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Nutrition counseling for non-communicable disease management

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Nutrition counseling for non-communicable disease management

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Editorial: Nutrition counseling for non-communicable disease management

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Editorial on the Research Topic
Nutrition counseling for non-communicable disease management

Introduction

Globally, non-communicable diseases (NCDs) like cardiovascular disease, diabetes, cancer, chronic respiratory diseases, infertility, and obesity are the main contributors to mortality and morbidity. The primary modifiable factor influencing the diagnosis and progression of NCDs is often diet. Changing lifestyle habits can be challenging without support; therefore, nutritional counseling by health professionals is essential.

Nutrition counseling refers to the guidance provided by a health professional with specialized training in nutrition to help individuals make healthy food choices and develop sustainable eating habits. Traditionally, nutrition counseling involves a one-on-one approach, where the health professional collects information about knowledge and current habits and then provides tailored recommendations to the individual. Given the limited evidence that the one-on-one counseling approach leads to improved lifestyle behaviors, alternative methods have been explored that include counseling with theories and frameworks, family and social network involvement, and the use of technology. Results from these various approaches showed positive improvements; however, identifying a single approach that is more effective in improving dietary habits than others are challenging.

This Research Topic features 11 articles in which 66 authors from Australia, China, Cyprus, Italy, Iran, Mexico, Singapore, Saudi Arabia, and the United States, addressed aspects of nutrition counseling with various NCD states.

Initially, Worthington et al. illustrated the importance of nutritional trial design to improve dietary behaviors through a small sample of 12 interviews. Based on their findings, the most common techniques to enhance participant compliance were extensive screening protocols, designing the studies with several behavioral-change techniques, approaches from other successful studies, and considering potential participant barriers.

There was an exploration toward healthcare workers in Italy, who were deemed as working in high stress environments, and their risk for NCDs by Pirrello et al.. From the 273 respondents, some did not adhere to a healthy lifestyle and were at risk for a NCD. For example, 33.7% of the respondents indicated that they wanted to increase their

intake of fruits and vegetables weekly, yet 27.5% implemented this change. Even though working in a healthcare facility may create an assumption that one adheres to healthy lifestyles, current habits and workload may prevent one from changing and adapting to a lifestyle that is most suitable to reduce NCDs. A study conducted by Alqarni et al. with a total of 1,068 healthcare professionals, found that 58% believed the ketogenic diet could enhance the quality of life for adults with chronic obstructive pulmonary disease (COPD). Specifically, the research emphasized the therapeutic potential of this diet in managing COPD, particularly regarding its anti-inflammatory properties and ability to modify symptoms.

Wang et al. discovered how a body roundness index could help in identifying those at risk for NCDs among 2,319 females from the 2013-2019 NHANES dataset. The large-scale cohort Chinese study conducted by Li et al. explored the relationship between body composition in early pregnancy and the risk of developing gestational diabetes mellitus (GDM), which was shown to be negatively correlated with free-fat mass and lean mass but positively associated with percentage of body fat and fat mass. The findings support the idea that routine prenatal care should include body composition measurements to enable the early identification and prevention of GDM. Qiu et al. explored nutritional status by using CONUT (Controlling Nutritional Status) and NRI (Nutritional Risk Index) among 2,427 individuals on peritoneal dialysis with potential effect on all-cause mortality. At least in this population, 79.1% of individuals were identified at nutritional risk with the NRI whereas 76.6% were identified at nutritional risk with CONUT. Regardless of the instrument, one who had been classified as severe nutritional risk had higher mortality. Each instrument can detect nutritional risk so it can be instrumental as a screening tool. Another study conducted by Ge et al. involving a cohort of 701 critically ill Chinese adults with intestinal obstruction (IO) demonstrated that a higher prognostic nutritional index (PNI)—which indicates their nutritional and immune status—correlates with a lower likelihood of dying during their hospital stay. The findings have significant clinical implications because incorporating the PNI, which is routinely used as a preoperative tool assessment, into the standard risk assessment protocol upon ICU admission enables clinicians to promptly identify patients with inadequate nutritional and immune profiles who are at a higher risk for adverse outcomes. The study conducted by Yu et al. examined the effectiveness of various sarcopenia screening methods among 300 adults with a bone tumor using the Asian Working Group for Sarcopenia screening tool. They demonstrated that the most effective approach for measuring muscle mass in the screening and follow-up of malnutrition involves combining SARC-F, SARC-Calf, and SARC-F+BEM measurements, serving as an alternative to ionizing imaging methods.

Michail et al. developed a questionnaire to assess nutritional knowledge, perceptions, and sustainability for a plant-dominant low-protein diet in adults with chronic kidney disease (CKD). This study points out the need to address culture-based dietary habits to benefit people at risk or with CKD throughout the nutritional care process. Furthermore, a higher dietary quality can reduce the frequency and severity of migraine episodes as identified by the Iranian study conducted by Feyzpour et al.. The authors concluded that prioritizing overall diet quality instead of concentrating solely on individual macronutrients or micronutrients is a promising approach for improving the prognosis and overall condition of individuals suffering from migraines. Finally, a study by Sevilla-González et al. explored how a tailored nutrition care process could be implemented for individuals with metabolic diseases in both inpatient and outpatient settings in Mexico. From the researchers and clinicians who were able to implement this process, it was successful. However, for this to be successfully implemented within other countries and populations, a thorough review and discussion needs to take place.

Overall, these studies involved diverse populations from around the world, allowing for adaptability and testing in other groups. The findings will contribute to developing a more effective consensus on the best approaches to use during nutrition counseling aimed at improving lifestyle habits and ultimately reducing NCDs globally.

Author contributions

JA: Writing – original draft, Writing – review & editing. SJ: Writing – original draft, 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.

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Investigating the relationship between diet quality, lifestyle and healthy eating index with severity and migraine attacks: a cross-sectional study

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Background: Migraine is a disabling neurovascular disorder often associated with comorbidities such as mental health disorders, cardiovascular diseases, and metabolic syndromes. While certain dietary triggers have been identified, the impact of overall diet quality on migraine severity and frequency is not well understood. This study aimed to evaluate the association between diet quality, lifestyle factors, and the Healthy Eating Index (HEI) with migraine severity and frequency.

Methods: A cross-sectional study was conducted on 280 patients aged 18–50 years newly diagnosed with migraines. Dietary intake was assessed using a 147-item Food Frequency Questionnaire (FFQ), and diet quality was evaluated using the Lifelines Diet Score (LLDS) and HEI. Migraine-related disability and severity were assessed using the Migraine Disability Assessment (MIDAS) questionnaire and the Visual Analogue Scale (VAS), respectively. Logistic regression models were applied to examine the association between diet quality and migraine outcomes.

Results: Higher LLDS and HEI scores were significantly associated with reduced odds of migraine-related disability. Participants in the highest LLDS tertile had an odds ratio (OR) of 0.68 (95% CI: 0.42–0.96; $p = 0.02$) for migraine disability. Similarly, the highest HEI tertile was associated with an OR of 0.58 (95% CI: 0.41–0.88; $p = 0.025$). For pain intensity, the highest tertile of LLDS showed an OR of 0.55 (95% CI: 0.38–0.75; $p = 0.026$), while the HEI showed an OR of 0.62 (95% CI: 0.45–0.85; $p = 0.03$).

Conclusion: Higher diet quality, as measured by LLDS and HEI scores, is inversely associated with migraine severity and frequency. These findings suggest that dietary improvements may be a viable strategy for managing migraine symptoms.

KEYWORDS

migraine, diet quality, healthy eating index, lifestyle factors, migraine severity

Introduction

Migraine is a debilitating neurovascular condition characterized by severe headaches, often accompanied by photophobia, phonophobia, nausea, vomiting, and heightened sensitivity to movement (1). It is frequently associated with mental health conditions, including depression and anxiety, sleep disturbances, chronic fatigue, and cardiovascular risk factors such as hypertension, diabetes, hyperlipidemia, and obesity (2–4). It is among the most common neurological disorders, with an estimated 14–15% of headache sufferers receiving a diagnosis of migraine (5). A recent meta-analysis found that the prevalence of migraine in the general population of Iran is 15.1% (6). The economic burden is significant; a systematic review reported annual healthcare costs ranging from £6,443 to £53,446 in some countries (7).

While the mechanisms underlying migraines remain unclear, environmental, hormonal, psychological, and dietary factors are potential contributors (8, 9). Certain foods, such as chocolate, caffeine, cheese, and alcoholic beverages, have been identified as common triggers (10–12). Dietary components may influence migraine pathophysiology through mechanisms involving neuropeptides, receptors, ion channels, inflammation, nitric oxide release, and vasodilation (13).

Although the evidence is limited, certain dietary interventions such as the ketogenic diet (14), elimination diets, and diets rich in anti-inflammatory foods show potential as effective approaches to managing migraines (15). However, individuals typically consume a variety of foods and nutrients simultaneously rather than in isolation, emphasizing the need to explore the combined effects, interactions, and cumulative impacts of diverse dietary components on migraines. Analytical methods, such as dietary pattern analysis and evaluations of overall diet quality, provide a more holistic understanding of the relationship between diet and migraines (13, 16).

Recent studies have examined the relationship between diet quality or dietary diversity and migraine attacks, finding that lower diet quality or diversity is associated with a higher frequency of attacks (17, 18).

However, to date, no studies have evaluated the combined effects of the LLDS and HEI on migraine severity and frequency. This study aims to address this gap by investigating the relationship between diet quality, lifestyle factors, and HEI with the severity and frequency of migraines.

