($N = 11$) for 8 weeks. Three meals per day were provided. Outcomes presented here include dietary intake of isoflavones, n-3 and n-6- PUFAs, which were assessed using three-day food records at baseline and 8 weeks. Baseline and 8-week mean intake within groups were compared using the Wilcoxon signed-rank test and between control and intervention groups by a two-sample *t*-test.

Results: The WFPB intervention participants increased their daily consumption of total isoflavones from a mean of 0.8 mg/day to 14.5 mg/day ($p < 0.0001$) and decreased the n-6:n-3 ratio of their diet from a mean of 9.3 to 3.7 ($p < 0.0001$). Within the WFPB group, linoleic acid (n-6 PUFA) consumption decreased by a mean of 3.8 g ($p = 0.0095$), from 12.8 g/day to 9.0 g/day; total n-3 PUFA consumption increased by a mean of 1.1 g ($p = 0.0005$), from 1.6 g/day to 2.7 g/day.

Conclusion: Transitioning to a WFPB diet resulted in significantly increased isoflavone intake and decreased n-6:n-3 ratio in women with breast cancer.

KEYWORDS

breast cancer, isoflavones, omega-3 polyunsaturated fatty acids, omega-6 polyunsaturated fatty acids, omega-6/-3 ratio, plant-based diet, soy, vegan diet

1 Introduction

Patients with breast cancer are often interested in nutrition (1–3) and are commonly recommended to adhere to dietary patterns rich in, but not limited to, minimally processed plant-based foods (4, 5). Plant-rich dietary patterns, or plant-based diets, include a spectrum of different diets, including a Mediterranean diet, Dietary Approaches to Stop Hypertension (DASH) diet, vegetarian, vegan, or a whole-food, plant-based (WFPB) diet. A WFPB diet, studied here, focuses on eating fruits, vegetables, whole grains, legumes, nuts, and seeds while minimizing or fully avoiding animal-based products, added oils, and processed foods.

Beyond dietary patterns, there remain important questions regarding the effect of specific dietary compounds on cancer risks. In particular, patients may ask about isoflavones or certain dietary fats. Isoflavones are found most abundantly in soybeans and foods derived from soybeans. They are a major class of phytoestrogens, which are naturally occurring plant compounds that are structurally similar to estrogens (6). They have a wide range of biologic effects. Phytoestrogens are weakly estrogenic as well as anti-estrogenic and can affect the cell cycle, apoptosis, genetic expression, endogenous steroids, angiogenesis, and also have antioxidant properties (6).

Concern about the potential carcinogenicity of isoflavones was raised based in part, on findings from experimental animal research testing various levels of isolated isoflavones (7–11) and *in vitro* data, but these concerns have not been supported by epidemiologic studies of isoflavones consumed as foods in the diet. A 2006 meta-analysis of 18 cohort and case–control studies found that high soy intake was modestly associated with a reduced risk of breast cancer (12). Three more recent meta-analyses (13–15) also found that high soy isoflavone intake was associated with reduced breast cancer risk in women without breast cancer, though this inverse association was not as strong in cohorts of Western women, who have lower intakes of isoflavones than Asian populations (15). Furthermore, other meta-analyses found that high soy isoflavone intake was associated with better outcomes in women with breast cancer (16, 17).

Similarly, omega-6 polyunsaturated fatty acids (n-6 PUFAs) and omega-3 polyunsaturated fatty acids (n-3 PUFAs), both essential fatty acids, have been studied in cancer risk. N-6 PUFAs are found in widely used vegetable oils like corn and soybean oil as well as nuts and seeds, whereas n-3 PUFAs are found in flax and chia seeds, cold-water fatty fish or fish oils, select plant oils, walnuts and fortified foods (18, 19). It has been suggested that humans evolved on a diet containing an omega-6 to omega-3 PUFAs ratio (n-6:n-3) of 1:1 (20, 21). The modern Western diet, however, has a n-6:n-3 ratio of 10–20:1 (22, 23). One recent meta-analysis shows that a higher n-6:n3 ratio is associated with an increased risk of breast cancer (24), and some research has shown that this fatty acid ratio is associated with inflammation and associated metabolic health (22, 25), but the evidence is far from settled.

Despite the interest in isoflavones and essential fatty acids there has been limited research to characterize the content of these compounds in either the typical Western diet of patients with advanced breast cancer or a WFPB diet. Given the questions around these food compounds, as well as the interest in plant-based diets, the purpose of this paper is to describe the changes in the intake of isoflavones, linoleic acid (n-6 PUFA), and n-3 PUFAs during a randomized controlled trial in women with metastatic breast cancer utilizing a WFPB dietary intervention.

2 Materials and methods

We conducted a randomized, controlled trial of a WFPB diet among women with stable stage IV breast cancer undergoing treatment. Our findings for feasibility, quality of life, and cardiometabolic and cancer-related biomarkers are published separately (26, 27). In this sub-analysis, we analyzed isoflavones, linoleic acid (n-6 PUFA), and N-3 PUFAs of the WFPB intervention diet and its n-6:n-3 PUFAs ratio using three-day food records at baseline and 8 weeks (final). Linoleic acid was used as a proxy for measuring total n-6 PUFAs given the vast majority was provided by linoleic acid.

2.1 Study selection, inclusion, and exclusion criteria

Study participants were recruited from oncology clinics at the University of Rochester Medical Center and local support groups. Eligibility criteria included: women with stage IV breast cancer with any estrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2 status, who were expected to live at least 6 months by their oncologist, and on a stable treatment regimen for the past 6 weeks with no expected changes in the next 4 weeks, were eligible for the study. Exclusions included inability to tolerate a normal diet, an active malabsorption syndrome, eating disorder, uncontrolled diarrhea, recent consumption of a vegan diet, major surgery within 2 months, current insulin, sulfonylurea, or warfarin use, glomerular filtration rate < 30 mL/min/1.73 m2 or serum potassium >5.3 mmol/L on twice within 90 days, current smoking, illicit drug use, drinking ≥7 alcoholic beverages per week, food allergies or intolerances to plant-based foods, or psychiatric disorder impairing ability to give consent.

2.2 Study design

Participants were randomized 2:1 to two arms: a WFPB diet or a usual diet. Given this was a dietary intervention, participants and study staff could not be blinded to the participants' group assignments. Participants in the control arm were instructed to continue their usual diets for 8 weeks and received phone calls from a study physician at weeks 2 and 6 to assess for adverse events and treatment changes. Participants in the WFPB arm received 3 meals and one side dish per day for 8 weeks and had weekly education visits and a brief weekly phone call with the study physicians. The *ad libitum* WFPB diet consisted of fruits, vegetables, whole grains, legumes, nuts, and seeds. Soy foods and minimal amounts of added sugars were allowed. Every four weeks, there were a total of 84 provided meals (3 meals/day), out of which 16 meals contained small amounts of tofu or soybeans in the entrée (edamame or tofu in a stir fry, or tofu mixed into a sauce, for example). Participants were not required to eat the provided meals and could add their own food in place of or in addition to the provided meals as long as it was 'on-plan'. The diet excluded animal products and added oils and solid fats. A daily multivitamin (Centrum Women) was provided to all participants in both groups.

2.3 Data collection and statistical analysis

Participants completed 3-day food records at baseline and 8 weeks on provided paper forms after instruction from the team's study coordinator. Participants then received a call from a dietitian within 1–2 days of completing their food record to clarify pertinent details. One intervention participant did not complete a final 3-day food diary and was not included in our analysis. The nutrient contents of 3-day food records were analyzed using the Nutrition Data System for Research (NDSR) version 2017 (Nutrition Coordinating Center, University of Minnesota, Minneapolis, MN) and statistical analysis was performed using SAS 9.4 (SAS Inc., Cary, NC, United States).

Within-group changes in nutrient content between the baseline and final 3-day food records were analyzed using the Wilcoxon signed-rank test, given non-normal distribution. The between-group difference in change of each nutrient was assessed using the Wilcoxon two-sample test. These tests were performed for isoflavones (daidzein, genistein, glycitein, and total isoflavones) and omega PUFAs (linolenic acid, total omega-3 PUFAs, linoleic acid, and linoleic acid: total n-3 PUFAs ratio), kilocalories, and macronutrients. All statistical tests of significance ($\alpha < 0.05$) were two-tailed.

3 Results

Thirty-two participants were enrolled ($n = 21$ WFPB and $n = 11$ control) and 30 completed the study ($n = 20$ WFPB and $n = 10$ control). Table 1 summarizes the energy and macronutrients consumed at baseline and 8 weeks. Within the WFPB group, the intervention resulted in significant changes in energy and the percentage of total kilocalories from fat and carbohydrates (energy and both macronutrients, all $p < 0.0001$) but not protein. Compared to controls, intervention participants had larger changes in both energy (−310.4 ± 111.3 (SE) kcals, $p = 0.0108$) and percentage of total kilocalories from fat (−15.2 ± 3.7% of total kcal, $p = 0.0044$). The control group did not significantly change their diet, except for decreased energy intake ($p = 0.0371$).

All isoflavones increased significantly ($p < 0.0001$) within the WFPB intervention group (Table 2). The WFPB intervention participants increased their daily consumption of total isoflavones from a mean of 0.8 ± mg/day to 14.5 ± 3.2 mg/day ($p < 0.0001$). Within the WFPB group, daidzein, genistein, glycitein, and total isoflavones, increased significantly on average by 5.3 ± 1.2 mg/day, 7.3 ± 1.7 mg/day, 1.2 ± 0.3 mg/day, and 13.7 ± 3.2 mg/day, respectively (all $p < 0.0001$). No significant differences were observed within the control group. Between group differences in change were significant for each isoflavone and the total isoflavones (all $p < 0.01$).

Table 3 summarizes the observed amounts of omega PUFAs, including linolenic acid (n-3 PUFA), total n-3 PUFAs, linoleic acid (n-6 PUFA), and linoleic acid: total n-3 PUFAs ratio (n-6:n-3). Within the WFPB group, the consumption of all PUFAs changed significantly ($p < 0.001$). The WFPB intervention significantly decreased the linoleic acid to total omega-3 PUFAs ratio (n-6:n-3) from a mean of 9.3 ± 0.9 to 3.7 ± 0.3 ($p < 0.0001$). Within the WFPB group, linoleic acid (n-6) consumption decreased by 3.8 ± 1.3 g/day ($p = 0.0095$), from 12.8 ± 1.1 g/day to 9.0 ± 0.6 g/day; the total n-3 consumption increased by 1.1 ± 0.3 g/day ($p = 0.0005$), from 1.6 ± 0.2 g/day to 2.7 ± 0.3 g/day as a result of increased non-marine alpha-linolenic acid consumption. Within the control group, the only significant change in omega PUFAs was decreased intake of linolenic acid from 2.4 ± 0.5 g/day to 1.6 ± 0.4 g/day ($p = 0.0488$). Between group differences in change were significant for linolenic acid ($p = 0.0009$), total n-3 PUFA ($p = 0.0031$), and the n-6:n-3 ratio ($p = 0.0015$), but not linoleic acid.

4 Discussion

To the best of our knowledge, this is the first description of isoflavone, linoleic acid (n-6 PUFA), and omega-3 PUFA intake in a WFPB diet among women with breast cancer. We observed that our WFPB intervention increased the consumption of isoflavones and non-marine alpha-linolenic acid (n-3 PUFA) while decreasing linoleic acid (n-6 PUFA). The linoleic acid to omega-3 PUFAs (n-6:n-3) ratio decreased from 9.3:1 to 3.7:1.

The baseline isoflavone intake in our cohort of women with metastatic breast cancer was very low but is consistent with other studies, which have found that Americans generally consume less than 1 mg/day (28, 29). In China and Japan, by contrast, some estimates of mean daily isoflavone intake have ranged from 20-50 mg/day or more (30, 31). Trials of isoflavone supplements on various outcomes utilize supplements of 25–300 + mg/day (32, 33). Thus, the total isoflavones consumed in our study, 14.5 mg/day, on a whole-food, plant-based diet with the inclusion of modest amounts of soy foods (~1 meal with a soy component every other day) could be described as no more than a moderate amount in a global context, even though it was roughly 20-fold more than the intervention group consumed at baseline.

Among observational studies, the beneficial inverse association of isoflavone intake and breast cancer diagnosis, recurrence, and mortality appears only after intake exceeds 10 mg/day (16, 34). While there remain many uncertainties regarding the effect of isoflavones on breast cancer, these observational studies offer support for the idea that increasing isoflavone to the level observed in this intervention is likely to be safe and potentially may offer benefits. Because our study was limited to 8 weeks and included many more changes than just isoflavones, we cannot draw any conclusions from our study regarding the increased isoflavones and their potential effect on cancer progression.

Apart from their effect on cancer progression, a meta-analysis of 16 pooled randomized control trials showed that isoflavone intake

TABLE 1 Macronutrients.

	Control diet (CON) n = 10			Intervention diet (WFPB) n = 19			Between group differences in change at week 8	
	Baseline	8 weeks	Difference	Baseline	8 weeks	Difference	Difference	p-value
Energy (kcal)								
Mean ± SE	1590.2 ± 140.0	1431.2 ± 126.8	−159.1 ± 63.8*	1782.2 ± 75.8	1312.8 ± 57.4	469.5 ± 73.1***	−310.4 ± 111.3	0.0108
Median (25–75%)	1572.5 (1379.0–2047.5)	1459.4 (995.8–1683.2)	−129.6 (−244.6–1.3)	1752.1 (1468.0–2124.8)	1293.4 (1127.2–1510.2)	−416.0 (−690.6– −220.2)		
Fat % of total kcal								
Mean ± SE	36.2 ± 1.8	36.0 ± 4.2	−0.2 ± 3.6	36.9 ± 1.4	21.4 ± 1.2	−15.5 ± 1.9***	−15.3 ± 3.7	0.0044
Median (25–75%)	37.5 (31.8–38.7)	38.6 (29.9–45.2)	1.7 (−4.5–6.1)	36.9 (30.9–42.1)	21.4 (18.3–25.2)	−14.7 (−23.7– −9.9)		
Carbohydrate % of total kcal								
Mean ± SE	46.6 ± 3.0	47.4 ± 6.2	0.8 ± 5.2	49.9 ± 1.9	68.9 ± 1.6	19.0 ± 2.3***	18.2 ± 4.9	0.0078
Median (25–75%)	49.2 (43.7–51.2)	50.9 (35.2–554.5)	−0.05 (−11.2–2.1)	46.7 (43.7–55.9)	67.6 (66.5–74.0)	22.1 (13.1–27.9)		
Protein % of total kcal								
Mean ± SE	19.5 ± 2.8	18.9 ± 2.1	−0.7 ± 1.8	14.8 ± 0.6	14.5 ± 0.4	−0.3 ± 0.7	−0.4 ± 2.0	0.7333
Median (25–75%)	16.5 (14.5–26.9)	18.4 (15.4–21.9)	0.7 (−3.4–3.2)	14.4 (13.5–16.5)	14.6 (12.9–15.7)	0.5 (−1.6–1.0)		
Dietary cholesterol (mg/day)								
Mean ± SE	217.1 ± 44.1	188.2 ± 37.8	−28.9 ± 55.6	214.2 ± 24.0	7.5 ± 4.2	−206.7 ± 24.3***	−177.8 ± 52.1	0.0343
Median (25–75%)	186.3 (109.8–317.9)	188.5 (91.6–222.2)	−42.9 (−173.6–104.1)	186.7 (132.4–269.2)	0.0 (0.0–1.7)	−164.4 (−254.0– −123.3)		
Dietary Fiber per 1,000 kcal								
Mean ± SE	16.6 ± 1.9	14.7 ± 1.4	−1.9 ± 1.6	12.5 ± 1.3	30.7 ± 1.4	18.1 ± 1.7***	20.0 ± 2.6	0.0108
Median (25–75%)	15.2 (12.1–20.2)	14.5 (9.7–18.0)	−0.4 (−4.5–2.1)	23.0 (8.3–14.3)	29.2 (27.4–35.6)	19.1 (11.4–23.4)		

*p < 0.05 for within-group change. ***p < 0.0001 for within-group change.