Methods

Study setting

This cross-sectional study involved 280 patients, aged 18–50 years, who were newly diagnosed with migraines and referred to the neurology clinic at Vali-e-Asr Hospital in Zanjan, Iran, between March 2023 and July 2024.

Study population and sample size

In this cross-sectional study, the population consisted of all patients aged 18 to 50 years who visited the neurology clinic at Vali-e-Asr Hospital in Zanjan. The sample size was calculated using G*Power software, referencing the study by Mirzababaei et al. (18). Based on the variability in migraine attack frequency, a statistical power of 80%, and a type I error rate of 5%, the required sample size was estimated to be 245 participants. To account for a potential 10% dropout rate, this number was adjusted to 265 participants. Ultimately, 280 individuals were enrolled to further increase the study's power.

Eligibility criteria included being aged 18 to 50 years, attending the neurology clinic for the first time, not adhering to any specific diet, having a confirmed migraine diagnosis by a neurologist based on the International Classification of Headache Disorders (ICHD-3) criteria, and a willingness to participate. Exclusion criteria encompassed a history of kidney, liver, pancreatic, or cardiovascular diseases; diabetes; cancer; neurovascular or vasculitis disorders as reported by the patient or documented in medical records; malnutrition [Body mass index (BMI) < 18.5]; pregnancy; menopause; or refusal to complete the questionnaire. Participants with incomplete questionnaires, changes in treatment type, lack of cooperation, or implausible caloric intakes (above 4,000 kcal or below 600 kcal) were also excluded.

Sampling method

A flowchart illustrating the study design, including participant eligibility, recruitment, and data collection processes, is provided in Figure 1. Participants were recruited using convenience sampling. Three researchers stationed at the neurology clinic of Vali-e-Asr Hospital identified patients recently diagnosed with migraines. Patients who met the inclusion criteria and agreed to participate were enrolled as study subjects. After a neurologist confirmed each patient's migraine diagnosis based on the ICHD-3 criteria, patients were referred to the research team for further procedures. The study objectives were thoroughly explained, and informed consent was obtained from all participants. Eligible individuals, as defined by the inclusion and exclusion criteria, then underwent data collection, which included anthropometric measurements, a FFQ, a physical activity questionnaire, the MIDAS questionnaire, and the VAS.

The MIDAS questionnaire assessed the impact of migraines on participants' daily lives over the past 3 months. It quantifies disability by measuring the number of days migraines interfered with work, household responsibilities, and social or leisure activities. MIDAS scores are categorized into four levels: little or no disability (score 0–5), mild disability (score 6–10), moderate disability (score 11–20), and severe disability (score 21 or higher). This tool provides a comprehensive evaluation of the burden of migraine-related disability, complementing the VAS's assessment of pain intensity (19).

Pain intensity was measured using the VAS, a widely recognized tool for subjective pain evaluation. Participants rated their pain on a scale from 0 to 10, where 0 represented 'no pain' and 10 indicated 'the worst possible pain.' The VAS is straightforward to administer and provides a reliable, quantitative measure of pain intensity, suitable for tracking changes over time (20).

Data collection tools

Food intake data were collected using a validated 147-item FFQ, which has been confirmed by previous studies (21, 22). Dietary intake

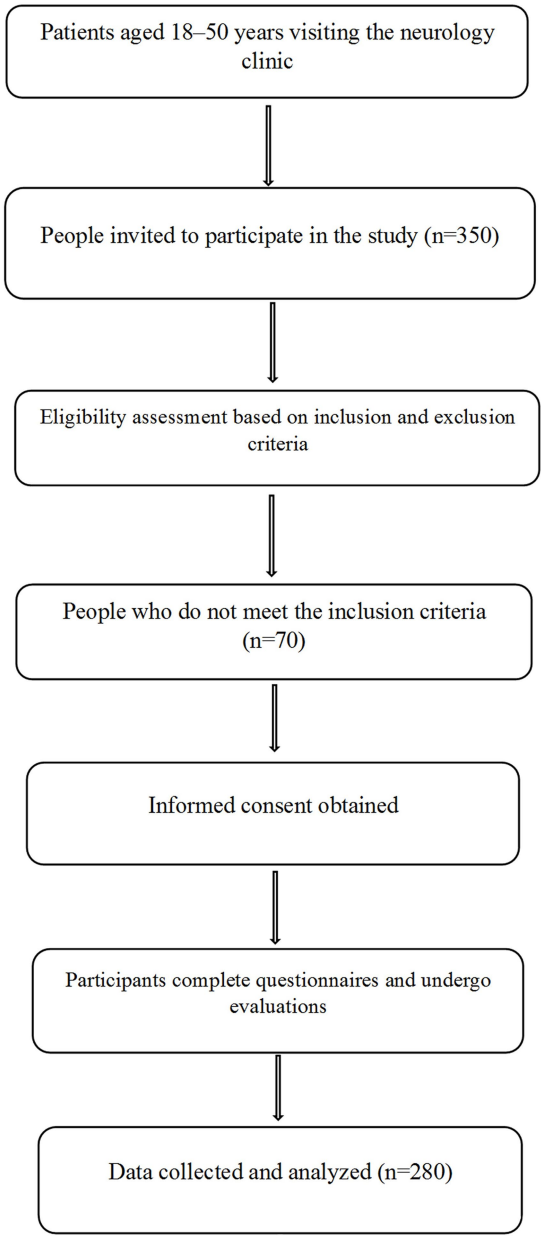

FIGURE 1
Flowchart of participant selection and study implementation.

analysis was conducted using N4 software, which converted all measurements into grams. All participants were newly diagnosed with headache conditions, and all questionnaires were completed by trained researchers. The FFQ assessed dietary intake over the past year, with participants recalling the frequency of food consumption (daily, weekly, or monthly).

FFQ data were analyzed to estimate dietary intake, with all measurements converted into grams using N4 software. Diet quality and HEI scores were calculated based on the FFQ data, using the USDA food composition table (23) to estimate energy and nutrient intake. Physical activity was recorded using the Iranian version of the International Physical Activity Questionnaire (IPAQ) (24), and anthropometric measurements were obtained from patient records.

The Pittsburgh Sleep Quality Index (PSQI) (25) was used to assess sleep quality among participants over the previous month. The PSQI is a validated self-reported questionnaire consisting of 19 items grouped into seven components: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction. Each component is scored from 0 to 3, with higher scores indicating poorer sleep quality. The total PSQI score, calculated by summing the component scores, ranges from 0 to 21, with a score above 5 indicating poor sleep quality. Trained researchers administered the PSQI and provided clarification to participants when necessary. A total score of 6 or higher indicates inadequate sleep quality.

The social status score was evaluated using a structured questionnaire designed to capture key socioeconomic factors, including educational attainment, occupational status, and income level. Each dimension was assigned a specific weight based on established scoring guidelines for social stratification. Educational attainment was categorized into three levels: primary education or lower (score = 1), secondary education (score = 2), and higher education (score = 3). Occupational status was classified as unemployed (score = 1), semi-skilled or skilled labor (score = 2), and professional or managerial roles (score = 3). Income was stratified into three tiers based on local economic benchmarks, with lower income (score = 1), middle income (score = 2), and higher income (score = 3). The final social status score was calculated by summing the scores from these three components, yielding a composite score ranging from 3 to 9.

Dietary indices

In this study, diet quality was assessed using two primary indices: LLDS and HEI. The LLDS is a food-based dietary quality index that evaluates adherence to dietary guidelines by scoring the intake of specific food groups associated with positive health outcomes. LLDS includes the consumption of nine food groups: vegetables, fruits, whole grain products, legumes and nuts, fish, oils and soft margarines, unsweetened dairy, coffee, and tea, which have been shown to have positive effects on health, and three food groups: red and processed meat, butter and hard margarines, and sugar-sweetened beverages, which negatively affect health. Individuals' food intake was expressed in grams per 1,000 kcal. For each food group, intake was divided into 1 to 5 quintiles, with 5 points awarded for the highest intake and 1 point for the lowest intake of positive food groups. For negative food groups, 5 points were awarded for the lowest intake and 1 point for the highest intake. The sum of the scores from the 12 components resulted in an LLDS score ranging from 12 to 60 (26, 27).

The HEI is calculated by assessing adherence to dietary recommendations across 13 components that represent various aspects of a balanced diet. These components include nine categories for food adequacy (e.g., total fruit, whole fruit, total vegetables, greens and beans, whole grains, dairy, total protein foods, seafood and plant proteins, and fatty acids) and four categories for foods to limit (e.g., refined grains, sodium, added sugars, and saturated fats). Each component is scored based on the proportion of intake that meets or exceeds the dietary recommendations. For adequacy components, higher intakes yield higher scores, while for moderation components, lower intakes of items like added sugars and saturated fats result in

higher scores. Scores for each component range from 0 to a maximum component score (typically 5 or 10 points), and the sum of all component scores provides a total HEI score, which ranges from 0 to 100. Higher total HEI scores reflect closer adherence to dietary guidelines and, therefore, a higher-quality diet (28).

Data analysis method

Statistical analyses were performed using SPSS version 26 (IBM Corp., Armonk, NY, United States). Continuous variables were summarized as means ± standard deviations (SD) if they followed a normal distribution, or as medians and interquartile ranges (IQR) for non-normally distributed data. Categorical variables were presented as frequencies and percentages. The Kolmogorov–Smirnov test was used to assess the normality of continuous data.