TABLE 2 Isoflavones.

	Control (CON) $n = 10$			Intervention (WFPB) $n = 19$			Between group differences in change at week 8	
	Baseline	8 weeks	Difference	Baseline	8 weeks	Difference	Differences	p-value
Daidzein (mg)								
Mean ± SE	1.5 ± 0.7	0.2 ± 0.1	−1.2 ± 0.7	0.3 ± 0.1	5.6 ± 1.2	5.3 ± 1.2***	−6.5 ± 1.4	0.0001
Median (25–75%)	0.3 (0.1–1.7)	0.2 (0.1–0.2)	−0.07 (−1.6–0.05)	0.1 (0.1–0.3)	3.9 (0.9–8.7)	3.9 (0.8–8.5)		
Genistein (mg)								
Mean ± SE	2.2 ± 1.2	0.3 ± 0.1	−1.9 ± 1.2	0.4 ± 0.2	7.6 ± 1.7	7.3 ± 1.7***	−9.2 ± 2.1	0.0008
Median (25–75%)	0.2 (0.1–2.6)	0.2 (0.1–0.3)	0.0 (−2.4–0.1)	0.1 (0.1–0.3)	5.7 (1.0–14.3)	5.2 (0.9–14.1)		
Glycitein (mg)								
Mean ± SE	0.3 ± 0.1	0.0 ± 0.0	−0.2 ± 0.1	0.1 ± 0.0	1.2 ± 0.3	1.2 ± 0.3***	−1.4 ± 0.3	0.0008
Median (25–75%)	0.0 (0.0–0.4)	0.0	0.00 (−0.4–0.0)	0.0	0.8 (0.1–1.9)	0.7 (0.1–1.8)		
Total isoflavones (mg)								
Mean ± SE	3.9 ± 2.0	0.6 ± 0.2	−3.3 ± 2.1	0.8 ± 0.4	14.5 ± 3.2	13.7 ± 3.2***	−17.1 ± 3.8	0.0012
Median (25–75%)	0.4 (0.1–4.7)	0.3 (0.2–0.5)	−0.1 (−4.3–0.1)	0.2 (0.1–0.7)	10.8 (1.9–24.7)	10.0 (1.9–24.4)		

***$p < 0.0001$ for within-group change.

TABLE 3 Omega-3 and linoleic (omega-6) fatty acids.

	Control (CON) $n = 10$			Intervention (WFPB) $n = 19$			Between group differences in change at week 8	
	Baseline	8 weeks	Differences	Baseline	8 weeks	Differences	Differences	p-value
Linolenic acid (g/day)								
Mean ± SE	2.4 ± 0.5	1.6 ± 0.4	−0.8 ± 0.3*	1.4 ± 0.2	2.7 ± 0.3	1.2 ± 0.3**	−2.0 ± 0.4	0.0009
Median (25–75%)	1.9 (1.7–3.1)	1.4 (1.2–1.8)	−0.7 (−1.2– −0.4)	1.4 (0.9–1.9)	2.3 (1.9–3.4)	1.2 (0.5–2.1)		
Total omega-3 FA (g/day)								
Mean ± SE	2.6 ± 0.5	1.9 ± 0.5	−0.7 ± 0.4	1.6 ± 0.2	2.7 ± 0.3	1.1 ± 0.3**	−1.7 ± 0.5	0.0031
Median (25–75%)	2.0 (1.8–3.0)	1.4 (1.3–1.8)	−0.7 (−1.4–0.1)	1.4 (0.9–2.0)	2.3 (1.9–3.4)	1.0 (0.3–1.5)		
Linoleic acid (g/day)								
Mean ± SD	15.5 ± 3.3	11.6 ± 1.8	−3.9 ± 2.9	12.8 ± 1.1	9.0 ± 0.6	−3.8 ± 1.3**	−0.1 ± 2.7	0.5556
Median (25–75%)	15.1 (8.2–18.0)	12.5 (7.1–16.4)	−4.9 (−6.4–1.9)	11.3 (9.1–16.8)	8.7 (7.1–10.9)	−3.2 (−7.8–0.5)		
Linoleic acid/total omega-3 FA ratio								
Mean ± SD	7.1 ± 1.1	7.6 ± 1.2	0.5 ± 1.3	9.3 ± 0.9	3.7 ± 0.3	−5.5 ± 0.8**	6.0 ± 1.5	0.0015
Median (25–75%)	8.4 (3.5–9.3)	9.1 (3.5–9.2)	0.7 (0.2–3.5)	9.2 (7.6–10.3)	3.3 (2.3–5.0)	−5.4 (−6.8– −2.8)		

*$p < 0.05$ for within-group change. **$p < 0.01$ for within-group change.

improved overall cognitive function and memory in adults via mechanisms involving decreased inflammation and oxidative stress (35). This is particularly relevant given that cognitive impairment occurs in 45% of breast cancer patients receiving chemotherapy (36). While increasing isoflavone intake, intervention group participants in this study reported clinically and statistically significant increases in perceived cognitive function, including in areas of memory, concentration, and attention, as measured across several validated questionnaires (27). It is not possible to attribute this strictly to isoflavones, however, given the plethora of related dietary changes and metabolic changes occurring simultaneously.

Concurrent with the changes in isoflavones, the WFPB diet had a significantly lower n-6:n-3 PUFAs ratio resulting from higher n-3 PUFAs and lower linoleic acid (n-6 PUFA) consumption. The effect of these changes on breast cancer progression is inconsistent across studies, but compelling animal research (37) along with some observational studies (38–41) suggest that if there is an effect, it is likely to lower breast cancer risks. However, the issue is further complicated by the potentially different effects of different sources of n-3 PUFAs. Here, study participants increased plant-sourced alpha-linolenic acid (ALA) intake without increasing intake of docosahexaenoic acid (DHA) or eicosapentaenoic acid (EPA), the downstream metabolites of ALA that are commonly consumed preformed in marine animal foods (fish and seafood). While research has often focused on DHA and EPA intake instead of ALA, a case–control study found that women with higher levels of ALA in breast tissue were less likely to have breast cancer (38). Further, the significantly decreased omega-6 intake is likely to enhance the conversion of ALA to EPA and DHA, increasing their serum levels (42–44).

There has also been evidence relating n-6 and n-3 PUFAs intake to cardiometabolic outcomes (22, 45), though there are inconsistent findings here as well, particularly because of observations that higher n-6 PUFA intake is associated with lower cardiovascular risks (46). Our dietary intervention, lower in n-6 PUFA and higher in n-3 PUFA, resulted in multiple cardiometabolic and hormonal improvements, including intentional weight loss without signs of disease progression, reduced total and LDL cholesterol, insulin resistance, free testosterone, and IGF-1 (26). These cannot be attributed solely to changes in fatty acid intake, however, due to the multitude of simultaneous changes in nutrient intakes.

Our study has numerous strengths and limitations. We successfully implemented much larger dietary changes than many other nutrition interventions, in part because of the provided meals. This may however limit generalizability. Patients adopting a WFPB diet on their own may not make such large, rapid changes. Another limitation to generalizability is that different plant-based diets can be constructed differently, with differing amounts of soy foods, chia and flax seeds, etc. But while there will be variation in intake, this descriptive analysis of our study intervention provides a framework for the types of nutrient changes that might be expected with a WFPB diet, which has not previously been described.

In conclusion, the findings from the current study show that transitioning to a WFPB diet inclusive of small amounts of soy foods resulted in significantly increased intake of isoflavones, n-3 PUFAs, and reduced linoleic acid (n-6 PUFA) intake and n-6:n-3 PUFA ratio. While these changes were observed along with numerous cardiometabolic and quality-of-life benefits in this trial, the implications for breast cancer progression and survival require further study.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by University of Rochester Research Subjects Review Board. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

JL: Writing – original draft, Data curation, Visualization. EKC: Conceptualization, Data curation, Investigation, Methodology, Project administration, Resources, Supervision, Writing – review & editing, Formal analysis. EvC: Data curation, Formal analysis, Methodology, Resources, Writing – review & editing. LB: Project administration, Writing – review & editing, Data curation, Formal analysis, Investigation. NW: Investigation, Methodology, Project administration, Resources, Writing – review & editing, Data curation. LP: Conceptualization, Methodology, Project administration, Resources, Supervision, Visualization, Writing – review & editing. TC: Conceptualization, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Writing – review & editing.

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Conflict of interest

TC: royalties from general interest books about plant-based nutrition (Benbella Books, Penguin Random House) and income from a lifestyle medicine practice, TC, MD PLLC; EKC: conflicts of spouse (TC).

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fnut.2024.1338392/full#supplementary-material

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Caregiver perceptions of a pediatric produce prescription program during the COVID-19 pandemic

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Introduction: Produce prescription programs are rapidly expanding as a type of Food is Medicine intervention with prospects for mitigating food insecurity and reducing diet-related health disparities. Gaining insight into participant perspectives on program logistics and perceived impacts is crucial to program success and improvements.

Methods: Between May and June 2021, we conducted individual and small group interviews with 23 caregivers with children aged 1–5 years who participated in a produce prescription program from 2020 to 2021 in Texas, U.S. They were provided with a gift card to a major national grocery retailer to purchase fresh produce. The card was reloaded $60 monthly for 8 months with automatic roll-over of unused funds to the next month. Participants also received nutrition education in the form of two videos. A deductive analysis approach was employed, and NVivo qualitative data analysis software was used to perform coding and to assist with subsequent analyses.

Results: All 23 participants were female, with an average age of 37.5 years, and the majority identified as Hispanic/Latino (83%). About 43% of the families had three or more children. Six themes were generated from interviews. Three of these themes were related to program logistics: (1) ease of program use; (2) participant satisfaction with the incentive; and (3) desire for additional store options. The remaining main themes pertained to program impact: (1) the enhanced ability to purchase produce; (2) the usefulness of the nutrition education; and (3) persistent challenges encountered when preparing the produce for picky eaters and young children.

Conclusion: A pediatric produce prescription program was perceived as logistically easy and a helpful source of financial support for accessing fresh produce. Program features such as card-based incentive system and partnership with major grocery retailer were favored by participants. For future program design, it may be beneficial to consider collaborating with multiple grocery outlets and enhancing the intensity and targeting of nutrition education.

KEYWORDS

produce prescription programs, qualitative research, pediatric population, caregivers, food is medicine

1 Introduction

Suboptimal diet is a major risk for non-communicable diseases, including obesity, diabetes, cardiovascular disease, and cancer (1–3). In the United States, more than 45% of cardiometabolic-related deaths and $50 billion healthcare costs were attributable to poor diet in 2012 (1, 4). Despite a modest increase in overall dietary quality in the past decades, most Americans do not meet the recommended intake of fruits and vegetables (5–7). About 40% of children aged 2–5 years were estimated to have poor dietary quality according to the 2015–2016 National Health and Nutrition Examination Survey (NHANES) (8).

Moreover, diet-related disparities have worsened across multiple sociodemographic factors, especially by race, education, and economic status (7–9). These populations are also disproportionately affected by food insecurity, defined as inadequate access to sufficient and nutritious food for an active and healthy life. In 2021, U.S. households with children less than 6 years old had a higher rate of food insecurity (12.9%) than the national average (10.2%) (10). Compared with non-Hispanic White households with children, Black, Asian and Hispanic households with children were at increased risk for food insecurity and the gap widened since the onset of the COVID-19 pandemic (10, 11). Food insecurity is associated with compromised dietary quality, poor health outcomes, and negative implications for child development independent of poverty (12, 13). Children growing up in food-insecure environments are more likely to experience co-existing health consequences of inadequate nutrient intake and obesity (13, 14).

Food-insecure households often lack the financial and physical resources to access healthy foods like fresh produce and whole grains (15). Federal nutrition assistance programs such as the Supplemental Nutrition Assistance Program (SNAP), the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC), and school meals programs may alleviate hunger and food insecurity by providing resources to meet food needs. A national survey conducted by the U.S. Department of Agriculture showed that about 56% households experiencing food insecurity participated in one of the major nutrition assistance programs in 2021 (10). Additionally, it has been estimated that school meals (breakfast and lunch) may contribute to more than 40% of daily energy and nutritional needs for children living in low-income households (16). Yet, how these programs affect dietary quality and intake of specific food groups remain inconclusive. In fact, several studies observed no differences in fruit and vegetable intakes comparing program participants with income-eligible non-participants among U.S. children, highlighting potential areas for more targeted interventions (17–19).

Produce prescription programs, a type of Food is Medicine intervention, offer participants monetary incentives such as vouchers or debit cards to purchase fruits and vegetables at farmers market or grocery retailers (20–22). Patients who are food insecure and/or at risk of diet related chronic disease are screened and referred to the programs by their healthcare providers. Emerging literature on this type of program indicates that participation is associated with increased produce consumption, reduced food security, and improved cardiometabolic outcomes (20, 23, 24). These programs may present an opportunity to address diet-related health disparities through integrating food and nutrition strategies into the healthcare system. Healthcare providers engaged in these programs have reported that although there were challenges related to staff time, they perceived an increase in knowledge, confidence, and motivation to screen and address food insecurity. They also appreciated that programs provided a tangible way to assist their patients, especially for under-resourced patients who might not qualify for other assistance programs or in times of emergency (25, 26).

Although interest in research and healthcare policy related to food is medicine interventions is growing rapidly, programs prioritizing children are still limited. Only eight studies have aimed to understand the experience of caregivers in pediatric programs in the past decades (27–30). In more recent qualitative studies of pediatric produce prescription programs operated during the COVID-19 pandemic, themes from the perspectives of caregivers revealed exacerbated economic challenges related to the pandemic, adaptations made in response to program implementation, and perceived favorable program effects on healthy food access and family dietary habits (28–30). These previous studies underscored the diversity of experiences with produce prescription program, which could be affected geographic and temporal factors. Policy reports call for more qualitative research on the experiences of program participants to explore the effect of cultural and socioeconomic factors on program adoption as well as to identify program impacts and areas for improvement that are not otherwise captured in quantitative studies (23).

Most prior programs mainly used vouchers for farmers' market or fresh produce boxes, offering very limited variations on incentive form and redemption partners (e.g., voucher vs. card-based incentives). In this study, we focused on understanding how program participants perceived a card based pediatric produce prescription program that partnered with a main grocery outlet implemented during COVID-19 pandemic in Texas U.S. where more than 20% children faced food insecurity in 2021 (31), how participating in the program affected food access and dietary behaviors, and how programs might be improved to better serve their needs in the future.

2 Methods

2.1 Study design and sample

In May–June 2021, we conducted three individual and six group interviews (each ranging from two to seven participants) with a total of $n = 23$ caregivers who participated in a produce prescription program from 2020 to 2021 that was run through a community health center serving a low-income community in Texas, U.S. Eligible caregivers had at least one child aged 1–5 years. All 23 participants were female; their mean age was 37.5 years and 83% identified as Hispanic/Latino (see Table 1).

Caregivers were provided with a gift card to a major national grocery retailer, restricted to fresh produce purchases, that was reloaded with $60 monthly for 8 months. The primary nutritional educational support materials were the two nutritional education videos created for the program and the participants by the wellness coordinator and coach at the participating clinic. The videos were in English and provided via a private link. The first video was released in the first 3 months of the program, and the second video was released in the last 3 months of the program. The topics were "Do not Tell Your Kids to Eat Fruits and Vegetables!" for the first video (approximately

TABLE 1 Texas 2020-2021 produce prescription program participant characteristics (n = 23).

Age in years, mean (SD)[1]	37.5 (10.1)
Gender, n (%)	
Female	23 (100)
Hispanic, n (%)	
Yes	19 (82.6)
No	4 (17.4)
Race, n (%)	
White	21 (91.3)
Black/African American	1 (4.3)
Did not say	1 (4.3)
Children in household, n (%)[1]	
One	4 (18.2)
Two	8 (36.4)
Three	3 (13.6)
Four or more	7 (31.2)
Marital status, n (%)	
Married	10 (43.5)
Divorced	1 (4.3)
Widowed	1 (4.3)
Separated	3 (13.0)
Never married	6 (26.1)
Member of unmarried couple	2 (8.7)

[1]Missing value, n = 22.

30 min) and "How to Make Eating Healthy Too Easy" for the second video (approximately 60 min).

2.1.1 Interview procedures

Semi-structured interview guides were developed by the Tufts research team's qualitative research expert (SCF) with input from research team members; the non-profit organization that implemented the produce prescription program evaluated in this study; and the program coordinator at the partnering clinic. The interview guide consisted of two key topic areas: "program logistics" concerning participants' perceptions on logistics and setup of the program; and "experiences with the program" concerning participants' experiences with using the program and program impact. A total of six main questions, each with multiple sub-questions, were included in the interview guide (Table 2).

Interviews (individual and small group) were conducted online using the Zoom videoconferencing application either by the qualitative expert or by study team members whom she had trained. Verbal consent was obtained at the beginning of each interview session. Interviews lasted 21–61 min. All interview sessions were recorded and transcribed verbatim. Study participants received a $50 gift card for remuneration. The protocol was reviewed and deemed exempt by the Tufts University Health Sciences Institutional Review Board.

2.1.2 Analysis

The interviews were recorded, transcribed, and coded using NVivo qualitative data analysis software. We used a directed qualitative content analysis approach, which is fundamentally deductive (32). We drafted initial codebooks based on the interview guides. We then conducted reviews of the transcripts and added codes for topics that arose in the data. Once the codebooks were established, the qualitative expert and the study administrator (ZL) independently coded one transcript. Inter-rater reliability testing identified minor differences in interpretation; coding decisions were reviewed line-by-line and resolved. The codebooks were revised accordingly, mainly by clarifying code definitions, and all transcripts were subsequently coded by the study administrator. Final themes were reviewed and refined by the study team and presented at monthly investigator meetings.

3 Results

Six themes were identified, three in each of the two key topic areas of the interview guide—Program Logistics and Program Impact.

3.1 Program logistics

Overall, program participants had positive perceptions about the logistics of the produce prescription program. There were three major themes related to participants' experiences: (1) ease of use; (2) satisfaction with the incentive; and (3) desire for additional store options.

3.1.1 Ease of use

In this program, participants received a gift card to a major national grocery retailer that automatically reloaded $60 each month. Any remaining balance rolled over into the next month. The gift card could be used for any fresh fruits or vegetables. The major theme was that the program and the card was easy to understand and use. Many participants used it at self-checkout, just like any gift or debit card.

> *"… it was easy. You just go in, select what you want, go and check out. Rather you have other merchandise or whatever, it would already separate it, it would pay for what it knew it was supposed to take off, so it was just super easy. I was surprised how easy it would be" [white female, 41-year-old, with one child].*
>
> *"I believe it was easy. You would get a text message saying when it was loaded. You were able to call to figure out how much you still had left. Yeah it was simple. It was not hard at all" [white female, Hispanic, 25-year-old, with four children].*
>
> *"I didn't have any problems with the setup. I heard about it. I contacted my contact at the at [clinic] he got right back with me. And any emails I got on what was to be expected, and what I was supposed to do was very easy to understand and follow" [white female, 44-year-old, with two children].*

Participants perceived store employees as friendly and helpful with the produce prescription. Only a few participants had issues with the program, and any questions were addressed quickly and satisfactorily by the program coordinator at the partnering clinic. A few had issues using

TABLE 2 Program participant interview guide.

Topic 1: Program logistics
For the first set of questions, I'm going to ask about how the program was set up.
1 Talk about how easy or hard it was to understand how to use the program.
a What, if anything, helped you to better understand the program? [probes: clinic staff, materials]
2 As you know, the program used a reloadable Walmart gift card. I'd like to ask about using the gift card itself.
a What worked for you? [probes: delivery system, ease of use]
b What did not work for you?
c Describe any problems you had using the card at Walmart.
i What problems, if any, did you have with the store employees when you were using the card? [probes: they did not know what it was, they treated you poorly]
d What other stores or places to get food would you have wanted to be part of the program? Tell me the reasons.
e Tell me your thoughts about the amount of the gift card.
i What amount would have been more helpful?
Topic 2: Experiences with the program
For the next set of questions, I'd like to find out more about your experiences with the program.
3 Think back to when you were deciding whether to do this program. What were you hoping to get out of it?
a Talk about whether the program helped you in the ways you thought it would.
i How could the program change to best meet your needs?
b What, if anything, surprised you about the program?
4 Now, I'd like to hear more about your experiences with the fruits and vegetables that you got as part of the program.
a What did you usually get with the card?
b How did you usually use them?
i Who in your household ate the fruits and vegetables?
c What did your children think about the fruits and vegetables?
d How easy was it to get fruits and vegetables that you and your children are most familiar with?
e Tell me about any new fruits and vegetables that you tried because of the program.
i What, if anything, surprised you about what you tried?
ii What did your child(ren) think about the new fruits and vegetables?
f In what ways, if any, did your children change what they thought about any fruits or vegetables?
g Tell me about the best moments you had when using the fruits and vegetables from the program. [probes: what made you proud? What was the most fun? What was the best meal you made?]
h Describe the biggest challenge you had with the fruits and vegetables that you got as part of the program. [probes: children would not eat the food; did not know how to prepare the food; food went to waste]
i What, if anything, could be added to the program to help you make better use of the fruits and vegetables?
5 Now I'm going to ask about some other parts of the program besides the card. Tell me your thoughts about the educational videos.
a What were you hoping to learn from them?
b What, if anything, did you learn that was new?
c What other topics would have been helpful?
d What did you think about using a video to receive this information?
e Some people were asked to set goals at the beginning of the program. What can you tell me about any goals you set?
i How helpful was it to set goals?
6 Overall, what did you like best about this program?
a What about this program was the most challenging?
b Talk about whether you would do this program again.
i If you were going to do the program again, what would you do differently?
c If you were trying to get a friend or family member to join a program like this, what would you tell them?
d In what ways, if any, did doing this program affect your experience in the clinic?
i How did the pandemic affect how often you come to clinic?
ii What could the clinic staff have done to make the program better for you?
e How did your experience with this program compare to any other food programs that you have done? [probes: WIC, food pantries, summer meals for kids]

the card the first time, but everything went smoothly after they figured out how to use it and what was covered by the card.

> *"In the beginning, it was trying to figure it out and everything, but yes. The fruit and vegetables, I didn't know even to get the ones that were bagged or just plain without having them bagged, but it was easy, except in the beginning. When I used it twice and then after that, it was fine" [white female, Hispanic, 60-year-old, with one child].*

A subtheme was that the program was logistically easier than the Special Supplemental Nutrition Program for Women, Infant, and

Children (WIC). Participants described several advantages to the program, such as being able to use the card at the self-check-out (which they could not do with WIC benefits), not needing to look for specific items like WIC tagged items when purchasing fruits and vegetables and being able to roll the incentive over to the next month. And a few also mentioned quicker responses to their questions and feeling less judged or embarrassed when using produce prescription card than WIC.

> *"Using that card self-checkout was a lot easier because whenever we have to use WIC, we cannot go to self-checkout, you have to go to the cashier. Sometimes, you're just going for fruits and vegetables, you can just go straight to your self-checkout and it's a lot easier to use that" [white female, Hispanic, 35-year-old, with six children].*

3.1.2 Satisfaction with the incentive

A second major theme was that participants were satisfied with the incentive amount. They described the amount as appropriate and useful, regardless of household size.

> *"It was a good amount. For me, it's just me and my son, but he is a big fruit lover. He loves all kinds of fruits. So I would use it every month and he really enjoyed it also" [white female, Hispanic, 28-year-old, with one child].*

> *"I think the amount was a really good amount. We're a family of five, now six, but that was, I think more than enough. Especially with the fruits and vegetables, sometimes they can be costly, but I think it was a good amount for us" [female, Hispanic 29-year-old, with four children].*

> *"Yes, and I agree also. The vegetables, not so much the vegetables, but I think some of the fruits can be a little bit more pricey during certain seasons, so it was very helpful with that amount" [white female, Hispanic, 41-year-old, with five children].*

Many participants stated that the incentive allowed them to purchase produce with less financial stress, especially when produce prices were high or when income had been reduced due to the effects of the COVID-19 pandemic. Moreover, many participants appreciated that the program provided extra funds specifically focused on fruits and vegetables. Participants also appreciated the flexibility of the incentive, allowing them to make their own choices of fruits and vegetables based on their preferences and needs.

> *"I personally love that we had choices, and we could make our own choice. We didn't just … here's a bag of food or here's your meals for the week. We could pick and choose what we wanted, what we liked. We didn't have to go and turn around and pass on the blessing to somebody else because we just can't utilize it because nobody likes it, or there's allergy, or whatever. I really enjoyed being able to pick and choose what we got" [white female, Hispanic, 35-year-old, with two children].*

The only major issue with the incentive that participants described was that it could not be used on frozen fruits and vegetables.

> *"The only downfall that I personally wished would be maybe frozen fruits and vegetables included, that would have been ideal because I noticed that sometimes I was like I want to go get them, but not, I don't think they're going to be eaten as much this weekend or whatever, because of our schedule and knowing that it was more of a chance of the produce going bad, not to mention me personally, [participating grocery store] doesn't have the best produce" [white-female, Hispanic, 39-year-old, with six children].*

3.1.3 Desire for additional store options

A third major theme was that more stores should be included in the program. Participants cited several reasons for wanting more options, including convenience and a better selection and quality of produce.

> *"I definitely think it would have been an improvement had it been contracted with somebody else like [statewide grocery store] or in addition to. That would have been really beneficial, in my opinion. Just because the quality of the produce really and the selections" [white female, Hispanic, 35-year-old, with two children].*

> *"I honestly prefer [health food store], like their fruits. I wish that would have been an option" [white female, 32-year-old, with two children].*

> *"Personally, I get all my groceries from [statewide grocery store], so I would have to make a separate trip in order to go to [participating grocery store], which isn't close to the [statewide grocery store] that I go to, but have to make an additional trip in order to get the fruits and veggies because I couldn't justify getting them at [statewide grocery store] and paying for them when I could get more and use the card" [white female, Hispanic, 36-year-old, with three children].*

Only a few other logistical factors with the program were mentioned. A few participants suggested having a program app where the incentive balance and nutrition education could be easily accessed. Related to COVID-19 concerns, some participants stated that being able to purchase produce online and having access to mental health videos or support would have been helpful.

3.2 Program impact

Most participants said that all members in the household ate and benefited from the fruits and vegetables purchased using the program. There were three main themes related to program impact. The first was the ability to purchase a greater quantity and variety of fruits and vegetables; a second was the usefulness of the nutrition education; and a third was challenges related to preparing the produce so that it was acceptable to children.

3.2.1 Purchasing a greater quantity and variety of fruits and vegetables

The overarching theme was that participants were able to purchase more produce because of the program. The program enabled participants to purchase more fruits and vegetables that they or the family liked and would normally buy.

> *"My little one loves bananas and eats one every day. Whereas before, I would purchase them a little bit more sparingly, I purchased it more because we had the extra amount to use" [white female, Hispanic, 36-year-old, three children].*

> *"My kids enjoyed it as well. My oldest is six and my youngest is one. In between, there's a two-year-old and a five-year-old. But they would love to pick their own fruit. They miss being able to get so much at one time. They would pack their lunch bags with fruits and vegetables instead of candy and chips. They really liked it, especially my daughter with the carrots and her ranch. I don't know where it went!" [white female, Hispanic, 25-year-old, with four children].*

> *"Every time I would tell my son I'm going to go to [participating grocery store], he would always already know that it was going to be like we're going to go buy fruits and vegetables. He really enjoyed being able to get the fruits he wanted, especially he loves grapes. [laughs] He already knew he could get, instead of just getting one bag, he could get two. He loved it" [white female, Hispanic, 28-year-old, with one child].*

The program allowed participants to purchase a wider variety of produce, and to be adventurous in trying new types. It also allowed participants to buy more produce that they knew their families enjoyed, but that were usually too expensive. For instance, people used the card to purchase more expensive items like cherries and avocados that they would typically buy in small quantities or not at all. A few participants also mentioned buying more higher-quality produce.

> *"Yes, we're exploring different things. Like the coconut, they hadn't been exposed to the coconut. Different bananas that they have, different carrots that they have; I was definitely able to think outside the box and try something different" [white female, Hispanic, 44-year-old, with seven children].*

> *"We were able to get better greens. Then also, I enjoyed that if my son wanted the plums or something, I wasn't just looking at the price and be like, 'No, we're only going to get the apples that are on sale this week.' I could get the ones that were 50 cents more a pound and not feel guilty that I was taking away some other food item from our grocery budget that I wasn't going to be able to get that week to make our meals. They were so excited that they could go pick their fruits and vegetables out without worrying about mom being like, 'No, let's get the cheaper ones' [laughs] So that was nice" [white female, 32-year-old, with two children].*

3.2.2 Nutrition education

In this program, nutrition education consisted mainly of two educational videos. Participants described learning new ways to add more fruits and vegetables to their children's diets. Some additionally mentioned new cooking tips and the benefits of consuming fruits and vegetables. Several participants commented that they were already familiar with the video content but felt that it served as a useful reminder.

> *"I thought the videos were a good resource for reminders for me. Life gets so busy, and then I would see the messages, so I'd be like you know what, I'm going to sit down for a second and watch this. And then I'd be like okay, now I need to get moving, get back on track, quit eating chips woman, and go and get something else healthier, you know. Just like a -- when the video is there I'd be like oh yeah, I'm trying to do better, I'm not trying to snack on all this garbage all the time" [white female, 41-year-old, with one child].*

> *"I enjoyed them. I thought he did a good job presenting the material. They weren't long, it wasn't a drawn-out, long, boring video. It's things that are important, like dealing with picky eaters, and hiding the vegetables. I know there was a portion on one of the videos about exactly what I'm trying to do right now. They were very pertinent to what I was doing at home" [white female, Hispanic, 35-year-old, with two children].*

While the overall theme was on the helpfulness of the nutrition education, several participants had contrasting perspectives. One participant with very young children said that the tips given in the videos were not helpful in getting her kids to eat more fruits and vegetables and try new things. A few participants did not watch or watched only one video. They were either too busy or did not feel motivated to do so.

3.2.3 Challenges

Despite the increased access to fruits and vegetables, a third theme was that participants still sometimes struggled with ways to prepare fruits and vegetables so that their family members would like and eat them. Several participants expressed a desire for new recipes and cooking tips, as well as how to properly feed very young children.

> *"I think, well, for me, trying to cook vegetables for my granddaughter is real hard because she's a picky eater. She'll eat cheese, she'll eat crackers, she'll eat almost every fruit there is. Vegetables are just really hard…We can't hide the green. I was thinking just now, maybe I should try to hide cauliflower in there because that's white. I think that would be the most challenging thing that I found, was trying to hide something. It was easier just to give her fruit and cheeses because we knew she would eat that. At two and three years old, the fight is just not there for me anymore" [white female, Hispanic, 59-year-old, with one child].*

> *"The biggest challenge for me, the vegetable, it was asparagus, the spinach, and the broccoli and all like that it's pretty cool because I could put it in the smoothies, but the asparagus, I cannot. I try to*

> *grill them, I try to put them in salads and grill them or bake them, that's a challenge still right now, ongoing. But she will eat some. One of these days she's going to like them. I'm going to prepare, and they'll like them" [white female, 60-year-old, Hispanic, with one child].*

4 Discussion

This qualitative study explored caregivers' perspectives on a pediatric program implemented during the COVID-19 pandemic among under-resourced families in Texas. In general, parents found the program to be logistically easy, with incentives perceived as adequate, regardless of household sizes. Moreover, program participants shared their experiences of reduced financial obstacles to acquiring fresh produce and an enhanced capacity to purchase a wider variety of fruits and vegetables. Participants expressed that maximizing choice, including the types of produce offered (i.e., frozen in addition to fresh) and ability to access more retail grocery stores was important. Many participants described the experience of the program as easier than WIC and less stigmatizing. Challenges and considerations for future program development included the need for increased grocery store involvement and the provision of recipes.