Comparisons of baseline characteristics and dietary intake across tertiles of the indices (e.g., LLDS and HEI) were performed using appropriate statistical tests. For quantitative variables, one-way analysis of variance (ANOVA) was applied if the data were normally distributed. For non-normally distributed data, the Kruskal-Wallis test was used. For qualitative variables, chi-square tests or Fisher's exact tests were employed, as appropriate. When significant differences were identified using ANOVA, Tukey's *post-hoc* test was performed to determine pairwise differences between tertiles. To evaluate associations between diet quality indices and migraine outcomes, multivariate logistic regression models were used. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for two primary outcomes: migraine-related disability, assessed by the MIDAS questionnaire, and migraine pain intensity, measured using the VAS. Three hierarchical models were constructed to control for potential confounders:

Model 1: Adjusted for total energy intake (kcal/day) and BMI. Model 2: Included additional adjustments for gender, social status score, sleep quality, and physical activity. Model 3: Further adjusted for daily water intake (glasses/day), salt consumption habits, and family history of migraines. Also, $p < 0.05$ was considered statistically significant for all analyses. All tests were two-sided, and results were reported with exact p where possible to enhance interpretability.

Results

The mean age of participants was 35.19 ± 6.92 years, and the mean weight was 74.55 ± 16.52 kg. None of the participants were following a specific diet. As shown in Table 1, participants' baseline characteristics and dietary intake varied across the tertiles of the LLDS and HEI. Additionally, the mean daily water intake among participants was 4.61 ± 2.69 glasses. Most participants (54.7%) were female, and 58.87% were married. Employment status varied, with 37.15% of participants being homemakers, 27.86% self-employed, and 34.99% either employed or students. About 49.65% of participants had never smoked, while 30% were current smokers. Physical activity levels were predominantly low, with 43.92% reporting low activity, 37.5% moderate, and 18.58% high. No significant differences in age, weight, BMI, or physical activity levels were found across the tertiles of the LLDS and HEI scores ($p > 0.05$). However, individuals in the highest tertile of both the LLDS and HEI reported significantly better sleep quality compared to those in the lowest tertile ($p < 0.001$).

TABLE 1 Overview of qualitative and quantitative variables in the study.

Variable (qualitative)		Frequency	Percentage
Gender	Female	153	54.7
	Male	127	45.3
Education level	High school diploma or lower	110	39.3
	Associate's or Bachelor's degree	130	46.4
	Master's or Doctorate	40	14.3
Employment status	Homemaker	104	37.15
	Self-employed	78	27.86
	Employee or Student	98	34.99
Marital status	Married	164	58.87
	Single or divorced	116	29.3
Smoking status	Never smoked	139	49.65
	Current smoker	84	30
	Former smoker	57	20.35
Family history of migraine	No	173	67.8
	Yes	107	38.2
Medication use	Yes	129	46.1
	No	151	53.9
Preference for salty foods	Yes	103	36.78
	No	177	63.22
Adding salt during meals	Yes	163	58.20
	No	117	41.8
Physical activity level	Low	123	43.92
	Moderate	105	37.5
	High	52	18.58
Variable (quantitative)		**Mean**	**SD[1]**
Age (years)		35.19	6.92
Height (cm)		170.41	7.49
Weight (kg)		74.55	16.52
Waist circumference (cm)		89.48	14.15
Hip circumference (cm)		104.25	12.17
BMI		27.36	5.69
Waist-to-hip ratio		0.84	0.07
Daily water consumption (glasses)		4.61	2.69
Physical activity (MET/Min/day)		134.29	36.19
Social status score		5.91	2.87

[1]Standard Deviation.

Table 2 presents the variations in baseline variables and dietary intake across the tertiles of the LLDS and HEI scores. The results show no significant differences in age, weight, BMI, or physical activity

TABLE 2 Baseline quantitative variables and dietary intakes of individuals across LLDS and HEI score tertiles.

Variable	LLDS score tertiles				HEI score tertiles			
	T1 Mean ± SD	T2 Mean ± SD	T3 Mean ± SD	*p**	T1 Mean ± SD	T2 Mean ± SD	T3 Mean ± SD	*p**
Age (years)	34.28 ± 7.43	35.59 ± 8.34	34.40 ± 7.60	0.65	34.63 ± 8.49	35.22 ± 7.76	34.31 ± 8.15	0.71
Weight (kg)	76.18 ± 17.44	74.18 ± 16.37	74.56 ± 16.81	0.52	76.55 ± 17.83	75.19 ± 16.57	74.77 ± 16.47	0.63
BMI	27.65 ± 5.73	26.93 ± 4.77	27.18 ± 5.39	0.64	27.70 ± 5.82	26.69 ± 5.22	27.21 ± 5.31	0.59
Pittsburgh sleep quality index	6.83 ± 3.70	5.53 ± 3.35	4.32 ± 2.81	<0.001	6.95 ± 3.81	5.18 ± 3.19	4.25 ± 2.76	<0.001
Physical activity (MET/Min/day)	132.28 ± 35.73	136.22 ± 36.24	135.64 ± 33.45	0.78	129.25 ± 31.43	137.50 ± 35.72	134.83 ± 34.60	0.61
	T1 Mean ± SD	T2 Mean ± SD	T3 Mean ± SD	*p**	*p***	T1 Mean ± SD	T2 Mean ± SD	T3 Mean ± SD	*p**	*p***
Energy (kcal)	2626.36 ± 674.44	2419.87 ± 680.44	2576.37 ± 643.53	0.17	–	2649.38 ± 623.36	2576.25 ± 605.56	2514.34 ± 584.44	0.12	–
Carbohydrate (g/day)	354.46 ± 119.25	325.25 ± 105.23	339.23 ± 112.41	0.12	<0.001	372.19 ± 130.19	354.67 ± 127.44	332.40 ± 129.36	0.07	<0.001
Protein (g/day)	84.89 ± 23.19	79.45 ± 19.32	94.26 ± 21.15	0.04	0.003	77.67 ± 18.43	85.71 ± 20.34	96.71 ± 23.62	0.02	0.001
Fat (g/day)	109.41 ± 33.28	91.42 ± 27.83	86.43 ± 23.49	0.001	<0.001	107.57 ± 34.12	98.75 ± 26.43	89.47 ± 25.52	0.03	0.002
Monounsaturated fatty acids (g/day)	35.19 ± 12.44	29.49 ± 11.83	27.38 ± 11.32	0.11	0.01	33.21 ± 13.19	30.14 ± 11.56	28.43 ± 12.13	0.16	0.08
Polyunsaturated fatty acids (g/day)	22.19 ± 10.26	20.65 ± 10.43	18.57 ± 9.36	0.13	0.18	23.29 ± 11.76	20.83 ± 11.43	19.23 ± 10.76	0.19	0.23
Saturated fatty acids (g/day)	35.42 ± 14.26	26.75 ± 10.11	23.32 ± 9.83	<0.001	<0.001	36.59 ± 16.27	33.91 ± 13.73	26.47 ± 10.25	0.003	<0.001
Fiber (g/day)	44.26 ± 19.45	46.19 ± 21.63	51.76 ± 24.27	0.09	0.01	36.15 ± 18.73	45.12 ± 20.63	53.32 ± 23.44	<0.001	<0.001

*P**: Calculated by ANOVA, *P*****: Calculated by ANCOVA after adjusting for energy intake.

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TABLE 3 Multivariate logistic regression analysis examining the effect of LLDS and HEI on migraine-related disability.

Variable		Odds ratio (95% CI)	*p*		*p-trend*
LLDS	Tertile 1		Reference	–	0.02
	Tertile 2		0.52 (0.31–0.76)	0.002	
	Tertile 3		0.45 (0.26–0.69)	0.003	
HEI	Tertile 1		Reference	–	0.03
	Tertile 2		0.57 (0.40–0.79)	0.004	
	Tertile 3		0.49 (0.37–0.72)	0.002	
Model 1	LLDS	Tertile 1	Reference	–	0.02
		Tertile 2	0.56 (0.35–0.79)	0.002	
		Tertile 3	0.57 (0.37–0.81)	0.001	
	HEI	Tertile 1	Reference	–	0.01
		Tertile 2	0.59 (0.42–0.81)	0.005	
		Tertile 3	0.51 (0.38–0.75)	0.002	
Model 2	LLDS	Tertile 1	Reference	–	0.021
		Tertile 2	0.60 (0.38–0.87)	0.004	
		Tertile 3	0.65 (0.43–0.94)	0.023	
	HEI	Tertile 1	Reference	–	0.005
		Tertile 2	0.67 (0.45–0.95)	0.035	
		Tertile 3	0.54 (0.39–0.85)	0.003	
Model 3	LLDS	Tertile 1	Reference	–	0.022
		Tertile 2	0.62 (0.43–0.88)	0.014	
		Tertile 3	0.68 (0.42–0.96)	0.02	
	HEI	Tertile 1	Reference	–	0.003
		Tertile 2	0.70 (0.48–1.09)	0.075	
		Tertile 3	0.58 (0.41–0.88)	0.025	

Model 1: Adjusted for energy intake and BMI; Model 2: Includes Model 1 + gender, Social Status Score, sleep quality and physical activity; Model 3: Includes Model 1 and 2 + water intake, salt consumption and presence of a family history of migraine.

levels among the tertiles of LLDS and HEI scores ($p > 0.05$). However, individuals in the highest tertile of both LLDS ($p < 0.001$) and HEI ($p < 0.001$) reported significantly better sleep quality compared to those in the lowest tertile.