This study suggests that implementation of produce prescription programs increases purchasing power for fresh produce. Financial constraints have been recognized as a main barrier to access fresh produce among food insecure households, contributing to heightened exposure to poor-quality food, chronic psychological stress, and unhealthy eating behaviors (33). Our findings suggest that produce prescription programs may play a crucial role in alleviating financial stress associated with accessing healthy fresh produce. This perception is shared by other produce prescription participants across several qualitative studies reporting enhanced financial accessibility to healthy produce during the pandemic (28, 29, 34). In future studies of produce prescription programs, quantitative research may confirm the impact of these programs on both perceived financial stress, household food purchases, dietary intake, and health outcomes.

Moreover, our findings align with those of other produce prescription programs, some of which offered lower monthly incentives, yet reported a reduction in the financial barriers to meeting the recommended intake of fruits and vegetables (35, 36). Notably, all participants in our study perceived $60 per month as appropriate and helpful to obtain fresh produce for their families, although family sizes varied from 2 to 9. An effective and sufficient incentive dosage, however, may vary largely by geographic locations and socioeconomic status of participants. More research is warranted in identifying proper incentive amounts to meet the needs of families living with varying conditions and challenges. Additionally, standardizing produce prescription benefits across states through federal legislation or uniform Medicaid guidance could establish minimum standards for pediatric programs, creating consistency and predictability for patients and providers nationwide.

Importantly, participation in this produce prescription program enabled families to explore a greater variety of fruits and vegetables. Studies have shown that consuming a diverse array of fruits and vegetables is associated with better weight management, reduced inflammation, and lower risks of chronic diseases, independently from total intake (37). Both adult and pediatric programs collaborate with key stakeholders like healthcare providers, community organizations, and farmers markets/grocery stores to increase fruit and vegetable consumption and improve health outcomes. However, pediatric programs uniquely target children and families, aiming to cultivate healthy eating habits from a young age and foster family involvement. This early intervention is crucial because exposure to a diversified diet rich in fruits and vegetables fosters positive childhood food experiences, which ultimately contributes to the establishment of long-term healthy dietary behaviors (38, 39).

This is supported by existing research and our own findings. A qualitative study on a fruit and vegetable prescription program among low-income pediatric patients reported children engaging in more frequent tasting and increased acceptance of new fruits and vegetables (40). Moreover, observations by Zimmer et al. indicated that children were more likely to choose fresh fruits over processed snacks after enrolling in a Fresh Food Prescription delivery program (34). In our study, we also observed that parents and children became more adventurous in experimenting with new fresh produce. Produce prescriptions have the potential to facilitate the introduction of healthy foods and eating behaviors in early life and improve long term health outcomes. As such, they may emerge as a valuable strategy within healthcare system to address food and health disparities among children.

Beyond accessibility to fresh produce, nutritional knowledge and food preparation skills can affect the actual utilization and consumption of purchased fruits and vegetables. This becomes particularly crucial for parents with very young children and picky eaters. In both our study and the other qualitative studies of pediatric produce prescription programs, caregivers encountered challenges in preparing fruits and vegetables to get their young family members to try them (34, 40). Therefore, engaging and educating parents or caregivers is fundamental for program success. Incorporating nutrition education as a programmatic component, including food preparation and recipe ideas, may promote the usability of fruits and vegetables that families receive through produce prescriptions (41–43). In this Texas pediatric program, nutrition education was delivered through two 60-min videos due to COVID-19 restrictions, without in-person sessions. Many participants appreciated the usefulness of new perspectives and practical advice on consuming fruits and vegetables, in the convenient format of video that accommodated their busy schedule during the pandemic. However, a subset of participants indicated a desire for additional motivation and content tailored more closely to their specific needs.

A field scan released in 2021 revealed that 70% of produce prescription programs incorporated an educational component that was perceived as helpful in encouraging prescription redemption and produce consumption among participants (22). The report further acknowledged that traditional nutrition education may be insensitive to the existing situation (e.g., nutritional knowledge, culinary skill, and needs) of people whom it serves. Tailoring nutritional education, including cooking tips and recipes, to specific populations such as young children and elders while considering the feasibility and availability of their caregivers as well as effective formats of educational materials, may be needed for produce prescription programs targeting diverse populations to optimize their impact and better address the unique challenges faced by different communities.

Several features of the Texas pediatric program worked well for participants. Participants described advantages to gift cards as a mode of providing the incentive. Program cards helped streamline the check-out process by eliminating the need to separate fruits and vegetables. Participants could conveniently use the card at self-check-out, a feature that many enjoyed and preferred, whereas incentives distributed as vouchers may extend the checkout time to sort exact voucher amounts and eligible items (28, 44). A qualitative study among WIC recipients revealed that major barriers to shopping with WIC included finding eligible items, difficulty at check-out with WIC vouchers, and perceived stigma against WIC participants primarily by cashiers at checkout (45). These barriers may subsequently discourage the utilization of program incentives (44). The program cards, however, were not identified as being related to a specific program, such as SNAP or WIC, which may reduce perceived embarrassment and stigmatization for participants, therefore promoting incentive use and program satisfaction. This highlights the importance of investment in point-of-sale technology in future programming: seamless integration of produce prescription benefits into checkout systems could further streamline enrollment, potentially increase program utilization, and reduce administrative burdens as well as facilitate more robust data collection for program evaluation.

Transportation was not perceived as a consistent or major issue in this study, suggesting that partnering with grocery outlets may make using the incentive more convenient and feasible. Future programs could consider partnering with multiple grocery retailers to increase produce offerings so that participants would be able to choose where to redeem the incentive, which was important to many participants in our study and in others (35, 44, 46). Moreover, this program only covered fresh produce yet expanding eligible items to include minimally processed (e.g., no added sugar) frozen produce, that are as nutritious for meeting the needs of healthy diet, may increase the storability, use of purchase items, less frequent trips to stores (47). For program participants who face challenges in consuming fresh produce quickly enough or desire to minimize their trips to grocery stores due to personal needs or health concerns, inclusion of frozen produce is a good alternative and may enable them to benefit more from the program. These approaches may not only help with any transportation issues but also supports program participants' valued autonomy and preferences, fostering a positive program experience and potentially higher enrollment and usage.

Providing targeted funding for pilot programs to test and evaluate innovative produce prescription program models in diverse communities including rural areas is critical. These pilots can demonstrate model effectiveness and inform future expansion efforts to promote program accessibility across a wider range of locations and populations. Beyond programmatic components, clinic adoption and sustainability are pivotal factors for program success. Developing workflows for program implementation that align with existing systems, designating specific staff responsibilities related to the program, and scheduling post-enrollment follow-ups with patients can potentially improve operational efficiency and foster clinician engagement.

This study has several limitations. We sampled from one produce prescription program implemented during the COVID-19 pandemic in 2021, which restricts our findings to the unique circumstances and factors specific to this program. It is important to recognize that other programs may operate differently, at different locations and times, and insights from these programs could vary significantly. Moreover, the recruitment process relied on active responses from program participants. Those who responded may have been more actively engaged in the program or otherwise different from those who did not respond. This potential response bias may influence the perspectives captured in our study, potentially reflecting the viewpoints of a specific subgroup of participants. Nonetheless, demographic characteristics such as age, gender (all eligible program participants were female), race/ethnicity, marital status, or number of children in the household did not differ significantly between the 23 study subjects and the 33 who screened eligible for the study but did not participate. This offers some assurance that the data we have were from a group of program participants who were reasonably similar to the entire sample. Still, our findings might not fully represent the experiences and opinions of other groups who may be more marginalized or financially unstable.

5 Conclusion

Findings from this study highlight the perceived usefulness of a pediatric produce program prescription program in alleviating financial stress to access fresh produce and promoting fruits and vegetable intake among food-insecure families living in Texas during COVID-19 pandemic in 2021. Program features such as card-based incentive distribution, seamless check-out process and redemption at main grocery retailers were favored by participants. As interests in produce prescription programs continue to grow, future programs should consider partnering with diverse grocery retailers, including frozen produce, and integrating more tailored and targeted nutrition education and culinary support to better accommodate participants' needs, preferences, and circumstances, ultimately improving the program's effectiveness and impact.

Data availability statement

The datasets presented in this article are not readily available because original qualitative datasets will not be shared. Requests to access the datasets should be directed to zhongyu.li@emory.edu.

Ethics statement

The studies involving humans were approved by Tufts University Health Sciences Institutional Review Board. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their oral informed consent to participate in this study.

Author contributions

ZL: Data curation, Formal analysis, Project administration, Software, Writing – original draft, Writing – review & editing. FZ:

Conceptualization, Funding acquisition, Investigation, Writing – review & editing. SC: Conceptualization, Funding acquisition, Writing – review & editing. KH: Investigation, Writing – review & editing. LT: Conceptualization, Investigation, Methodology, Resources, Writing – review & editing. SF: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Software, Supervision, Validation, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

The reviewer MK declared a past co-authorship with the author SF to the handling editor.

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Piloting a brief assessment to capture consumption of whole plant food and water: version 1.0 of the American College of Lifestyle Medicine Diet Screener (ACLM Diet Screener)

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Background: Despite the availability of various dietary assessment tools, there is a need for a tool aligned with the needs of lifestyle medicine (LM) physicians. Such a tool would be brief, aimed at use in a clinical setting, and focused on a "food as medicine" approach consistent with recommendations for a diet based predominately on whole plant foods. The objective of this study is to describe the development and initial pilot testing of a brief, dietary screener to assess the proportion of whole, unrefined plant foods and water relative to total food and beverage intake.

Methods: A multidisciplinary study team led the screener development, providing input on the design and food/beverage items included, and existing published dietary assessment tools were reviewed for relevance. Feedback was solicited from LM practitioners in the form of a cross-sectional survey that captured information on medical practice, barriers, and needs in assessing patients' diets, in addition to an opportunity to complete the screener and provide feedback on its utility. The study team assessed feedback and revised the screener accordingly, which included seeking and incorporating feedback on additional food items to be included from subject matter experts in specific cultural and ethnic groups in the United States. The final screener was submitted for professional design, and scoring was developed.

Results: Of 539 total participants, the majority reported assessing diet either informally (62%) or formally (26%) during patient encounters, and 73% reported discussing diet with all or most of their patients. Participants also reported facing barriers (80%) to assessing diet. Eighty-eight percent believed the screener was quick enough to use in a clinical setting, and 68% reported they would use it.

Conclusion: The ACLM Diet Screener was developed through iterative review and pilot testing. The screener is a brief, 27-item diet assessment tool that can be successfully used in clinical settings to track patient dietary intakes, guide clinical conversations, and support nutrition prescriptions. Pilot testing of the screener found strong alignment with clinician needs for assessing a patient's intake of whole plant food and water relative to the overall diet. Future research will involve pilot testing the screener in clinical interventions and conducting a validation study to establish construct validity.

KEYWORDS

nutrition, diet, nutrition assessment, dietary screener, food frequency questionnaire, whole-food plant-based diet, FFQ, WFPB

Introduction

Health professionals have a need for brief dietary assessment tools that align with the recommendations they give patients. There is increased interest in implementing "food as medicine" or "food is medicine" and bridging what is known in nutrition research to clinical settings. This aligns with the approach to care practiced in the field of lifestyle medicine (LM), in which dietitians, health coaches, and other members of the interdisciplinary team work closely with physicians to support a coordinated care approach that incorporates the use of nutrition prescriptions (1).

Lifestyle medicine clinicians typically recommend a diet based predominantly on whole, plant foods and water as the beverage of choice. Increasingly, research finds that plant-based diets of all kinds are associated with lower risk for chronic disease (2), and are effective interventions for healthy weight loss (3), improvement of blood glucose control (4, 5), treatment of cardiovascular disease (6, 7), and even remission of type 2 diabetes (8, 9). In addition, plant-based diets can range in definition from vegan and vegetarian, to flexitarian, and even include other omnivorous diets such as Mediterranean and DASH that incorporate more unrefined plant foods than a typical Western diet (10). To support treatment protocols and behavior change in patients, LM clinicians need a questionnaire that has a low respondent burden, is easy and quick to implement in the context of brief patient encounters, and provides simple and straightforward feedback on the amount of whole plant food and water being consumed relative to the overall diet as captured by the screener (referred to from here on as "overall diet"). Additionally, the ideal questionnaire would provide sufficient information to thoroughly capture not only intake of whole foods, but also consumption of processed food and ultra-processed food, as nearly 60% of total energy intake in the United States comes from ultra-processed foods (11). Responses on such a questionnaire, or screener, would provide a clear path for health professionals to guide clinical conversations around dietary improvements with patients.

Dietary screeners, sometimes called scanners, are short dietary assessment tools designed to capture self-reported intake of particular aspects of an individual's diet in a quick and easy-to-use questionnaire format. Similar to a food frequency questionnaire (FFQ), screeners typically focus only on frequency of consumption (12) and ask about usual intake patterns over a period of time (e.g., the past 30 days or the past year) rather than exact quantities, portions, or brands consumed on a given day (13). Unlike FFQs, which are commonly designed to assess the whole diet by asking about multiple food groups and seasonal changes in intake, screeners often focus on a single nutrient (e.g., NutritionQuest's Fat Intake Screener) (14), food (e.g., Block Soy Foods Screener) (14, 15), or food component (e.g., Beverage Questionnaire) (16), or select food groups (e.g., NutritionQuest's Fruit, Vegetable, and Fiber Screener) (17). However, screeners have also been developed to capture several components across the diet [e.g., the Dietary Screener Questionnaire (18, 19) which captures fruit, vegetable, dairy/calcium, added sugars, whole/grains/fiber, red meat, and processed meat; or the Nova Ultra-processed Food Screener (20)]. There are a multitude of dietary assessment tools available, ranging from food records, 24 h recalls and FFQs to brief screeners of fewer questions, such as those from the Register of Validated Short Dietary Assessment Instruments (RSVSDAI) at the National Cancer Institute (NCI) (21). Each tool focuses on capturing a different aspect of the diet, therefore enabling different specific comparisons or analyses. Brief screener tools are often most appropriate for clinical settings in which diet is discussed, where there is limited time available to conduct assessments (22).

Due to their focus, simplicity, and shorter length, screeners capture less detailed information than dietary assessment tools such as 24-h recalls and food records. Despite this, their simplicity means they can be used to capture a general sense of an individual's or population's intake of dietary components of specific interest both quickly (in under 15 min) (23) and inexpensively when a great level of detail is neither necessary nor feasible. Screeners can be used to track changes in usual intake over time and to compare high and low levels of intake within a population (24). Where more detail or additional information is needed, screeners can be combined with other tools.

Each tool focuses on capturing a different aspect of the diet, therefore enabling different specific comparisons or analyses (21). Within the RSVSDAI at NCI (21), a validated brief dietary assessment that is a low-tech, simple questionnaire measuring whole plant food and water consumption does not exist. To fill this gap, this study team undertook the development of a new dietary assessment tool, the ACLM Diet Screener. The objective of this study is to describe the development and initial pilot testing of the screener, in preparation for future validation of this tool.

Methods

The screener development followed an iterative process beginning in September of 2021. A study team was assembled that included lifestyle medicine physicians, nutrition researchers, and staff from the sponsoring organization. The study team met weekly through August 2023, initially with the goal of developing a longer dietary intake questionnaire for use in research settings. However, discussion emerged about the need for a brief dietary assessment tool that could be used during patient encounters in clinical settings. Subsequently, the study team decided to create two tools: a longer dietary intake questionnaire for research use and a brief diet screener suitable for clinical encounters of limited duration. Initial development and pilot testing of the brief diet screener is presented here.