There were no significant differences in caloric intake across the LLDS ($p = 0.17$) and HEI ($p = 0.12$) tertiles. Regarding dietary intake, participants in the higher tertiles of LLDS and HEI had significantly higher protein and fiber intake, along with lower fat and saturated fat intake, even after adjusting for energy intake. Additionally, participants in the higher tertiles of LLDS and HEI had significantly lower intake of carbohydrates and monounsaturated fatty acids (MUFA) after adjusting for energy ($p < 0.05$).

Table 3 shows the relationship between LLDS and HEI scores and MIDAS using logistic regression analysis. As shown in Table 3, in the fully adjusted models, higher scores of LLDS and HEI were significantly associated with lower odds of migraine-related disability (OR = 0.68, 95% CI = 0.42–0.96, $p = 0.02$ for LLDS and OR = 0.58, 95% CI = 0.41–0.88, $p = 0.025$ for HEI).

Regarding the relationship between migraine pain intensity and diet quality, Table 4 presents the association between VAS and LLDS and HEI scores. In the fully adjusted model, participants in the highest tertile of LLDS had 45% lower odds of experiencing severe migraine pain compared to those in the lowest tertile (OR = 0.55, 95% CI: 0.38–0.75, $p = 0.026$). Similarly, those in the highest tertile of HEI exhibited a 38% reduction in the odds of severe migraine pain (OR = 0.62, 95% CI: 0.45–0.85, $p = 0.03$).

Participants in the highest tertile of LLDS and HEI scores exhibited lower odds of migraine-related disability and intensity. These findings suggest an association between diet quality and migraine outcomes, although the cross-sectional design of the study limits the ability to infer causality.

Discussion

This cross-sectional study found that higher diet quality, as measured by the LLDS and HEI, was associated with reduced severity and frequency of migraine symptoms. However, given the observational nature of the study and the relatively small sample size, these findings should be interpreted with caution. The results highlight a potential link between dietary improvements and migraine management, but they do not establish causality. Future

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TABLE 4 Multivariate logistic regression analysis examining the effect of LLDS and HEI on migraine pain intensity.

Variable			Odds ratio (95% CI)	*p-trend*	*p*
LLDS	Tertile 1		Reference	–	0.019
	Tertile 2		0.59 (0.44–0.81)	0.001	
	Tertile 3		0.43 (0.32–0.59)	<0.001	
HEI	Tertile 1		Reference	–	0.026
	Tertile 2		0.62 (0.45–0.83)	0.004	
	Tertile 3		0.45 (0.32–0.63)	0.001	
Model 1	LLDS	Tertile 1	Reference	–	0.015
		Tertile 2	0.63 (0.45–0.84)	<0.001	
		Tertile 3	0.45 (0.33–0.62)	<0.001	
	HEI	Tertile 1	Reference	–	0.018
		Tertile 2	0.66 (0.45–0.89)	0.016	
		Tertile 3	0.48 (0.34–0.69)	0.004	
Model 2	LLDS	Tertile 1	Reference	–	0.026
		Tertile 2	0.66 (0.45–0.89)	0.002	
		Tertile 3	0.49 (0.36–0.68)	0.019	
	HEI	Tertile 1	Reference	–	0.039
		Tertile 2	0.74 (0.53–1.07)	0.12	
		Tertile 3	0.57 (0.36–0.81)	0.023	
Model 3	LLDS	Tertile 1	Reference	–	0.003
		Tertile 2	0.68 (0.46–0.93)	0.017	
		Tertile 3	0.55 (0.38–0.75)	0.026	
	HEI	Tertile 1	Reference	–	0.046
		Tertile 2	0.78 (0.59–1.15)	0.18	
		Tertile 3	0.62 (0.45–0.85)	0.03	

Model 1: Adjusted for energy intake and BMI; Model 2: Includes Model 1 + gender, social status score, sleep quality and physical activity; Model 3: Includes Model 1 and 2 + water intake, salt consumption and presence of a family history of migraine.

research, including longitudinal studies and clinical trials, is necessary to confirm these associations and explore the underlying mechanisms.

Diet plays a crucial role in influencing health outcomes and the risk of chronic conditions, such as migraines (29, 30). Numerous studies have assessed the impact of individual nutrients or combinations of dietary components on the occurrence and intensity of migraines (13, 31–35). However, few studies have comprehensively assessed overall dietary patterns and their cumulative effects on migraine risk and management. By focusing on dietary quality as a whole, our study provides valuable insights into how a balanced and nutrient-rich diet can mitigate the debilitating effects of migraines.

The HEI-2015 defines high-quality diets as those that emphasize greater intake of nutrient-dense foods, including fruits, vegetables (particularly greens and beans), whole grains, dairy products, total protein sources, seafood, plant-based proteins, and healthy fatty acids (36). It also emphasizes limiting the consumption of sodium, refined grains, added sugars, and saturated fats. Such a diet not only provides essential nutrients required to maintain normal neural function but may also be associated with a reduction in the severity of migraine attacks (37). Similarly, the LLDS is a dietary assessment tool based on food-based principles aligned with the Dutch Dietary Guidelines (27). It evaluates diet quality by assessing adherence to these guidelines, offering insights into how specific dietary patterns may reduce migraine severity and frequency.

Recent studies have consistently shown a significant association between poor diet quality and the prevalence of migraines (29). Supporting our findings, one study demonstrated that healthy women with normal body weight had higher diet quality scores (HEI-2005) compared to those suffering from migraines (38). Similarly, Bakirhan's research aligns with our results, revealing a negative correlation between total HEI-2015 scores and VAS scores, suggesting that better diet quality is associated with lower migraine severity (39).

Furthermore, another study reported that individuals with migraines tend to consume more pro-inflammatory foods and exhibit lower overall diet quality compared to those without migraines (40). In line with these findings, Ghoreishy et al. observed that individuals with diets high in pro-inflammatory properties had a significantly greater risk of severe headaches compared to those with diets rich in anti-inflammatory foods, which were inversely associated with the frequency and severity of migraine attacks (41).

While the precise mechanisms underlying migraine attacks remain unclear, evidence suggests that inflammation plays a crucial role in their development (42). Additionally, an imbalance between oxidants and antioxidants is believed to contribute to the pathogenesis of migraines, potentially prompting the brain to initiate a homeostatic

and neuroprotective response to oxidative stress (37). The association between higher diet quality and reduced migraine symptoms observed in our study may be explained by the presence of antioxidants, unsaturated fatty acids, and dietary fiber in nutrient-dense foods. These components help mitigate oxidative stress and reduce neuroinflammation, potentially preventing or alleviating migraine episodes (39).

From an alternative perspective, it is worth noting that the HEI and LLDS share similarities with dietary patterns such as the DASH (Dietary Approaches to Stop Hypertension) and Mediterranean diets, particularly in their emphasis on fruits, vegetables, and legumes (43, 44). Previous studies have found that greater adherence to the DASH diet is associated with reduced headache severity and shorter headache duration per episode, highlighting the potential benefits of these dietary patterns in managing migraine symptoms (17, 18). Furthermore, studies have shown that the neuroprotective effects of the Mediterranean diet in preventing neurodegeneration are largely attributed to its abundance of bioactive compounds, phytochemicals, and phenolic substances (45–48). These components play a critical role in mitigating inflammation and oxidative stress, which are significant contributors to the development of neurodegenerative conditions and play a key role in the severity of migraine-related disability, as measured by the MIDAS.

As mentioned previously, a possible underlying mechanism for the findings of our study may involve the balance between antioxidants and oxidants, which could be linked to the occurrence of migraines and headaches. Neuroinflammation can result in vasodilation and sensitization of pain-sensitive neurons, primarily through the activation of nociceptors in the trigeminal system. When the trigeminal ganglion is stimulated, it triggers the release of neuropeptides such as substance P, neurokinin, and calcitonin gene-related peptide (CGRP) (49). CGRP plays a critical role in various physiological processes, including the dilation of cerebral and dural blood vessels and the release of inflammatory mediators. Elevated levels of these neuropeptides have been detected in the cerebrospinal fluid of individuals with chronic migraines (50). Additionally, inflammatory markers such as interleukin (IL)-1β, IL-6, and tumor necrosis factor (TNF)-α have been observed to increase, particularly during migraine attack phases (51).

Fruits and vegetables, rich in antioxidants, have potential therapeutic effects on migraines due to their bioactive compounds. For instance, indole-3-carbinol and sulforaphane, found in vegetables such as cabbage, broccoli, beets, parsley, spinach, and carrots, may act as CGRP antagonists, demonstrating effectiveness comparable to some medications in certain patients (52). Additionally, diets high in fiber can help reduce inflammation by modulating glucose absorption rates, altering gut microbiota, and decreasing the production of inflammatory cytokines (53). The fermentation of fiber by gut microbiota produces short-chain fatty acids (SCFAs), including butyrate, propionate, and acetoacetate. Among these, butyrate plays a critical role in regulating T-cell function, maintaining gut barrier integrity by enhancing the expression of tight junction proteins, and stabilizing hypoxia-inducible factor (HIF), which supports gut health and reduces toxin permeability (54).

Magnesium also plays a significant role in migraine pathophysiology. Fruits, vegetables, and legumes are excellent sources of magnesium, a mineral often found to be deficient in the plasma and brain tissue of individuals experiencing migraines. Magnesium is essential for mitochondrial energy production and contributes to various physiological processes, including vasoconstriction, inhibition of platelet aggregation, and regulation of serotonin secretion all of which are relevant for managing migraine symptoms (55).

This study is the first to present evidence of an association between the HEI, the LLDS, and migraine-related factors. Dietary data were collected using a validated FFQ, and participants with implausible calorie intakes (>4,000 or < 600 kcal) were excluded from the analysis. To ensure accuracy, interviews were conducted by three trained researchers.

Despite its strengths, this study has several limitations. First, its cross-sectional design precludes establishing causal relationships between diet quality and migraine outcomes. While the findings suggest associations, the temporal relationship between dietary intake and migraine symptoms cannot be determined. Second, the sample size, although sufficient for initial exploratory analyses, was relatively small and drawn from a single clinical setting. This may limit the generalizability of the findings to broader populations, particularly those with different sociodemographic or cultural backgrounds. Third, potential biases, such as recall bias, may have influenced the dietary data collected through the FFQ. Although the FFQ has been validated for the Iranian population, self-reported dietary intake is inherently prone to inaccuracies. Finally, while multivariable logistic regression models were used to adjust for confounders, the number of adjustment variables was limited. This raises the possibility of residual confounding from unmeasured variables, such as other dietary or lifestyle factors, genetic predisposition, or environmental influences. Future studies should aim to include a broader range of confounding factors and employ more robust statistical techniques to minimize bias.

Conclusion

Based on the findings of our study and the underlying mechanisms, managing overall diet quality, rather than focusing solely on individual macronutrients or micronutrients, appears to be a promising strategy for improving the prognosis and overall condition of individuals with migraines. However, further research is needed to validate the findings of the present 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 Zanjan University of Medical Science. The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent for participation in this study was provided by the participants' legal guardians/next of kin.

Author contributions

MF: Methodology, Writing – original draft, Writing – review & editing. FS: Data curation, Methodology, Writing – original draft, Writing – review & editing. GB: Conceptualization, Investigation, Writing – original draft. RM: Investigation, Methodology, Project administration, Writing – review & editing. MR: Writing – original draft, 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.

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Exploring how researchers consider nutrition trial design and participant adherence: a theory-based analysis

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Introduction: Nutrition trials are important for informing dietary and clinical guidelines. Central to the success of these trials is participant adherence to dietary behaviors. However, trials commonly experience poor adherence. This study seeks to understand if and how researchers consider supporting participant adherence to dietary behaviors and their relationship to using behavior change science when designing trials.

Methods: A mapping exercise was undertaken to create matrices that describe the landscape of current nutrition trials. A total of 12 researchers participated in semi-structured, one-on-one interviews. Transcripts were analyzed using (i) the theoretical domains framework (TDF) to identify themes in current practice and beliefs, and (ii) the capability, opportunity, motivation, and behavior model to identify barriers and enablers to using behavior change science in the design of nutrition trials.

Results: Twenty-two belief statements were identified across all 14 TDF domains and were conceptualized as 5 key themes with respect to designing nutrition trials to improve participant adherence: (i) what was done, (ii) how it was done, (iii) why it was done, (iv) adherence challenges, and (v) conflicting beliefs. Regarding using behavior change science when designing trials, some researchers felt this would be beneficial but lacked the knowledge and skills to do so, while others were skeptical of its value over the current experience-based practice.

Discussion: Researchers are motivated to encourage participant adherence to dietary behaviors, and, consciously and subconsciously, implement a range of strategies through non-systematic methods in their trials. Future publications would benefit from the explicit documentation of levels of adherence to dietary behaviors and strategies implemented to improve adherence.

KEYWORDS

patient adherence, nutrition trials, behavior change science, methods, research design, treatment adherence and compliance

Introduction

Nutrition intervention trials are key for informing dietary guidelines and clinical practices (1). Inherent to these trials, is the need for participants to perform certain dietary behaviors to answer questions about primary outcomes. Dietary behavior is an umbrella term that refers to all phenomena related to food choice, eating behavior, and dietary intake/nutrition (2). These can range from simple, such as taking a supplement or single food item, to more complex behaviors, such as changing whole dietary patterns. Hence, adherence to the dietary behavior, or the extent to which a participant actively follows an investigator's instructions on the behavior, is often a spectrum rather than binary; additionally, it may be part of the intervention arm only or part of both intervention and control arm, i.e., a trial process. Given the challenging nature of changing one's dietary habits, nutrition trials face a unique challenge in measuring and achieving adherence (3, 4). From here on, participant adherence specifically refers to adherence to dietary behaviors within a trial.

Commonly in trials, dietary behavior change is conceptualized as part of the intervention, where only participants in the intervention arm are asked to perform the target behavior. For example, participants in the intervention arm of a trial that looked at the metabolic effect of an adapted Mediterranean diet were asked to change their dietary pattern for 12 weeks, while the control arm was asked to continue their habitual diet (5). However, it is important to note that performing dietary behaviors may also be part of trial processes, whereby participants on all arms of a trial are required to perform that behavior. For example, in a study investigating the health effects of regular consumption of red meat compared to plant-based meat alternatives in young adults, both arms were required to adhere to a basal vegetarian diet (6). Indeed, a trial may involve dietary behaviors as part of the intervention and the trial processes. For instance, one crossover trial investigating kiwifruit consumption on intestinal function required participants to consume two kiwifruits daily for 3 days as the intervention arm, consume two isocaloric controls twice daily for 3 days as the control, and fast overnight prior to the MRI scan as part of the trial processes (7). Consequently, researchers may need to carefully design their trials to support participant adherence to multiple dietary behaviors of varying complexity and duration.

Nutrition trials exist on a continuum between efficacy trials, where adherence to a dietary behavior is required to elucidate the effect a food or dietary pattern has on human health, to effectiveness trials, where dietary behavior change is desired to understand its effect in a real-world setting (8). Central to the success of trials that lie closer to the efficacy end of the spectrum, is the need for participants to adhere to the dietary behavior change required within the trial (9, 10). Unfortunately, many nutrition trials suffer from low participant adherence and high attrition rates (7–10). For efficacy trials, the magnitude, or observed effect, of the dietary intervention on the primary outcome is dependent on the level of adherence. Poor adherence decreases the likelihood that the results reflect the true effect of the intervention (11). Measuring and reporting adherence to dietary behavior in both efficacy and effectiveness trials is essential for understanding its true influence on primary outcomes (12). However, there is often heterogeneous and insufficient documentation of adherence in nutrition trials (13–15). Consequently, it is important to support and measure participant adherence to dietary behaviors, as well as adequately report these efforts and their outcomes.

The design of a trial can either facilitate or hinder adherence (16). For instance, using behavioral strategies, such as goal setting and self-monitoring, has been shown to improve adherence to lifestyle interventions (17). When considered through the lens of behavior change science, these strategies are known as behavior change techniques (BCTs) and are defined as the "active ingredient" that brings about behavior change (18, 19). Despite research advocating for transparent and replicable methodology, little is documented about how or why researchers select and implement certain BCTs to enhance adherence to dietary behaviors, whether that be for the intervention or trial processes. Behavior change frameworks provide a systematic, theory-based way of selecting BCTs that are most likely to bring about change. Over recent years, these frameworks have been applied to improve the design of interventions aimed at changing health and environmental behaviors and are returning promising results in terms of efficacy (20, 21). Additionally, public health guidelines advocate for the use of such frameworks within strategy design (22). Consequently, using behavior change science, such as frameworks to select BCTs, not only in the design of lifestyle interventions but within the design of trials involving any dietary behavior, is likely a promising avenue to enhance participant adherence.

Given the breadth of nutrition trials, an important starting point for this research is to understand current trends in the types of nutrition trials being conducted, including conditions of interest, the complexity of interventions, levels of adherence, and the type of dietary behaviors trials involved. Additionally, this will identify a representative pool of researchers as potential participants across nutrition trials to interview. As such, the primary aim of this research is to understand the behavioral factors that drive nutrition researchers' selection of strategies within the trial design to enhance participant adherence to dietary behaviors. Additionally, these researchers' relationship to using behavior change science when designing trials involving dietary behavior changes will be investigated, and strategies to support future researchers in using behavior change science will be considered.

Objectives

The purpose of this research is threefold:

i To describe the current landscape of nutrition intervention trials, including types of trials being conducted, conditions of interest, the complexity of interventions, and the types of dietary behaviors involved, and to identify the levels of adherence within these.
ii To identify behavioral determinants that influence how researchers design nutrition trial components to support participant adherence to dietary behaviors.
iii To understand researchers' relationships with behavior change science, as well as the barriers and enablers to its use in the design of nutrition trials.

Methods

The Consolidated Criteria for Reporting Qualitative Research (COREQ) checklist (23) was used to guide study reporting (Supplementary file S1).

Part 1. Conceptualizing nutrition trial areas

As the field of nutrition research is so broad, a mapping exercise was undertaken to identify areas of high research activity within it. The Clinical Trials Registry (clinicaltrials.gov) was searched for nutrition intervention trials that had results first posted in the past year (1 June 2022–1 June 2023). A limited date range was selected to retrieve a manageable sample size. For 'Other Terms', "nutrition OR diet" was entered. Filters included selecting trials classified as interventions, conducted among adults (18+ years), that accepted healthy volunteers, and with recruitment marked as completed. A matrix was created that described the type of dietary intervention and condition investigated. Definitions of intervention types were as follows:

Simple intervention: trials in which the primary purpose is to investigate a supplement, drug, or single nutrient.

Dietary intervention: trials in which the primary purpose is to investigate a specific dietary pattern or combination of dietary components.

Multi-component intervention: trials in which the primary aim is also to change another behavior (e.g., physical activity) alongside diet.

Device and/or procedure intervention: trials in which the primary purpose is to investigate a device or medical procedure (e.g., gastric band).