The following resources relevant to plant-based dietary patterns were reviewed to identify gaps in food items recorded or analyzed by existing assessments or scores, as well as to identify potential foods and beverages for inclusion on the screener: (1) a theoretical analysis of a whole food, plant-based dietary pattern (25), (2) United States Dietary Guidelines and MyPlate (26), (3) the Vegetarian Food Guide Pyramid (27), (4) the Healthy Eating Index (28), (5) the Alternative Healthy Eating Index (29, 30), (6) the DASH diet (31, 32), and (7) the Mediterranean Diet Score (33). Informed by these existing scores and resources, as well as food categories consistent with the ACLM dietary position statement recommending an eating plan based predominantly on a variety of minimally processed vegetables, fruits, whole grains, legumes, nuts, and seeds (34), the study team discussed food items to include and how to group them into categories most useful for LM clinicians, as well as possible categories representing frequency of consumption. A goal was set to differentiate between infrequent consumption and zero consumption of a food, to enable LM clinicians to continue more nuanced conversations with patients about dietary improvements.

An initial draft of the screener was created and informally shared with $N=81$ individuals (friends, family, and colleagues of the study team). Based on feedback that emerged, it was determined that food examples would be useful in understanding how to answer the screener. The team continued weekly meetings and developed food examples to provide context for how participants should interpret each food category when responding.

Finally, sets of additional questions on the following factors and dietary behaviors were included, based on relevance to long-term behavior change interventions: food security, supplement intake, food preferences, eating style, food preparation behaviors, and self-efficacy around healthy food intake. These questions are intended to be used as optional modules in situations where the healthcare practitioner would find the information useful for discussion during a clinical visit. The two-question food security screener was also included (35).

Two academic, senior scientists with expertise in nutritional epidemiology and dietary assessment methods, as well as a senior statistician with experience in dietary assessment were engaged as consultants to provide feedback on the structure of the screener questions and answer choices, taking into consideration the long-term goal of validation.

The screener, originally containing 25 items and asking about intake over the previous 4 weeks, was pilot-tested with an online survey administered to lifestyle medicine clinicians, with data collection from February 20, 2023 to April 18, 2023. This study was reviewed by the University of New England IRB.

Participants were recruited by the sponsoring organization through email, social media posts, and resharing online by individuals. Recruitment targeted healthcare practitioners, but non-practitioners were not specifically excluded and also participated. Individuals reviewed a participant information sheet and indicated that they were 18 years of age or older and consented to participate by beginning the survey. The survey captured demographics and medical practice status, degree and specialty, barriers and needs in assessing patients' diets, and characteristics of the practitioner's patient population. Participants then completed the screener itself and answered both multiple choice (Likert scales) and free text questions on the utility of the screener, their likelihood of using it, overall feedback on the screener, and possible formats summarizing intake reported on the screener. Time required to take the screener was assessed with start time and end time questions immediately before and after the dietary screener, as it was embedded in the larger survey. Finally, participants answered sets of optional questions on dietary behaviors and provided feedback about these questions using a Likert scale of how likely they were to use these optional questions. Participants were provided the opportunity to give unstructured, free-text feedback on any aspect of the screener or other questions.

Quantitative data were descriptively analyzed using SAS software 9.4 (Cary, NC, United States). Survey responses were included in this analysis if respondents answered questions on start time, end time, and the last multiple-choice question asking for screener feedback on whether they preferred a pie chart or bar chart for presenting the results. Time required to take the screener was calculated after dropping $n=21$ outlier observations that appeared to be due to leaving the browser open for extended periods of time (>20 min). Screener feedback in the form of free-text data was coded into categories of responses by at least two members of the research team, with a third team member participating in discussions to resolve conflicts. Initially, the free-text data were evaluated by the entire research team in several of the weekly meetings to calibrate the coding. Responses that were difficult to code were brought to the team for evaluation throughout the coding process.

Once all the feedback about the screener was coded, the PI (MK) summarized the findings and first presented the research team with themes of feedback that were straightforward and easy to address (e.g., change wording in the screener, add examples of food items). Second, the PI highlighted themes of feedback that were less straightforward and merited group discussion, and these themes were discussed until consensus was reached around whether and how to revise the screener accordingly (i.e., adding new food categories or changing what was included in them). Finally, the group reviewed feedback that was deemed out of the scope of the project to verify consensus.

Once this initial phase of testing and review was completed, a second phase was initiated to expand and deepen the relevance for the following specific ethnic or cultural groups: African American, Hispanic/Latino, Asian American, Native American, and Indian American. This second phase was designed to maximize alignment with ACLM's values of diversity and inclusion, to make the screener relevant for as broad an audience as possible, and to respond to the feedback given by pilot testers asking for more culturally relevant and diverse food examples in the screener.

A three-step process was used to adapt the list of food examples. First, ChatGPT (December, 2023) was used for brainstorming to generate food examples for each of the categories with the following query:

> *Help me design a dietary screener. Create a list of commonly eaten foods from [XXX] culture that can be used in a nutrition screening questionnaire. Include 5–10 commonly eaten foods in each of the following categories: [insert food categories from screener].*

The query was run six times, replacing "XXX" above with "multiple ethnicities and cultures," "African American," "Hispanic Latino," "Asian American," "Native American," and "Indian American."

Second, between 2 and 5 subject matter experts (SMEs) were recruited for each of the specific groups and asked to review the list of food examples in the diet screener and propose additions or deletions based on their perspective and experience of that culture, with the ChatGPT suggestions provided as a brainstorming aid. Most SMEs were physicians or public health professionals, and all SMEs were members of their relevant demographic group, with the exception of one of the two SMEs reviewing the list of Native American foods, who self-describes as a non-Native public health nutrition researcher who has worked extensively with indigenous communities for over 30 years. Suggestions from SMEs for specific foods were incorporated into the list of example foods, but with a goal of only naming foods or ingredients; specific names of dishes were generally avoided for length reasons.

Third, previously published work on validated dietary screeners or FFQs developed for these specific populations were reviewed. When available, the actual questionnaire or food items were compared to the food examples list in the drafted ACLM Diet Screener. The following list of methods papers and questionnaires were consulted: the Block FFQ adapted for a Hispanic audience (36), a regional FFQ adapted for use among white and African-American adults in the southern United States based on the National Cancer Institute's Health Habits and History Questionnaire (37), an FFQ developed for African-American women in the midwestern United States (38), the Dietary Screener Questionnaire adapted for an Asian American audience (39), a dietary screener adapted for a Chinese American audience (39), a dietary questionnaire adapted for use in the India Health Study (40), a food frequency questionnaire developed among Canadian First Nations in north-western Ontario (41), an FFQ developed for the Navajo Nation (42), an FFQ developed to evaluate a nutrition intervention for the Apache in Arizona (43), and the OPREVENT2 FFQ that was an expansion of the Block FFQ (44), developed to be used for southwestern and midwestern Native American peoples. In addition, the Block 2014 FFQ (45, 46) and the Harvard semiquantitative FFQ Grid 2007 were reviewed (47, 48).

Food examples from the existing tools that fit into the ACLM Diet Screener categories and were not already included were added.

A scoring procedure was developed through discussion by the PI and several members of the research team. The scoring (Figure 1) was based on summary scores for frequency of whole plant foods consumed out of total foods reported, and water consumed out of total beverages reported. The final version of the screener including example food lists and the scoring procedure were approved by the study team. Following approval by the team, the screener was then submitted to a professional designer to create a colorized PDF version with photos depicting the food examples as well as a simpler, printer-friendly, black and white PDF version. For ease of use in online settings, images of the food examples were made available.

Results

The pilot test survey was viewed 4,651 times with $n = 1{,}330$ total responses (both complete and incomplete). A total of $n = 505$ completed the entire survey, with $n = 539$ answering the critical feedback question and being included in the main analysis, and $n = 518$ being included in the analysis to calculate mean time required to take the screener.

Mean age of participants was 49 years (SD = 12, range 19–80). Reported working status was as follows: 86% answered yes to being in active practice, 6% answered no, 4% reported being in training, and 1% reported being retired/not working, and 2% preferred not to answer. Participants reported practicing in all 50 states, with the most frequently reported states being California (8.0%), New York (5.9%), and Florida (5.2%). Twenty-one percent of the sample reported practicing outside of the United States. Fifty-one percent of respondents were physicians (MD/DO), 15% advance practice providers (NP, PA, APN, and DNP), 15% other clinical/patient care

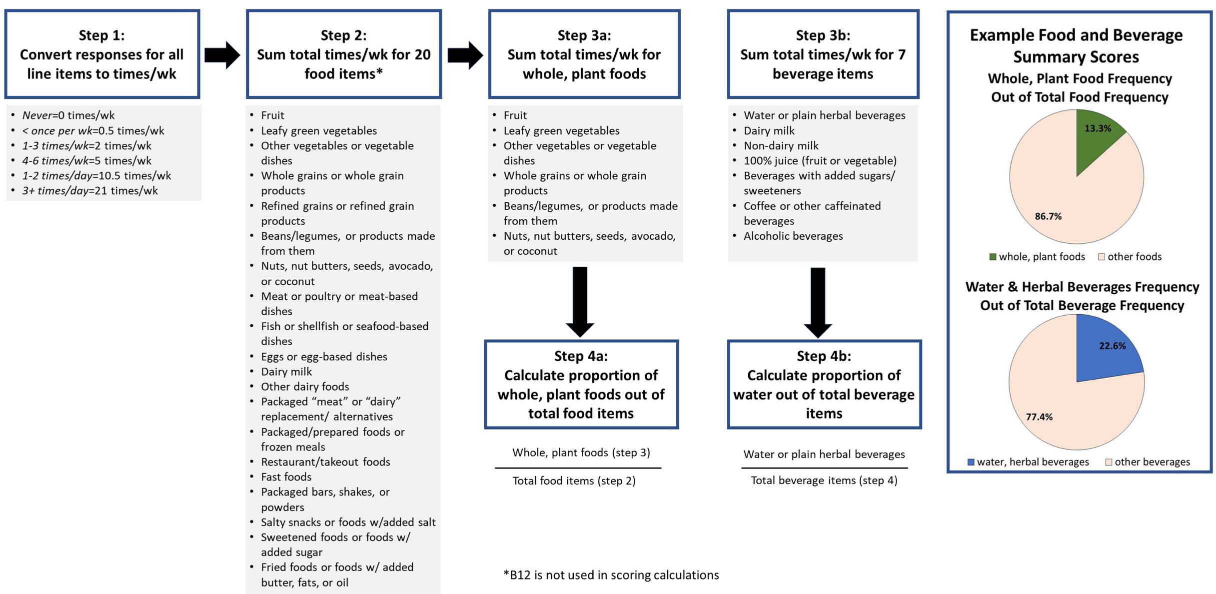

FIGURE 1
Scoring the ACLM Diet Screener.

fields (chiropractic, physical therapy, dietitian/nutritionist, and occupational therapy), and 7% nursing (RN, LPN). Physicians reported being boarded in over 20 different medical specialties (American Board of Medical Specialties), with family medicine (31.9%), internal medicine (13.5%), and preventive medicine (7.8%) being the top reported.

Table 1 presents characteristics of practitioners, patients, and the practice. A total of 77% of participants identified as female and 74% as white. A total of 81, 41, and 26% of participants reported serving patient populations with substantial numbers (at least 20%) of white, Black or African-American, and Asian patients, respectively. Participants also reported substantial numbers of patients facing a variety of risk factors for health disparities, with the top three being low-income (56%), food insecure (45%), and racial, cultural, or ethnic diversity (44%). Thirty-six percent of participants reported serving patient populations with substantial (≥20%) numbers of Hispanic patients. Fifty-eight percent of participants reported they promote or prescribe a specific diet to their patients and were asked to specify which diet or diets they prescribe. Of those, 48% prescribed a whole-food, plant-based diet, 39% prescribed a plant-predominant diet, 20% prescribed a Mediterranean diet, 16% prescribed a diet personalized to a specific patient/health condition, and 15% prescribed a whole food (minimally processed) diet.

The majority of participants reported assessing diet either informally (62%) or formally (26%) during patient encounters, and 73% reported discussing diet with their patients all or most of the time. Participants also reported facing some barriers (60%) or significant barriers (21%) to assessing diet. The top reported barrier was limited appointment time (45%).

Table 2 presents participant feedback on the screener. A majority of participants indicated they thought the screener captured the information they would want to know about patients' diet very well (51%), somewhat well (30%), or extremely well (14%). Eighty-eight percent believed the screener was quick enough to use in a clinical setting, and 68% reported they would use it. Of these, participants reported they would use it most (46%), some (21%), or all (26%) of the time. Participants responded to the question asking if frequency without serving size was enough information with a "yes, frequency is enough information" (36%), "no, I would want to know about serving sizes" (31%), and "probably frequency alone is enough, but I'm not sure" (25%). After being presented with two examples, a bar chart and pie chart (Figure 1), of how to graphically present the summary scores, the majority of participants preferred the pie chart to the bar chart (70 vs. 12%). As far as potential missing items, 52% reported nothing they themselves ate was missing from the screener, 24% suggested additional foods should be added, and 8% suggested additional beverages should be added. When asked if there was anything else that would be important for them to know, a variety of topics were suggested, including other foods (15%), portion sizes (13%) eating behavior/preferences/allergies (12%), timing and/or frequency of eating (11%), and more detail about the food/diet (10%).

The following key themes emerged from analysis of the final, free-text feedback question asking for any additional suggestions, which the team discussed and determined how to proceed: (1) feedback was positive, and participants seemed satisfied (no action); (2) some participants wanted more detail, portion sizes, or more questions were desired (study team felt these can be addressed in the planned long screener); (3) participants desired support in their practice that the

TABLE 1 Respondent characteristics, practice, and patient population ($n = 539$).

	Mean (SD)
Age	49 (12)
	N (%)
Gender	
Female	415 (77.0)
Male	118 (21.9)
Non-binary/non-conforming	1 (0.2)
Prefer not to answer	5 (0.9)
Race	
White	397 (73.7)
Asian	69 (12.8)
Other	28 (5.2)
African American	25 (4.6)
American Indian or Alaska Native	5 (0.9)
Native Hawaiian or Other Pacific Islander	2 (0.4)
Prefer not to answer	20 (3.7)
Racial demographics within patient population (respondent estimated 20% or more of patients)	
White	435 (80.7)
Black or African-American	223 (41.4)
Asian	139 (25.8)
Prefer not to answer	50 (9.3)
American Indian or Alaska Native	24 (4.5)
Native Hawaiian or Other Pacific Islander	17 (3.2)
Ethnicity within patient population (respondent estimated 20% or more of patients Hispanic)	195 (36.2)
I prescribe or promote a specific diet to patients	314 (58.3)
(If yes) Diet prescribed/promoted	
Whole-food, plant-based	150 (47.8)
Plant-predominant	122 (38.9)
Mediterranean	62 (19.7)
Personalized to patient/health condition	51 (16.2)
Whole food/no or low processed food	46 (14.6)
Low carb/Keto	20 (6.4)
DASH Diet	18 (5.7)
Low fat	18 (5.7)
Self-described healthy diet/MyPlate	17 (5.4)
High/adequate protein	6 (1.9)
Other/not codable	10 (3.2)
Risk factors for health disparities faced by substantial numbers of patients (respondents estimated at least 20%)	
Low-income/underserved	302 (56.0)
Food insecurity/low access to healthy options	240 (44.5)
Racially, ethnically, and/or culturally diverse	237 (44.0)
Uninsured/underinsured	156 (28.9)

(Continued)

TABLE 1 (Continued)

	Mean (SD)
Low literacy	149 (27.6)
None of the above	123 (22.8)
Housing insecurity	119 (22.1)
Exposure to violence/trauma	116 (21.5)
Low English proficiency	115 (21.3)
Prefer not to answer	21 (3.9)
Do you assess diet with your patients?	
Yes, I discuss it during the visit informally	333 (61.8)
Yes, I do a formal assessment with a questionnaire or other tool	142 (26.4)
No, I would like to, but I face barriers	31 (5.8)
I am not a practitioner or am not practicing	24 (4.5)
No, it is not relevant in my practice	5 (0.9)
Prefer not to answer	4 (0.7)
With approximately what proportion of your patients do you discuss diet?	
All/most	393 (72.9)
Some	94 (17.4)
A few	25 (4.6)
None	15 (2.8)
Prefer not to answer	12 (2.2)
Do you face barriers when assessing patient's diets?	
Yes, significant barriers	112 (20.8)
Yes, some barriers	320 (59.4)
No	80 (14.8)
Not applicable/prefer not to answer	27 (5.0)
What are the major barriers you face when assessing patients' diets? ($n = 528$)	
Limited appointment time	239 (45.3)
Patient's nutrition knowledge/understanding dietary habits	115 (21.8)
Patient's ability/willingness to make changes	104 (19.7)
Recall/reporting bias	85 (16.1)
Lack of practitioner tools	65 (12.4)
Accuracy of assessment tools	57 (10.8)
Patient honesty about diet	55 (10.4)
Patient's financial instability/cost of healthy food	34 (6.4)
Patient's culture-familiarity w food-alignment of tool cuisine	30 (5.7)
Other[a]	144 (27.3)

[a]Includes wants more detail/more complete info/portion size/nutrients; unclear about portion size; compliance; relationship with patient; poor habits/lifestyle; response was not codable (did not answer question); lack of pay for assessment; not relevant to current practice; access to healthy foods; family/friends/social pressure; and patient lack of time.

screener cannot address, such as improving the doctor-patient relationship, patient honesty/recall bias, or patient economic circumstances (no action); (4) needs were identified that the screener already aims to address, such as brevity or the desire for a validated tool, or for questions that existed in the optional question list (continue as planned toward eventual validation); and (5) participants desired components that were already planned, such as translation (continue as planned toward translation, starting with Spanish). Overall, positive feedback was provided in regard to the value of the optional questions on food preferences, behaviors, self-efficacy and knowledge, and food insecurity (data not shown) (Table 3).