A second matrix was created that described the type of dietary behavior in the trial (e.g., simple or complex) and the reported level of adherence. In addition, the incorporation of dietary behavior change into nutrition trials was considered by authors as desired or required. In trials investigating the effect of complex interventions, dietary behavior change is often desired of participants as a direct outcome of the intervention. For example, an intervention evaluating the effectiveness of a multi-component, community-based healthy eating program aims to encourage participants to change their dietary behavior as a result of the intervention. On the other hand, trials evaluating the physiological or psychological effect of consuming a specific supplement, nutrient, food, or dietary pattern require participants to change their behavior. For example, an efficacy trial investigating the impact of a low-fat diet on bile production requires participants to adhere to a low-fat diet to elucidate the primary outcome of the study.

Data for these matrices were extracted from the information published on clinicaltrials.gov, attached files (e.g., protocols), and associated publications. Of note, not all trials from the search had published articles with relevant data on adherence and as such were coded as 'data not available' in the second matrix.

Part 2. Interviews

Sampling and recruitment

All corresponding authors from the articles identified in Part 1 were contacted via email inviting them and/or their co-authors involved in the trial design to participate in one-on-one interviews; this convenience sample was deemed reflective of a range of articles reporting high, low, and insufficiently reported adherence to dietary behaviors. Upon expression of interest following this email, they were sent a second email with an attached participant information sheet (PIS) and consent form. Potential participants were told author AW would be the interviewer and provided brief information on her research in the PIS; no other interviewer characteristics were provided. Consenting authors of articles will hereon be referred to as 'researchers'.

Previous literature has recommended that a minimum of 10 interviews be conducted for initial data analysis, followed by three additional interviews until data saturation is reached, that is, there are three consecutive interviews where no new themes arise (24). Hence, to identify when this stopping criterion was reached, data were analyzed concurrently with progressive collection.

Data collection

Semi-structured qualitative interviews were conducted, and video was recorded on Zoom (version 5.16.10, Zoom Video Communications Inc.) between 29 August 2023 and 23 November 2023. An interview topic guide was developed using the Theoretical Domains Framework (TDF) and the Capability, Opportunity, Motivation, Behavior (COM-B) model (18). The topic guide was refined by a discussion between two researchers experienced in using the TDF and COM-B models following mock pilot interviews. The final version can be found in Supplementary file S2. There were two main parts to the interview. The first part aimed to understand the determinants that influence how researchers design nutrition trial components to support participant adherence to dietary behaviors. The second part aimed to understand researchers' relationship to behavior change science, and their barriers and enablers to using it in nutrition trial design.

All one-on-one interviews were conducted by AW who is a New Zealand Registered Dietitian; at the time of the interviews, she was a full-time PhD student and had 3 years of experience in running focus groups and one-on-one interviews, as well as training in using the Behavior Change Wheel, the TDF, and BCT taxonomy version 1 (BCTTv1). The interviewer adapted the order of questions within the topic guide to facilitate the natural flow of conversation and took field notes throughout. The interviews lasted up to 60 min.

Data analysis

Audio transcripts were exported using the Zoom software and then checked by AW that they had been transcribed verbatim. Identifying information, such as names and organizations, was removed. Transcribed interviews were sent to researchers within 1 week for them to amend or withdraw parts of the transcript; at this stage, they were provided the opportunity to add further written comments at the end of the transcript. Researchers were given a 2-week timeframe for this task from the date the email was sent; they did not provide feedback on the overall findings.

Returned transcripts were uploaded to NVivo (Version 12) for theory-based content analysis. A coding guideline (i.e., a set of explicit statements of how the TDF is to be applied to a specific data set) was developed by AW and TC (Supplementary file S3) (25). This was used by AW to deductively code statements into the most relevant TDF domain. A second author (TC) independently coded two of the first four transcripts, and discrepancies between coders were discussed to iterate the interview script and coding guideline to ensure that all relevant data were being captured and accurately coded. Specific belief statements were then inductively generated within each theoretical domain by AW; belief statements are statements that summarize a collection of responses with a similar underlying belief influencing the target behavior (26). Where possible, frequency counts of certain belief statements across all interviews were generated by counting

once within each interview. Relevant theoretical domains were identified by the (1) relatively high frequency of specific beliefs, (2) presence of conflicting beliefs, and (3) evidence of strong beliefs that may affect the target behavior (27). Additionally, the BCTTv1 was used to classify strategies researchers reported using to enhance participant adherence (19); each BCT was recorded only once across all transcripts to demonstrate the range of techniques used as opposed to the frequency.

Results

Part 1. Conceptualizing nutrition trial areas

The search returned 55 registered trials. For the purpose of this study, the authors were interested in adherence to eating behaviors, and consequently, trials not involving an act of consumption were excluded ($n = 7$). Additionally, 11 studies were excluded as they focussed on other topics (e.g., smoking cessation and physical activity). The remaining 37 trials were categorized by the intervention type [i.e., simple, dietary, complex, or device (Table 1)] and health condition related to the primary outcome.

Table 1 shows a high proportion of nutrition trials had a primary outcome related to obesity ($n = 12$). In terms of intervention type, there were a similar number of simple ($n = 16$) and complex interventions ($n = 14$) reported. The majority of trials had a primary outcome that was physiological ($n = 31$) rather than behavioral. Complex interventions tended to be longer than 4 weeks, while simple interventions were shorter in duration.

Table 2 shows that, of the studies that had data available, the majority ($n = 15$) did not report adherence in sufficient detail, if at all. In trials that required behavior change, there was a mix of simple and complex dietary behaviors; of those with high adherence, all intervention supplements or food were provided. Of the identified studies, all desired behaviors were complex, did not provide the totality of food, and half had insufficient or no adherence to the behavior reported.

Part 2. Interviews

Participant characteristics

Twelve researchers responded and consented to participate (50% female), while no response was received from the other researchers. The majority of researchers worked in the United States ($n = 9$), while the remaining individuals worked in Italy, the United Kingdom, and New Zealand. The majority of researchers ($n = 8$) were principal investigators of the trial they were identified through; other roles included research dietitians ($n = 2$), a study coordinator ($n = 1$), and a principal scientist ($n = 1$). All researchers were involved in the design and conduct of the trial described in the publication they were identified through. Researchers reported having between 5 and 45 years of research experience, with an average of 18 years. Two researchers considered themselves experts in behavior change science. With this sample size, it was deemed that sufficient depth of understanding of the phenomenon had been reached.

Interview part 1. How do researchers design nutrition trials to support participant adherence?

Twenty-two belief statements were identified, covering all 14 TDF domains, and can be conceptualized as 5 key themes with respect to designing nutrition trials to improve participant adherence to dietary behaviors. The themes are (i) what was done, (ii) how it was done, (iii) why it was done, (iv) adherence challenges, and (v) conflicting beliefs (Table 3). TDF domains are included below in parentheses for further context.

TABLE 1 Matrix of nutrition trials with results published on clinicaltrials.gov between June 2022 and June 2023.

Primary intervention type Condition[&]	Simple	Dietary	Multi-component interventions	Device	Total studies
Obesity	B* X* X* X* X* X	X* X X	X X	X	12
Healthy (establishing food safety, biomarker, etc.)	X* X* X		B		4
Osteoarthritis/osteoporosis			X X		2
Pregnancy		X	X X		3
Cognitive function	X* X				2
Cardiovascular disease	X		B X		3
Diabetes Mellitus	X	X	B B X		5
Gastrointestinal health	X* X* X	X			4
Other (aging, cancer)			B* X		2
Total Studies	16	6	14	1	37

B, behavioral primary outcome; X, physiological primary outcome; *, Intervention ≤ 4 weeks.
[&]The condition of the trial's primary outcome focussed on preventing, improving, or understanding.
Definitions of intervention types:
Simple intervention: trials in which the primary purpose is to investigate a supplement, drug, or single nutrient.
Dietary intervention: trials in which the primary purpose is to investigate a specific dietary pattern.
Multi-component intervention: trials in which the primary aim is also to change another behavior (e.g., physical activity) alongside diet.
Device and/or procedure intervention: trials in which the primary purpose is to investigate a device or medical procedure (e.g., gastric band).

TABLE 2 Adherence of nutrition trials with results published on clinicaltrials.gov between June 2022 and June 2023.

Dietary behavior Adherence	Required	Desired	Total studies
Higher (>80%) or statistically significant change	S* S* S* S* S* C* C*	C C	9
Lower (<80%) or no statistically significant change		C C C	3
Not reported in sufficient detail	S* C	C C C C C C	8
Not reported within the article	S* S* S C C C	C	7
Data not available[&]	S* S* S* S* S* C* C* C*	C C	10
Total studies	23	14	37

*All intervention supplements or food provided.
[&]Results of identified trials in the registry were not published at the time of the search.
S—Simple dietary behavior: behavior that requires minimal steps, e.g., taking a pill, supplement, or performing a one-off behavior.
C—Complex dietary behavior: a behavior that is a combination of different behaviors, e.g., changing multiple dietary behaviors to follow a dietary pattern.
Required—behavior participants need to perform within a trial to maintain validity.
Desired—behavior desired of participants as a direct outcome of the intervention.

What was done?