The mean time to complete the screener was 3.4 min (SD = 2.4, range 1–20), using $n = 518$ responses with plausible values.

Following discussion, revision, and generation of multiple iterations of the screener, the final review of other diet assessment tools did result in the addition of a few items, not previously included. These were lard from the OPrevent FFQ (44), grits from the Block 2014 FFQ (45, 46), honey and molasses from the DSQ modified for use in the India Health Study (40), tamales and organ meat from the FFQ for the nutrition intervention for the Apache (43), mayonnaise from the FFQ developed for use in the southern United States (37), moose from the FFQ developed for Canadian First Nations (41), and chokeberries from the FFQ developed for the Navajo Nation (42).

The final version of the screener included 27 items, of which 19 were food categories, seven were beverage categories, and one was a nutrient or supplement (B12). Food categories included Fruit; Leafy green vegetables; Other vegetables, or vegetable dishes; Whole grains or whole grain products; Refined grains or refined grain products; Beans/legumes, or products made from them; Nuts, nut butters, seeds, avocado, or coconut; Meat or poultry or meat-based dishes; Fish or shellfish or seafood-based dishes; Eggs or egg-based dishes; Other dairy foods; Plant-based meat alternatives/mock meats; Dairy alternatives; Packaged/prepared foods or frozen meals; Restaurant/takeout foods; Fast foods; Packaged bars, shakes, or powders; Salty snacks or foods with added salt; Sweetened foods or foods w/added sugar; Fried foods or foods w/ added butter, fats, or oil. Beverage categories included Dairy milk; Non-dairy milk; Water or plain herbal beverages; 100% juice (fruit or vegetable); Beverages with added sugars/sweeteners; Coffee or other caffeinated beverages; and Alcoholic beverages. The final item was B12 supplement or B12-fortified foods. B12 was not included in the scoring.

The frequencies offered as answer choices were never, less than 1x/week, 1–3x/week, 4–6x/week, 1–2x/day, and more than 3x/day. Portion sizes were not assessed.

Summary scores for total whole plant food frequencies as a proportion of total food frequencies and total water frequency as a proportion of total beverage frequencies are quantitatively calculated as per the instructions displayed in Figure 1. For the purpose of clinical conversations with patients, and based on pilot testers' preferences, we suggest displaying individual summary scores in a pie chart format and describing the scores as the proportion of whole plant foods out of total foods and proportion of water out of total beverages.

The ACLM Diet Screener Version 1, scoring instructions, and related materials can be accessed at https://lifestylemedicine.org/dietscreener.

Discussion

This study details the iterative development of a brief diet screener that assesses intake of whole, plant foods in comparison to overall intake, provides summary scores to highlight the proportion of total plant food and total water consumption, and is appropriate for use by clinicians in brief patient encounters. The screener can be quickly reviewed by a physician, dietitian, or other member of a patient care team without quantitative analysis, simply by viewing the answers. Alternatively, if time and/or resources allow, a graphical summary of the output could be generated, as shown in Figure 1. A patient's answers can be used to guide conversations around current diet, possible goals for behavior change, and to support tracking changes over time and use of nutrition prescriptions. This study followed a richly iterative process with robust pilot testing to gather feedback on the utility of the screener and possible improvements, laying a strong foundation for eventual validation.

To the authors' knowledge, there are no existing dietary assessments that include all the characteristics of the screener developed here, specifically (1) capturing consumption of whole plant foods separately from other foods, (2) capturing the consumption of refined foods, foods with added sugar/salt/fats, or other unhealthy prepared/packaged foods, (3) capturing juice separately from fruit, (4) providing an answer to record zero consumption of a food item separately from infrequent or minimal, (5) made available freely to the public, and (6) generating summary scores capturing a dietary pattern of whole, plant foods in comparison to the overall diet. For these reasons, the ACLM Diet Screener is useful for clinicians writing nutrition prescriptions.

A number of tools exist for assessing diet, varying in length from single-question fruit and vegetable screeners to more comprehensive fruit and/or vegetable screeners (49) as well as questionnaires aimed at assessing fruit and vegetable intake along with overall diet (Block, Harvard semiquantitative FFQ) (36, 50). Of the 61 brief tools categorized as addressing fruit and vegetable intake on the RVSDAI at NCI (21), none adequately capture a picture of the overall diet, while simultaneously capturing total whole plant food intake and distinguishing between refined and unrefined foods. Additionally, none provide a simple summary measure that is clinically relevant by being both understandable and actionable for a patient. Supplementary Table 1 presents key characteristics of these tools. Among the RVSDAI tools, the number of question items ranged from 1 to 74, with the majority questionnaires having between 20 and 40 items.

In addition to assessment tools, there are also various scores and indices that can be applied to evaluate an individual's diet, assuming the correct assessment was used to gather the data and provide the information needed for that evaluation. Some of these include the Healthy Eating Index (HEI) (51), Alternative Healthy Eating Index (AHEI) (29, 30), Mediterranean Diet Score (33), and the DASH Online Questionnaire (31, 32). The summary scores produced are often useful in research, and might be useful in clinical settings if data collection were possible. Each score focuses on different aspects of the diet, usually including both food and nutrient components. Our screener scoring is a simple calculation, enabling rapid feedback and straightforward interpretation by patients, without requiring nutrient calculations or complex statistical analysis. This is a strength of the screener, which makes it more accessible to users.

The ACLM Diet Screener fills the need for a clinical tool that LM practitioners can use to efficiently review dietary intake and, thus, begin a conversation around nutrition. Despite the knowledge that dietary intake significantly affects health, it is documented that practitioners have limited time to engage in a discussion of diet and lifestyle with their patients. For example, one recent study suggested that during a typical office day, physicians are only able to spend 27% of their time with patients directly, while nearly 50% of their time is allocated to administrative work including electronic health records (52). In the current study, 21% of respondents indicated significant barriers when it comes to assessing patient's diets, and an additional 60% of respondents indicated some barriers. Nearly 50% of participants reported limited appointment time as a barrier to assessing patients' diets. The ACLM Diet Screener is intended to be completed in less than 5 min and may be offered to patients to complete in the waiting room or before arriving at their visit. If scoring is applied, it may also serve as a tool to allow practitioners to review, within a matter of minutes, a snapshot of a patient's dietary intake by viewing two summary scores representing consumption of (1) whole, plant foods and (2) water/plain herbal beverages. Importantly, 88% of respondents indicated that the screener was quick enough to use in a clinical setting.

While administering the screener electronically may be convenient for many patients and practitioners, a paper version is also available to be used in settings where resources do not allow for electronic data capture. In the long-term, we aim for the creation of a digital resource, such as an app, that would not only allow for electronic data capture via a smartphone but also produce a graphical summary of the data, such as presented in Figure 1, to further guide the practitioner in their conversation with a patient.

Sixty-eight percent of respondents indicated that they would use the screener, which highlights the utility of this tool. Furthermore, 95% reported that if they were to use the tool in clinical practice, it would capture the information that they would want to know (64% extremely or very well). With respect to the screener, over half of the participants reported that no items they ate were missed by the screener, and 22% reported that there was no other important information not captured by the screener.

The inclusion of food examples specific to African American, Hispanic/Latino, Asian American, Native American, and Indian American populations in the United States makes this screener unique. Currently, tools do exist for African-American, Hispanic/Latino, Asian-American, Native-American, and Indian-American populations; however, to the authors' knowledge there is no single tool that attempts to generalize to all these populations, making our screener more flexible for a wider variety of patient populations.

While the screener is not intended to provide a comprehensive assessment of overall dietary intake, it focuses on whole, plant foods and water as these are two dietary components that are known to be lacking among individuals eating a standard American diet. In addition, it is well-established that plant-predominant diets, as well as diets low in processed foods, are effective for not only disease prevention, but also play a role in treatment of many chronic diseases, particularly cardiometabolic conditions (53). Adequate water intake is essential to health and noncommunicable disease prevention (54, 55). Clinical studies have clarified the benefits of water hydration and the avoidance of damage caused by fluid imbalance in both extracellular and intracellular water levels, particularly kidney dysfunction, kidney stones, poorer cognitive performance and brain function, and increased heart rate (56). Water's importance for the prevention of nutrition-related noncommunicable diseases has emerged more recently because of

TABLE 2 Respondent feedback on ACLM Diet Screener (n = 539).

	n (%)
If you were to use this tool in clinical practice how well does it capture the information you would want to know about patients?	
Extremely well	77 (14.3)
Very well	272 (50.5)
Somewhat well	163 (30.2)
Not very well	17 (3.2)
Not well at all	6 (1.1)
Prefer not to answer	4 (0.7)
Respondents reporting that screener was quick enough to use in a clinical setting	473 (87.8)
Is frequency without serving size enough information?	
Yes, frequency is enough information	192 (35.6)
Probably frequency is enough, but I'm not sure	135 (25.1)
Probably frequency alone is NOT enough, but I'm not sure	44 (8.2)
No, I would want to know about serving sizes	166 (30.8)
Prefer not to answer	2 (0.4)
Would use the screener	368 (68.3)
(if yes) Approximately how often do you anticipate that you would use this screener in clinical practice? (n = 368)	
All of the time/with all my patients	97 (26.3)
Most of the time/with most of my patients	170 (46.2)
Some of the time/with some of my patients	77 (20.9)
Occasionally/with a few of my patients	14 (3.8)
Not applicable	7 (1.9)
Prefer not to answer	3 (1.0)
Do you prefer a bar chart or pie chart format for visualizing scoring and starting the conversation and/or educating patients?	
Pie chart	377 (69.9)
Bar chart	62 (11.5)
Both	68 (12.6)
Neither	23 (4.3)
Prefer not to answer	9 (1.7)
Is anything missing that you ate but that was not captured by the screener? (n = 402)[a]	
Nothing missing; satisfied with screener	210 (52.2)
Foods	98 (24.4)
Beverages	31 (7.7)
More detail about food and beverages	30 (7.5)
Supplements	28 (7.0)
Eating/cooking behavior/food prep	28 (7.0)
Food or beverage reported but already captured by screener	25 (6.2)
Not codable/did not answer question	14 (3.5)
Portion size	11 (2.7)
Is anything else missing that would be important for you to know as a practitioner but that was not captured by the screener? (n = 422)[a]	
Nothing missing; satisfied with screener	92 (21.8)
Food	62 (14.7)
Portion sizes	53 (12.6)
Eating behavior/preferences/allergies/	51 (12.1)
Timing and/or frequency of eating, including fasting	47 (11.1)
More detail about food/diet/energy intake/calories	42 (10.0)
Supplements	38 (9.0)
Food preparation	31 (7.3)
Non-codable/not answering question	22 (5.2)
Other[b]	115 (27.3)

[a]Free-text coded responses.
[b]Includes other health behaviors/risk factors; health literacy/nutrition knowledge; barriers/social determinants of health; beverages; scoring, interpreting, presenting data; water intake (amount/timing); tobacco/alcohol/drug consumption; different data collection method; patient goals/commitment/patient perception of health and eating.

the shift toward large proportions of fluids coming from caloric beverages (55). Calories taken in from beverages promotes central adiposity and increase risk for all cardiometabolic conditions, i.e., diabetes and heart disease (57–60). Average water intake in the United States is lower than recommended and is of particular concern in higher-risk groups such as Hispanic populations and older adults.[60] Further, an estimated 20–22% of water intake comes from food, which is of particular concern in the United States where fruit and vegetable intake is known to be lower than recommended (55). The ACLM Diet Screener, uniquely aims to differentiate between not only whole plant-based foods vs. refined and non-plant-based foods, but also water vs. other beverages, which can help clinicians address the displacement of water with caloric drinks.

Strengths of this study included the richly iterative process used to develop the screener, the thorough review of SMEs with expertise in different cuisines, and the review of other previously validated tools. One limitation of this study is that the sample providing feedback were members of a professional organization for lifestyle medicine practitioners. While their feedback may not represent the general population of practitioners in theb United States, it does represent the sample of practitioners who have a high interest in food as medicine and a need for a screener assessing intake of unprocessed plant foods. It is also important to note that a relatively small proportion of invited participants completed the survey, yet this low response rate is not surprising for a research study in a population of busy healthcare professionals.

Another limitation of the screener itself is that foods are counted, when appropriate, in more than one category, such as foods that are refined and contain added sweeteners and fats. Thus, while the screener may be useful for initiating discussions around diet in a clinical setting, it may not accurately measure actual dietary intake. Similarly, while the line item for "water or plain herbal beverages" was created intentionally, with the goal of assessing unsweetened and non-caffeinated water intake, it may not accurately reflect total water intake or hydration status. Water, in particular, may be difficult for some people to quantify in terms of frequency if sipping continuously from a water bottle. The ability of the screener to quantify both food and beverage intake will be further assessed in a future validation study. In addition, the

TABLE 3 Top[a] feedback for changes to language, accuracy, efficacy, or clarity and action/planned action ($n = 252$).

Feedback	n (%)	Action/Planned action
No suggestions	128 (50.8)	N/A
More detail: define food categories, more examples	31 (12.3)	Added many more food examples; added images for clarity.
Translate to other languages	23 (9.1)	Plan to translate to Spanish first, then other languages if/when resources allow.
Add images of foods	16 (6.3)	Added images.
Revisit format of screener	13 (5.2)	Plan to offer paper version and eventually an electronic version; plan to translate to Spanish and eventually other languages; and added images and food examples.
Add food examples from more specific cultures/ cuisines	10 (4.0)	Sought input from subject matter experts as well as reviewed other tools to incorporate a broader variety of foods in food examples.
Issues with health literacy/ assess patient comprehension	8 (3.2)	Added additional food example details, as well as images.
Include portion sizes	8 (3.2)	Plan for long format questionnaire.

[a]Feedback reported by at least 3% of the sample.

calculation of the summary score for beverages, which does group beverages contributing toward nutrient requirements (dairy milk, plant-based milk, and juice) with beverages that provide empty calories (sugar-sweetened beverages and alcohol). However, as discussed, water consumption is frequently inadequate in the United States, and increasing water consumption is often a goal in lifestyle medicine practice. While some consumption of energy-containing fluid may positively contribute toward nutrient requirements, water should be the beverage of choice, as noted in the Dietary Guidelines for Americans (61) and Canadian Dietary Guidelines (62). The summary score can be used to draw attention to overall fluid consumption for goal setting.

Future research will first involve conducting a pilot study to utilize the screener in a small number of clinical practices. Such a study will assess use of the screener in a real-life, clinical setting, as well as including usefulness of the scoring. A formal validation study will be conducted to validate the screener against multi-day food records, first in the general United States population and later in specific ethnic and cultural groups to ensure relevance.

Conclusion

The ACLM Diet Screener was developed through iterative review and pilot testing. The screener is a brief, 27-item diet assessment tool that can be successfully used in clinical settings to track patient dietary intakes, guide clinical conversations, and support nutrition prescriptions. Pilot testing of the screener found strong alignment with clinician needs for assessing overall dietary patterns of patients. Future research will involve pilot testing the screener in clinical interventions and conducting a validation study to establish construct validity.

Data availability statement

The datasets presented in this article are not readily available because individuals may request access to the data by contacting the corresponding author. Requests to access the datasets should be directed to mkarlsen@lifestylemedicine.org.

Ethics statement

This study involving humans was approved by University of New England Institutional Review Board. The study was conducted in accordance with the local legislation and institutional requirements. The ethics committee/institutional review board waived the requirement of written informed consent for participation from the participants or the participants' legal guardians/next of kin because this was deemed a low-risk study. Participants were asked to review a participant information sheet with details of the study, and consent was implied by starting the survey. Written informed consent was not required by the IRB.

Author contributions

MK: Project administration, Writing – original draft, Writing – review & editing, Conceptualization, Formal analysis, Investigation, Methodology, Supervision. KS: Project administration, Writing – original draft, Writing – review & editing, Data curation. KP: Data curation, Writing – review & editing. KC: Writing – review & editing. SH: Data curation, Writing – review & editing. EC: Writing – review & editing. SF: Writing – review & editing.

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Conflict of interest

Three co-authors were staff employed by the American College of Lifestyle Medicine (MK, KS, and KP), and two co-authors received consulting payments from the American College of Lifestyle Medicine (KC and SH).

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fnut.2024.1356676/full#supplementary-material

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Implementation of a virtual, shared medical appointment program that focuses on food as medicine principles in a population with obesity: the SLIM program

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Background: Multimodal lifestyle interventions, employing food as medicine, stand as the recommended first-line treatment for obesity. The Shared Medical Appointment (SMA) model, where a physician conducts educational sessions with a group of patients sharing a common diagnosis, offers an avenue for delivery of comprehensive obesity care within clinical settings. SMAs, however, are not without implementation challenges. We aim to detail our experience with three implementation models in launching a virtual integrative health SMA for weight management.

Methods: Eligible patients included individuals 18years of age or older, having a body mass index (BMI) of 30kg/m^2 or 27kg/m^2 or greater with at least one weight related comorbidity. The Practical, Robust Implementation and Sustainability Model (PRISM), Plan, Do, Study, Act (PDSA), and the Framework for Reporting Adaptations and Modifications-Enhanced (FRAME) models were applied to guide the implementation of the Supervised Lifestyle Integrative Medicine (SLIM) program, a virtually delivered, lifestyle medicine focused SMA program, in a weight management clinic within a major health system. We describe how these models, along with attendance for the initial cohorts, were used for decision-making in the process of optimizing the program.

Results: 172 patients completed the SLIM program over two years. Attendance was lowest for sessions held at 8:00 AM and 4:00 PM compared to sessions at 10:00 AM, 1:00 PM, and 3:00 PM, leading to only offering midday sessions (p = 0.032). Attendance data along with feedback from patients, facilitators, and administrative partners led to changes in the curriculum, session number and frequency, session reminder format, and intake visit number.

Conclusion: The use of implementation and quality improvement models provided crucial insight for deployment and optimization of a virtual, lifestyle medicine focused SMA program for weight management within a large healthcare system.

KEYWORDS
shared medical appointment, lifestyle medicine, food as medicine, implementation science, obesity

Introduction

Obesity has become a global epidemic, with two billion people currently living with excess weight and projected estimates that more than half of the world's population having overweight or obesity by 2035, according to the World Obesity Atlas (1). In response to increasing evidence suggesting that lifestyle modifications are effective in treating obesity, the U.S. Preventive Services Task Force is currently recommending intensive, multimodal lifestyle programs that focus on effective dietary strategies, physical activity, and behavior change as the first-line treatment of obesity (2).

The Diabetes Prevention Program (DPP) demonstrated that intensive lifestyle intervention (ILI) was effective for weight loss and preventing or delaying the onset of type 2 diabetes. In its randomized design, participants in the ILI treatment group lost significantly more weight than those in the metformin only and placebo groups (3). Notably, the ILI featured in the DPP utilized the "Food as Medicine" paradigm to treat and reverse disease, establishing a healthy dietary pattern as a foundation for treatment. By strategically using food as a therapeutic tool and making deliberate choices about the types and quantities of foods consumed, individuals with obesity can achieve sustainable weight loss (4–6), reduce the risk of obesity-related comorbidities (7, 8), and improve their overall quality of life (9).

While these results are promising, using the Food as Medicine paradigm in primary care or clinical settings is challenging due to the limited time during usual appointments dedicated that is inadequate for intensive lifestyle counseling. The most common format of healthcare delivery involves a brief 15-to-20-min visit for an acute complaint, management of chronic disease or wellness checkup, which may include basic lifestyle counseling but is typically not enough time to develop a cohesive plan for weight management (10). The adjunctive use of Shared Medical Appointments (SMAs) can successfully address this issue by providing patients with cost-effective appointments dedicated to intensive lifestyle counseling and weight management planning (11). These medical appointments, facilitated by a physician, involve a small group of patients with a common diagnosis and can last 60-to-120-min. Patients receive clinical care such as check-ins with a physician, physical exams, medication management, patient education, and peer support (12, 13). SMAs have been shown to improve patient access, self-efficacy, self-care (13), clinician and patient satisfaction (14), and clinical outcomes (11, 15), while reducing cost (15) and repetition of health information by the practitioner due to the group session format (16). Notably, patients with obesity who attend weight management SMAs have been found to sustain significantly more weight loss for up to 12 months compared to patients who receive the standard of care (17).

Despite the advantages of SMAs, many clinics still do not offer them, possibly due to implementation barriers such as resource allocation, scheduling challenges, and lack of staff familiarity with associated billing and reimbursement procedures (12, 18, 19). Difficulty with patient recruitment and low program adherence have also been barriers to program sustainability (20). The lengthy, multi-session format of most SMA programs has also elicited patient feedback about scheduling conflicts, hardship in obtaining transportation and childcare, and complaints about extended visit lengths (21). Even with reports of numerous challenges in implementation, few feasibility papers have examined the process of program implementation and adaptation (22), which may provide valuable insight for clinics interested in establishing SMA programs of their own (16).

The 2013 AHA/ACC/TOS Guideline for the Management of Overweight and Obesity in Adults call for additional research in "effective methods of delivering lifestyle interventions remotely" (23). Virtual delivery of SMA programs may reduce overhead costs and improve treatment reach by minimizing patient barriers such as access to transportation, distance to the clinic, and access to childcare (21) but may prove challenging in other ways like access to a stable internet connection and use of web-based video conferencing (24).

The Supervised Lifestyle Integrative Medicine (SLIM) program is a virtual, lifestyle medicine-focused SMA program delivered as an adjunct to traditional clinic-based obesity treatment. We describe our use of the Practical, Robust Implementation and Sustainability Model (PRISM) implementation model and the Plan, Do, Study, Act (PDSA) and Framework for Reporting Adaptations and Modifications-Enhanced (FRAME) quality improvement models to implement and adapt the SLIM program to be acceptable and sustainable within a large healthcare system.

Methods

Patients and setting

Patients were referred to the SLIM program by physicians at the University of California, San Diego (UCSD) Center for Advanced Weight Management. We received support from the Center for Integrative Health, the UCSD Department of Family Medicine, and the UCSD Bariatric and Metabolic Institute early on to ensure a sustainable home for the program and a referral pipeline. Upon referral, eligibility was confirmed independently via medical record review by the research team and the patient navigator, who also interviewed patients individually. The inclusion criteria were being 18 years of age or older, having a body mass index (BMI) of 27 kg/m^2 or greater with weight-related comorbidity, or a BMI of 30 kg/m^2 or greater. Participation in the program was determined based on insurance eligibility. During enrollment, patients were informed that they would receive medical care in a group setting and that the program would be delivered virtually through Zoom video conferencing. The patient navigator received verbal confirmation

TABLE 1 Initial and updated SLIM curriculum.

Session	Initial	Updated
1	SMART goal setting	Welcome to SLIM
2	5 pillars of a healthy diet	SMART goal setting
3	Overcoming triggers	5 pillars of a healthy diet
4	Sleep hygiene	Principles of positive psychology and strengths-based thinking, self-compassion
5	Environmental influences	Cognitive Behavioral Therapy (CBT), applying CTFAR, environmental influences
6	Stress management	Hunger and snacking, sugars, intuitive eating, mindfulness
7	Grocery shopping, whole grains	Physical activity
8	Protein, fat, sodium	Meal prepping, grocery shopping, food labels
9	Meal prepping	Calorie density, types of carbohydrates
10	Strengths-based thinking	Sleep hygiene, stress management, social connection
11	Gratitude	Relapse prevention
12	Hunger and snacking, sugars	Gratitude
13	Physical activity	
14	Leisure time, reducing sedentary behavior	
15	Social support	
16	Sustainability and weight reduction maintenance	

that the patient had stable internet access, a device to access the visits, and were comfortable using the required technology. Patients signed an agreement that medical information disclosed by others during visits would not be shared outside of the medical visits. An exemption was granted by the University of California Human Research Protections Program for the retrospective collection of attendance and demographic data from the electronic medical record.

SLIM program intervention

The SLIM program is an intensive weight management intervention developed at UCSD. It comprises a series of virtual, SMAs to deliver a Lifestyle Medicine-based curriculum to patients to improve their weight management and health outcomes. The curriculum was developed following the key tenets of Lifestyle Medicine: whole-food, plant-predominant diet, regular physical activity, restorative sleep, stress management, reduction of risky behaviors, and positive social connections. There was an intentional focus on leveraging healthy eating patterns to improve patients' metabolic health profile and was intended to be delivered as an adjunct to traditional clinic-based obesity treatment.

Each curriculum session was approximately 1–2 h in length and covered various topics in lifestyle medicine, including but not limited to nutrition, culinary medicine, exercise, sleep, and stress. The curriculum format for each session was structured with the following components: welcome/ice breaker activity and introductions, educational session on a lifestyle medicine-related topic (Table 1), discussion, questions and answers, and ending with medication adjustments or any other specific activity that was needed to support patients. Sessions included speaker lectures, group discussions, and other group exercises to create an interactive, two-way learning environment. To foster trust and connection among both patients and facilitators, each session began with a reminder that the SMA was considered a "safe space" for self-disclosure and a statement that all information shared would remain strictly confidential within the group session.

Food as medicine-based topics comprised more than a third of the curriculum content. They included dedicated sessions on fundamental topics such as caloric density, nutrition, and the benefits of incorporating legumes, whole grains, and seasonal produce into everyday diets. Although plant-based diets were strongly emphasized, patients were introduced to various other balanced diets, including MyPlate (25), DASH (26), and Mediterranean diets (27, 28), and advised to select one that would be most appropriate for their socio-cultural background. Patients were encouraged to abandon "fad"-based thinking about dieting and reframe their understanding of nutrition in a holistic fashion that would be sustainable for long-term dietary change. The curriculum also emphasized "real-world" applications of culinary medicine in a dedicated session about grocery shopping strategies, understanding nutritional labels, meal planning, preparation, and batch cooking. Recipe and meal sharing were strongly encouraged throughout group discussions and other "show-and-tell"-based activities.

Behavioral change techniques and mental health-related topics, including mindfulness, mindful self-compassion, and cognitive behavioral therapy (CBT) were fundamental and interwoven throughout every topic in the SLIM curriculum. Each session began with a guided mindful meditation session followed by a "Rose, Bud, Thorn" activity to provide patients with time to reflect upon and share their stories of success, challenges, and opportunities for growth since the prior session. Behavioral change techniques (29) like Specific, Measurable, Achievable, Realistic, and Timely (SMART) goal setting (29) for initiating and maintaining change were repeatedly emphasized and practiced throughout each session. Cognitive behavioral therapy-based techniques and models were also used in various sessions to contextualize negative thoughts and feelings about lifestyle change and guide patients in overcoming psychological barriers to sustaining their lifestyle goals. The curriculum also included an entire session about relapse prevention (29) with an emphasis on resilience, problem solving, self-care, and self-compassion. Full-length curriculum materials and details are freely available online on our program website.[1]

1 http://slim.ucsd.edu

Initial implementation design

Upon enrollment into the SLIM program, patients received one, 60-min, one-on-one intake visit with an attending physician certified in Obesity Medicine and Lifestyle Medicine. Patients were introduced to the program, a lifestyle and weight history was taken, and baseline anthropometric and laboratory studies were performed including routine vitals, height, weight, waist circumference, complete metabolic panel (CMP), fasting insulin, lipids panel, C-reactive protein (CRP) and thyroid-stimulating hormone (TSH). If indicated, anti-obesity medications (AOMs) were also initiated at this time. The primary goal of the intake visits was to establish rapport with the patients, understand any psychosocial factors affecting their lifestyle, and determine readiness and barriers to change.

Following the intake visits, patients were assigned to a cohort and provided instructions to attend virtual SMAs via group Zoom calls. The original program began with 1 session each week for four sessions, then moved to 1 session every two weeks for 4 sessions (spanning 8 weeks or roughly 2 months), then 1 session every three weeks for 4 sessions (spanning 12 weeks or roughly 3 months), and finally 1 session monthly for 4 sessions (spanning four months). In total, the 16 sessions were completed sequentially and occurred over about 10 months. The SMAs were led by the same attending physician alongside a team comprised of a health coach and Preventive Medicine resident physicians.

After completing the 16 SMAs, patients were seen by the attending physician for two more follow-up in-person visits for laboratory studies, as well as a discussion of maintenance plans and future goals. Patients were encouraged to continue following up with the same physician and incorporating healthy lifestyle habits through referrals to community events, such as free cooking classes and group walks.

Implementation design and adaptation

PRISM-guided implementation design

We used multiple implementation science frameworks to create a structure to guide our implementation, evaluation, and adaptation of the SLIM program within the context of our organizational setting and patient characteristics. We used the Practical, Robust Implementation and Sustainability Model (PRISM) to inform our implementation approach, which is comprised of four key domains: (1) organizational and participant characteristics (patients and providers); (2) characteristics of the intervention from the organizational and participants' perspectives; (3) availability and sustainability of infrastructure/resources, and (4) the external environment and context (30). Our usage of the PRISM model and the key findings from each domain is presented in Figure 1.

PDSA-driven program adaptation with FRAME

Following the implementation design process using the PRISM framework, the SLIM program was implemented in rolling cohorts over three years. The Plan-Do-Study-Act (PDSA) model was used iteratively to adapt the implementation plan throughout active program administration. Adaptations made during the 'Study-Act' phases of PDSA were documented using parameters drawn from the Framework for Reporting Adaptations and Modifications-Enhanced (FRAME) model (31).

The PDSA model conceptualizes program testing cycles as a process of developing a plan to execute an implementation (Plan), carrying out the plan while gathering data (Do), analyzing the outcome data (Study), and using the data to adapt the next iteration of the implementation (Act) (32). Our PDSA cycles were operationalized through administration of the program for a span of three to six cohorts while conducting periodic research group meetings for review of feedback and outcome data collected. During these meetings, decisions were made to adapt the implementation plan on an ongoing basis using outcome data, team consensus, and input from patients, clinic staff, and administrative partners.

Adaptation decisions were systematically analyzed using FRAME to create structured and meaningful documentation along six domains – the adapted component, the nature of the adaptations, rationale, timing, fidelity, and post-adaptation evaluation. Using a structured documentation framework facilitated internal consistency in quantifying and qualifying the impact of our adaptations on implementation outcomes. A complete overview of the usage of implementation science (IS) frameworks to design and implement the SLIM program is outlined in Figure 1.