The majority of researchers ($n = 10$) reported that dietary adherence was defined in their trial (knowledge), while one said it was not, and another could not remember. Nine participants also reported measuring dietary adherence within their trial. The method of measuring adherence was dependent on dietary behavior. Types of measurements included self-reported questionnaires specific to the study behavior, collection of containers or food waste to prove consumption, 24-h recalls, doubly labeled water, witnessing food being consumed (e.g., via Zoom or photos), and blood biomarkers. Many researchers believed that trial design impacts a participant's ability to adhere (beliefs about consequences), and as such made compromises in the trial design to support participants. Additionally, many researchers highlighted that to improve adherence, they screened for people who were more likely to be adherent to their targeted dietary behavior when recruiting (skills). All researchers reported using strategies (skills) to enhance participant adherence that could be classified as BCTs. Using the BCTTv1 (19), 14 BCTs were identified across the transcripts (Supplementary file S4); few researchers described these strategies using BCT terminology.

How it was done?

Many researchers expressed how their experience in trials was primarily what informed trial design and their selection of strategies to support participant adherence (behavioral regulation). Additional aspects that informed chosen strategies to support participant adherence included using the literature and strategies used in similar trials (memory, attention, and decision processes), seeking advice from other members of their team or experts (social influences), and thinking about the potential participant barriers to the targeted dietary behavior (memory, attention, and decision processes). For some, thinking about supporting adherence was a conscious process, while for others, choosing strategies to support adherence was done implicitly.

Why it was done?

The majority of researchers ($n = 10$) saw it as part of their role to help participants be adherent (social professional role and identity) and felt highly motivated to achieve participant adherence (intention). Researchers saw it as important to encourage adherence, as poor adherence decreases the validity of the trial and wastes resources (reinforcement/beliefs about consequences). However, the study design and strategies chosen were influenced by the budget and time available for each trial (environmental context and resources).

Adherence challenges

One of the most common challenges voiced was difficulty achieving adherence due to trial participants "*just doing what they want to do*" (P2) (social influences). Additionally, researchers voiced accurately measuring dietary behaviors was a challenge due to believing existing measures of dietary assessment are flawed and difficult to conduct (beliefs about consequences). The complexity of the dietary behavior in question also impacted researchers' confidence levels, with more complex behaviors lowering confidence in their ability to conduct a study with high adherence (beliefs about capabilities). Together, these challenges contributed to feelings of stress or frustration regarding adherence (emotion).

Conflicting beliefs

Three domains had the presence of conflicting belief statements. The majority of researchers voiced the importance of achieving good participant adherence. For some, it was one of the highest, if not the highest, priority, while for others, achieving the trial outcome or recruitment took priority (goals). Researchers also differed in their expectations of participants adhering; one group held an expectation that participants would adhere to dietary behaviors in their trial, while another group was hopeful but not certain they would adhere (optimism). Finally, researchers differed in how much they thought about participant adherence when designing their trial; some had developed a habit of thinking about it from the start of trial design, while others reported not giving it a lot of thought, despite recognizing its importance (behavioral regulation).

Interview part 2. Barriers and enablers to using behavior change science

Supporting quotes can be found in Supplementary file S5.

Capability

Many researchers expressed they do not have adequate knowledge about what behavior change science is, or how to use it in the design of nutrition trials. Confidence levels in their perceived ability to use behavior change science varied depending on their

TABLE 3 Determinants that influence how researchers design nutrition trials to support participant adherence to dietary behaviors.

Theme	Belief Statement (*theoretical domain*)	Illustrative quote
What was done	We defined and attempted to measure adherence to dietary behaviors in our trial (*knowledge*)	*"… we had to understand if they were adherent to the different diets, one which was a Mediterranean diet, another which was a lacto-ovo vegetarian diet. So we tried to estimate the adherence with two measures. One was the questionnaire…and we performed a 24 [hour] recall…" P5*
	We have implemented some strategies to try and improve adherence in our trial *(skills)*	*"So we actually gave our participants things like a large jug of olive oil. We collaborated with certain brands that provided walnuts or almonds, things like that. So, we tried to reinforce, you know, a diet that has a lot of evidence behind it" P4*
	When recruiting, we screen for people we think are more likely to be adherent (*skills*)	*"When you enroll people it's [important] to really make sure you get people who fully understand and are, I guess you could say fully, or are motivated. So find people who are motivated and want to change and want to do this study and want to want to follow my instructions." P8*
	We made compromises in the trial design to support participant adherence, as a good trial design can improve participant adherence (*beliefs about consequences*)	*"We kind of sacrificed this piece of it like controlling what really they are having because we thought that this would increase the feasibility and increase the generalisability of the study, you know. So, I think that for nutrition trials in particular, I think it's pretty tough to have a trial that is so controlled, because that's where I think adherence becomes more complicated." P3*
How it was done	Reflecting on my experience in trials helps me choose what strategies to use to support participant adherence (*behavioral regulation*)	*"So I was designing and doing different studies, and trial and error… So I think I would credit that to my postdoc and the ability to run all kinds of different studies and see what's worked." P8*
	We use the literature to inform what strategies we choose to improve participant adherence (*memory, attention, and decision processes*)	*"We try to understand what was has been done in the literature our best. We had some meetings before in order to understand how could we improve the adherence, and we found these strategies in the literature." P5*
	We consider what would stop participants from adhering when designing our trial (*memory, attention, and decision processes*)	*"We really tried to think about all the places that people make decisions about food and have something in place for every single one of those." P7*
	I seek advice from other members of my team, participants, or experts to help choose strategies that are more likely to improve adherence (*social influences*)	*"We discuss together when we decide to design study also for this [adherence] aspect. We have, we are a multidisciplinary team, so some are more involved in this aspect, some others less. We are all susceptible to this problem and we try to find a solution we can, we can do in this context." P5*
Why it was done	I am highly motivated to encourage participant adherence (*intention*)	*"[I'm] highly motivated, because it's actually quite a job getting participants to commit to something like that, and we do not want to have too many dropping out, or have to recruit large number to allow for that. So, it's pretty important the ones we get will stick with it, and that we do not need to allow for too many dropouts." P12*
	When designing a trial, it is part of my role to help participants be adherent (*social, professional role, and identity*)	*"I think that it's my role to really worry about how I'm going to get people to enroll and then to stay." P3*
	Poor adherence can mean we have to spend more time and money on our trial to make it work, so we try to think about it from the start (*reinforcement*)	*"Someone who's not adherent will potentially skew your results. Potentially, it means that you have to recruit more people and spend more money or spend more time or resources. So… that's the incentive to think about it in advance, and then come up with good strategies to make sure people adhere, because if they do not, your study might just not work." P11*
	Our choice of strategies to support adherence is influenced by our resources (budget, personnel, and time) (*environmental context and resources*)	*Interviewer: "Do you recall how you decided what strategies to use to improve participant adherence?"* *P10: "Usually it's budgetary, unfortunately…"* *"… It's one of those things that we have to be available when the participant needs you. But I think that's actually a big challenge to be available when people needed us, because we did not have the infrastructure where we could just always be on call." P3* *"…if they had all the money in the world they would use the best methods available as well, but sometimes, you know, the diet intervention methods they slowly get kind of chipped away in order to fit into the budget." P7*

(Continued)

TABLE 3 (Continued)

Theme	Belief Statement (*theoretical domain*)	Illustrative quote
Adherence challenges	Trial participants are only human and this can make it hard to achieve adherence (*social influences*)	*"The whole idea of adherence is impossible. And then a dietary intervention is impossible. I mean, they are not lab animals. So you just gotta have expectations. And I think granting agencies do not always realize that. And even reviewers that you need to be realistic…these are humans who go to work and parties in school and high school, and whatever grade they are in. And you know they are gonna eat things they are around that you do not want them to eat or they are not gonna keep track." P2* *"And knowing that participants are human and that they have their lives, you know, participating in studies is not their primary goal, maybe probably even secondary or tertiary and so working within those confines." P1*
	Measuring dietary behaviors to assess adherence is flawed and difficult *(beliefs about consequences)*	*"So we look at adherence more as session attendance or self-monitoring adherence. But we know that dietary measurement is so messy and so prone to errors that it does not seem like the ideal focus." P1* *"…it's all self-report so I have no way of to know if they really took it, but they seem to be." P2*
	My confidence to run a study with high adherence depends on the complexity of the dietary behavior (*beliefs about capabilities*)	*"I think it depends on how complicated your dietary intervention is… If you are trying to change a whole diet. and for a prolonged period, you know longer than for a couple of days, I imagine that would that that's not something I've had, I've done, but I think that that would be extremely challenging, and I'm not sure that I would have huge amount of confidence doing that level of nutritional or dietary intervention" P11*
	Promoting adherence can be stressful or frustrating for me (*emotion*)	*"I get feelings of a little bit of stress, because I remember how challenging it was." P4*
Conflicting beliefs	Achieving good participant adherence is important, but recruitment or achieving the outcome takes priority (*goals*) vs. Achieving good participant adherence is one of the highest priorities for us (*goals*)	*"The goal was weight management, and so our supervision was more focused on were they meeting the expected weight trajectory rather than were they meeting our standards related to dietary adherence." P1* vs. *It's one of the highest priorities… if our participants are not adhering to the diets, my job is pointless, you know. So it's high priority. P7*
	I was hopeful participants would adhere, but not widely optimistic they would (*optimism*) vs. I expected participants to adhere to the desired dietary behavior because we made it easy for them (*optimism*)	*"We're not forcing them to be in the trial. They know what they are getting into. So, I mean, I do not know if I would say I'm widely optimistic, but I think it should work." P2* vs. *"Yes, I expected them to, because it wasn't a particularly difficult ask and we had quite clear instruction and it wasn't over a prolonged period of time, so there was, there should not have been much to stop them from being able to adhere to it. We made it very simple for them." P11*
	I do not give a lot of thought to participant adherence (*behavioral regulation*) vs. I think about participant adherence from the beginning of trial design (*behavioral regulation*)	*"It's not something I've actually given a lot of thought to, participant adherence, even though it's obviously very important." P12* vs. *"I think you have to think out [participant adherence] ahead of time… you just have to do that extra work." P6*

area of expertise and years of experience designing trials. For instance, dietitians with training in using behavior change science reported higher confidence levels. One behavior change expert expressed concern at other researchers using behavior change science when outside their area of expertise, describing it as "*contains a lot of subtleties that come from years of experience*." Researchers suggested further training in applying behavior change science and having real-life examples to work from to increase confidence in their capability. Many were confident in their skills to do so if training was provided.