Outcome measures and data analysis

Qualitative data informally collected from the implementation included feedback from key partners (e.g., health coaches, patients, clinic staff, and directors) and patients. Data was collected using a combination of *ad hoc* conversations and feedback sessions following cohort cycles, during which feedback regarding the patients' satisfaction with the SMAs and the lifestyle medicine interventions was actively solicited. Input from key partners and patients guided adaptations to the program design and implementation.

Quantitative attendance data for SLIM patients who participated during year one and year two was collected from the UCSD Epic electronic medical record database to analyze attendance stratified by sessions and cohorts. For the quantitative analysis, statistical methods were performed with IBM SPSS Standard v29 to examine the effect of varying session days and times on patient attendance. Session-level attendance was defined as the number of attendees present as a percent of the number of patients scheduled. The correlation between session-level attendance and program adaptations was assessed using an independent samples *t*-test. For a power level of 90%, at least 56 patients need to be in each comparison group.

Results

Patient demographics

172 patients completed the SLIM program over three years (age: 51.2 ± 14.6 years; 76% female, 23% male, 1% nonbinary) (Table 2). 4 cohorts finished in year 1, 8 in year 2, and 11 in year 3, with cohort sizes reaching a maximum of 17 patients. Out of those who completed the program, baseline metabolic data was complete for 130 patients: BMI was 37.2 ± 7.5, kg/m^2, LDL cholesterol was 107 ± 33 mg/dL, triglycerides were 129 ± 63 mg/dL, and HbA1c was 5.6 ± 0.6%.

Attendance

Attendance data for years 1 and 2 are included in this analysis as year 3 was ongoing at the time of analysis (Table 3). The average

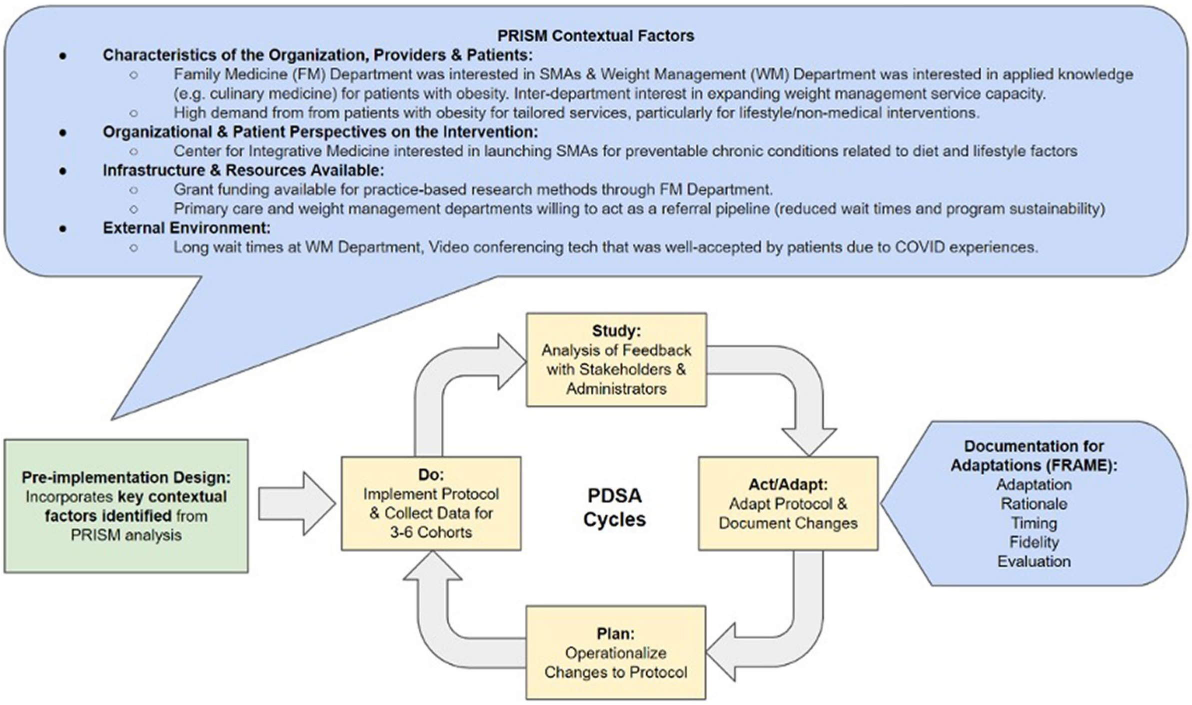

FIGURE 1
Application of implementation science frameworks.

attendance rate was lowest for cohorts 10 and 11, which had session times at 8:00 AM and 4:00 PM, respectively. The independent samples *t*-test revealed, among this sample of 199 sessions held during years 1 and 2, that sessions held at 8:00 AM or 4:00 PM had statistically significantly lower attendance rates ($M = 0.42$) than those who attended other sessions ($M = 0.49$) [$t_{(197)} = -1.867$, $p = 0.032$].

Program adaptations

Table 4 shows the application of the Framework for Reporting Adaptations and Modifications-Enhanced (FRAME) model, which was used to provide a structured overview of adaptations made to the SLIM program during the first three years of program implementation. A combination of qualitative and quantitative data prompted adaptations to program implementation and content in an effort to meet the needs of patients, health coaches, clinic staff, physicians, and department leaders. Modifications made during year 2 included encouraging patients to communicate outside of the SLIM program session times as a source of social support (29) and refinement of the didactic material shared in group sessions to emphasize self-talk (29), self-belief, and a positive relationship with physical activity. Year 3 modifications centered around program execution with goals of improving attendance and clinic workflow.

Updated SLIM program

The SLIM program was updated after 12 cohorts of participants over two years of PDSA development cycles. Currently, upon enrollment into the program, participants are scheduled for 3, one-on-one intake visits with a physician certified in Obesity Medicine and Lifestyle Medicine. During these 30-min-long visits, patients are introduced to the program, a complete lifestyle and weight history is taken, and baseline laboratory studies are established. If indicated, AOMs are also initiated at this time. Following intake, participants are assigned to a cohort and provided instructions to attend 12 weekly virtual SMAs via group Zoom calls. The SMAs are led by the same intake physician alongside a team variably composed of a health coach, registered dietitian, and/or Preventive Medicine resident physicians. Each session is approximately 120 min in length, and the session topics covered a wide range of patient education on diet, culinary medicine, exercise, sleep, stress, and behavior change techniques, including mindfulness, mindful self-compassion, positive psychology, and cognitive behavioral therapy (CBT). Each session includes speaker lectures, group discussions, breakout groups, and other learning exercises. Full-length curriculum materials and details are freely available online on our program website (see Footnote 1). Following the 12 SMAs, patients are seen by the intake physician for two more follow-up visits for laboratory studies and discussion of maintenance plans and future goals. Comparison of the initial and updated SLIM curriculum can be found in Table 1.

Discussion

The PRISM, PDSA, and FRAME models were employed to mitigate barriers and optimize implementation of a virtual, lifestyle medicine focused SMA program, providing an adaptive approach to patient-centered care. Use of the PRISM model during

TABLE 2 Baseline demographic and metabolic variables.

Baseline demographic information	$n = 172$
Mean age, y (SD)	51.2 (14.6)
Sex, *n* (%)	
Female	130 (76)
Male	40 (23)
Nonbinary	2 (1)
Race, *n* (%)	
American Indian/Alaska Native	1 (1)
Asian	11 (6)
Black or African American	23 (13)
Native Hawaiian or other Pacific Islander	1 (1)
Other or Mixed Race	35 (20)
White	99 (58)
Unknown/Not Reported	2 (1)
Ethnicity, *n* (%)	
Hispanic or Latino	31 (18)
Not Hispanic or Latino	103 (60)
Unknown/Not Reported	38 (22)
Baseline metabolic data	$n = 130$
BMI, kg/m^2 (SD)	37.2 (7.5)
Lipids	
LDL, mg/dL (SD)	107 (33)
Triglycerides, mg/dL (SD)	129 (63)
Glucose, mg/dL (SD)	100 (15)
HbA1c, % (SD)	5.6 (0.6)

TABLE 3 Average attendance rate, year of program, day and time for each cohort ($n = 199$).

Program year	Cohort	Weekday or Weekend	Time	Average Attendance Rate	*n*
1	1	Weekday	8 AM	68%	11
	2	Weekday	10 AM	63%	12
	3	Weekday	1 PM	53%	13
	4	Weekday	1 PM	57%	14
2	5	Weekend	10 AM	57%	17
	6	Weekend	1 PM	33%	18
	7	Weekday	1 PM	36%	15
	8	Weekday	3 PM	60%	16
	9	Weekday	4 PM	37%	15
	10	Weekday	8 AM	32%	10
	11	Weekday	4 PM	29%	17
	12	Weekend	10 AM	40%	15

pre-implementation elucidated system and patient level barriers to program implementation and sustainability including departmental support, patient referral pipelines, and durable funding sources. Iterative rounds of the PDSA model led to identification of key factors influencing attendance and patient satisfaction such as optimal and nonoptimal session times, program structure and length, and education topics. Following identification of key factors, modifications based on these insights were systematically documented using the FRAME model.

We found session times of 8:00 AM and 4:00 PM had the lowest attendance. A possible explanation could be that these are common times when individuals start and end their workday making it likely they are in their work commute or actively working. Family needs such as transportation to school or to after school activities may also make those times challenging for individuals. Eisenstat et al. reports that in their experience, the optimal times of day for group medical visits depends on the population. For those working full-time, session times occurring before 8:30 AM and between 5:00 PM and 7:00 PM are best. For individuals who are retired, sessions between 12:00 PM and 2:30 PM are best (33).

Barriers to utilizing SMAs for chronic disease management in prior literature include inadequate administrative support and funding to develop and implement the program which impact scheduling and visit logistics and the establishment of a stable referral pipeline and, thus, a consistent revenue stream (22, 34). Walker et al.'s systematic review of SMAs for weight loss reported session time as a barrier to attendance, with sessions occurring during work hours attended the least. In addition, they point out that using implementation frameworks for planning and executing SMA programs are crucial, yet the use of such models in SMAs for weight loss have yet to be documented. Lastly, they report that the lack of early engagement with key partners as a limitation of prior studies of SMAs for weight loss (11). The use of implementation frameworks and quality improvement models such as PRISM, PDSA, and FRAME prevented many barriers to adoption seen in existing SMA literature. Identifying critical contextual factors and potential obstacles early through use of the PRISM model enabled us to address barriers to sustainability before implementation such as establishing departmental and administrative support, cultivating reliable patient referral sources, and securing the necessary resources and personnel. Executing regular cycles of the Plan-Do-Study-Act (PDSA) model allowed us to operationalize qualitative feedback from participants, health coaches, physicians, and staff and the quantitative data on attendance rates to optimize session times and refine the program structure, curriculum, and participant engagement strategies.

Limitations of this assessment include that the initial phase of the program was implemented in a real-world setting so there was not a control group and participants self-selected to enroll. Additionally, we were unable to collect all individual, social, and contextual variables influencing attendance. These variables may include but are not limited to socioeconomic status, geographical location, personal motivation, and unforeseen life events. Lastly, the virtual delivery of the SLIM program required that patients have access to the internet and videoconferencing technology which may be a financial or technological barrier, possibly leading to a patient population that is disproportionately from well-resourced areas and thus not representative of the general population.

Despite the limitations mentioned above, we believe the SLIM program is successful as its implementation has been sustained in the Center for Advanced Weight Management beyond its pilot phase and continues to grow in patient demand. The use of implementation

TABLE 4 Program adaptations using the FRAME model.

Adaptation	Description	When?	Program year	Whose need was addressed?	Why was the adaptation made?
Encourage patient communication outside of the program sooner	Rather than waiting until the end of the program to encourage patients to connect with one another outside of the program, patients are now prompted during session 3	2023	3	Patients	Early establishment of an accountability partner and support system to encourage lasting lifestyle change
Change program structure	The program structure changed from 4 sessions weekly, 4 sessions every 2 weeks, 4 sessions every 3 weeks, and 4 sessions monthly to 12 sessions weekly.	2022	3	Patients, Department Administration	Improve attendance
Changing reminder method	No longer using email as a reminder method, relying primarily on MyChart messages, text messages and phone calls	2022	3	Patients, Health Coach/ Facilitator	Improve attendance and participation, improve workflow efficiency
Changing session times	Removal of 8 a.m. and 4 p.m. sessions in response to attendance data providing insight into optimal session times (see Table 3)	2022	3	Health Coach/Facilitator	Improve attendance and participation, choose times with better attendance
Modified intake visit	Changed intake from 1, hour-long visit to 3, 30-min visits	2022	3	Physician, Department Administration,	If a patient cancels, only one appointment slot is lost; this gives patients other opportunities to meet with a physician before starting the program and enhances recruitment
Expansion of relapse sessions	Information added about Lapse vs. Relapse, addition of slides involving addiction and movement toward recovery	2021	2	Patients, Health Coach/ Facilitator	Improve mental health and motivation
Adding information on weight stigma	Information added to better address the weight stigma, to improve patient/participant self-compassion	2021	2	Patients	Improve motivation, Improve patient self-love
Leisure activity moved ahead of physical activity	Leisure activity moved before physical activity to highlight enjoyable forms of movement	2021	2	Patients	Improve fit of content to patient/participant goals in response to a desire for more and earlier physical activity information
Added positive psychology	Added positive psychology pillars like the PERMA (Positive emotion, Engagement, Relationships, Meaning, Accomplishments) model of wellbeing	2021	2	Patients, Health Coach/ Facilitator	Encourage focus on connection, gratitude, and living a meaningful life
Moved session on strengths	Moved the session on Strengths earlier in the curriculum	2021	2	Patients, Health Coach/ Facilitator	Encourage strengths-based thinking at the beginning of the program
Recommend patients communicate outside of the program	Assigning patient team leaders and maintaining communication through Text/WhatsApp, an effort to improve patient support through communication	2021	2	Patients	Improve attendance and participation; improve mental health and motivation; improve program comradery

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models to guide its feasibility continues to be relevant and will actively guide the shape and future of the SLIM program. Moving forward, we envision the increased use of patient-centered outcomes like quality of life, mental health status, symptom management, and patient satisfaction to tailor adaptations. Future efforts include a study of effectiveness as well as continued evaluation of program attendance, scalability, and durability.

In conclusion, the use of implementation frameworks and quality improvement models provides valuable insights by offering a practical and multi-faceted approach to implementing and adapting a virtual, lifestyle medicine focused SMA program for weight management in a healthcare setting. Ongoing efforts are needed to enhance patient engagement and ensure long-term sustainability. If successfully implemented, and ultimate effectiveness is demonstrated, virtual SMA programs that offer comprehensive lifestyle education focusing on food as medicine can leverage the widespread adoption of virtual healthcare to make a meaningful contribution to the global efforts to reduce obesity.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by University of California, San Diego Human Research Protections Program. The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent for participation was not required from the participants or the participants' legal guardians/next of kin in accordance with the national legislation and institutional requirements.

Author contributions

KK: Writing – original draft, Writing – review & editing, Conceptualization, Data curation, Formal analysis, Methodology. IM-M: Data curation, Formal analysis, Writing – original draft, Writing – review & editing. AS: Data curation, Methodology, Writing – original draft, Writing – review & editing. CC: Data curation, Project administration, Writing – review & editing. SS: Methodology, Writing – original draft, Writing – review & editing. AB: Project administration, Writing – review & editing, Conceptualization, Investigation. LM: Conceptualization, Project administration, Resources, Writing – review & editing. EG: Conceptualization, Project administration, Resources, Writing – review & editing, Funding acquisition. GK: Conceptualization, Project administration, Resources, Writing – review & editing, Funding acquisition. MT: Conceptualization, Funding acquisition, Methodology, Project administration, Resources, Supervision, Writing – original draft, Writing – review & editing, Investigation. DS: Writing – original draft, Writing – review & editing, Funding acquisition, Investigation, Methodology, Project administration.

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Conflict of interest

MT was employed by International Consulting Associates, Inc. Arlington, VA, United States.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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