Opportunity

In general, researchers responded positively about the acceptance of using behavior change science among them and their colleagues. Two researchers were skeptical that it would be encouraged by other researchers and reviewers. Additionally, a key enabler identified through the interviews for using behavior change science was collaboration and networking with colleagues, particularly those who have more experience in its implementation. Discussing with colleagues was perceived as a way for researchers to question and improve current practices. Researchers perceived limited time and

funding would stop them from using behavior change science in trial design. Access to resources, training, expertise, and literature was seen as enablers, as these were perceived to increase capability.

Motivation

Some researchers reported they would be motivated to use behavior change science if there was reinforcement from funding agencies. Equally, some researchers expressed how they had not thought about using it; it does not exist as a habit for them. About half of the researchers reported high motivation to use behavior change science in this context as they saw it as important for improving trial design and validity, and beneficial for the wellbeing of their participants. The other half of participants expressed lower motivation to use it, primarily due to the lack of evidence that it would lead to greater adherence than their current practices.

Discussion

Given that nutrition trials often suffer from poor adherence to dietary behaviors, this study sought to understand if and how researchers consider participant adherence to dietary behaviors when designing a trial. The qualitative aspect of this study identified that many researchers consider participant adherence as important and attempt to define, measure, and support dietary adherence, often by relying on methods that have worked in their own experience or those used in other trials. When probed about using behavior change science in the design of trials, one group of researchers felt this would be beneficial but lacked the knowledge and skills to do so. Another group of researchers were more skeptical about the use of behavior change science in this way without evidence that it works better than current practice.

The matrices echo previous literature, highlighting the issue of poor participant adherence across different types of nutrition trials (1). In particular, they demonstrate that trials involving complex behaviors in real-world settings are more likely to have poor adherence than those involving simple behaviors or those where all food is provided (i.e., controlled feeding studies). Indeed, the confidence level of researchers in their ability to run a trial with good adherence decreased as the complexity of the behavior increased. All researchers reported thinking about participant adherence to various extents when designing their trial, and as a result, implemented strategies to support their participants. Few researchers had a systematic process for doing this, relying instead on their own experiences or those of others. This selection process, based on intuition, experience, and assumptions, is used by many when designing interventions to change health behaviors, including clinicians (28), and is known as the "*It Seemed Like A Good Idea At The Time*" (ISLAGIATT) principle (18). This is not to say this method is ineffective, but it certainly is not transparent or replicable, as advocated for in research (29). Together, this could indicate a need for researchers to use different methods of selecting strategies for enhancing adherence depending on the complexity of behavior in question. From this research it could be inferred using the ISLAGIATT principle is sufficient for informing the design of trials involving simple dietary behaviors, while a more systematic, evidence-based method may be more effective for supporting adherence to complex dietary behaviors.

Many researchers looked to other articles to see what strategies they used to support adherence. Consequently, sufficient reporting in articles about how adherence was supported, such standardized reporting using the BCTTv1 (19), and the resulting level of adherence, is important to build a greater understanding of how this can be improved. Of course, from the lens of behavior change science, care needs to be taken with this method; transplanting what works for one behavior in one specific context and population is not guaranteed to work in another (30, 31), which could perpetuate the problem of poor adherence and its consequences on research validity and resource waste.

This is where providing a systematic method to select evidence-based BCTs, such as using behavior change frameworks, could play a key role. However, although all researchers viewed it as part of their role to enhance participant adherence, how many go about this is currently a self-taught, experienced-based art, as opposed to a systematic science. In our interviews, there was a consensus of insufficient knowledge and skills to apply behavior change science in trial design. Possible enablers suggested by researchers, and also aligning with expert recommendations (30), included providing further training on how to do so, or including behavioral scientists on the trial team. Additionally, some researchers were unmotivated due to the absence of evidence demonstrating that the use of behavior change science in this way would enhance adherence more than current practices. Indeed, the evidence base supporting this practice is still in its infancy, although it shows promising results (30, 32, 33). It is also important to note that there is little empirical evidence on the effectiveness of efforts to support adherence using the ISLAGIATT method (34).

The matrices highlight a potentially more imminent problem though. Despite the majority of researchers saying they define and measure adherence, as well as iterating the importance of it, the matrices indicate there is often no or inadequate reporting of dietary adherence. Additional literature also highlights this issue (15, 35). One possible reason for this is the lack of emphasis on documenting adherence to current reporting guidelines such as CONSORT. Recently, a Nutrition Extension for CONSORT was proposed and peer-reviewed (36, 37). An important addition is the requirement of articles to report the level of dietary adherence, or compliance with the intervention, in the trial and discuss the implications of adherence within the trial (36). This addresses previous research that has advocated for nutrition trials and reviews to report the definition and assessment of adherence in the methods and the resulting degree of adherence in the results (15).

Considering general compliance with CONSORT reporting guidelines is poor (35, 38), researchers may need additional support to comply with the CONSORT Nutrition Extension guidelines. For instance, dietary adherence must be measured to be reported. Researchers may need more support with selecting and implementing methods of dietary assessment, as doing so was viewed as a challenging aspect of trial design by researchers involved in this study. Framing the use of the CONSORT Nutrition Extension as behavior and applying learning from implementation science could add value and may be of use to facilitate uptake.

Strengths of this research include its basis on the TDF and COM-B model; this provided a systematic and thorough framework to explore the current beliefs and behaviors of researchers, such as

insight into how researchers make efforts to enhance participant adherence, something often not reported in the literature (35). Understanding current behaviors, what drives them, as well as barriers to using behavior change science, provides a foundation for designing support to change researchers' behaviors. However, the sample size, although diverse, was small and subject to self-selection bias, limiting its generalisability to other settings and populations. It was not powered to identify differences in beliefs and behaviors by researcher characteristics, such as their years of experience or background training, although these undoubtedly influence how one approaches designing a trial. Another potential limitation is we did not compare what researchers said they did, with what was reported in their article.

Conclusion

Researchers are motivated to encourage participant adherence and implement a range of strategies to do so, often through non-systematic methods. Some researchers perceived behavior change science to be a promising alternative to improve trial design, while others were skeptical of its value over current practice. To build the knowledge base of how participant adherence can be enhanced, future research would benefit from the explicit documentation of strategies implemented in nutrition trial design and the resulting level of adherence.

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 Auckland Human Participants Ethics Committee (UAHPEC) (reference UAHPEC25835). 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.

Author contributions

AW: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing. TC: Formal analysis, Methodology, Writing – review & editing. KG: Conceptualization, Methodology, Writing – review & editing. RR: Conceptualization, Writing – review & editing. AB: Conceptualization, Supervision, 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

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Adaptation of the nutrition care process for metabolic diseases in the Mexican population

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Background: The Nutrition Care Process (NCP) is a systematic framework designed to enhance the quality of nutrition care. Given the high prevalence of metabolic diseases in Mexican population, there is a critical need for tailored nutrition care strategies.

Objective: We aim to describe the adaptation of the NCP to manage metabolic diseases in Mexican individuals.

Methods: Our adaptation included a comprehensive literature review of clinical nutrition guidelines, by a structured consultation with experts to ensure clinical setting-specific and culturally appropriate modifications. A team of registered dietitians from two tier 3 hospitals, each with over five years of experience in metabolic disease management, customized the NCP's four core steps—assessment, diagnosis, intervention, and monitoring—to meet the specific needs of the Mexican population.

Results: We adapted the NCP to manage five common metabolic disorders: obesity, type 2 diabetes, kidney disease, metabolic dysfunction-associated steatotic liver disease, and dyslipidemia. Each step of the NCP was complemented by the development of educational materials designed to (1) enhance awareness of disease risk, (2) broaden their knowledge of nutritional management, and (3) provide tailored strategies for developing personalized action plans. The adapted NCP was implemented in clinical and research settings and the materials were documented as an online publication to facilitate widespread dissemination.

Conclusion: Our adaptation represents a significant advancement in the use of structured tools for nutrition care in Mexican populations, who face

disproportionately high rates of metabolic diseases. Further research is needed to assess the effectiveness of this approach in clinical settings.

KEYWORDS

nutrition therapy, educational, diabetes mellitus, obesity, metabolic diseases, population health

Introduction

Metabolic diseases, including obesity, Type 2 Diabetes Mellitus (T2DM), chronic kidney disease (CKD), Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD), and dyslipidemia, represent a significant global health challenge, particularly for Hispanic populations, where the rates of these disorders are disproportionately high. In Mexico, the 2022 National Health and Nutrition Survey (ENSANUT) indicates that 75.2% of Mexican adults are classified as overweight or obese (1). In 2021, this alarming rate was linked to 118,000 deaths attributable to elevated body mass index (BMI), with elevated BMI accounting for 55% of T2DM-related deaths and 41.1% of deaths from CKD (2). Dyslipidemia also significantly affects the adult population, with approximately 50% presenting some form of lipid disorder (3). Moreover, MASLD (previously known as NAFLD and later as MAFLD), represents a significant and growing public health challenge in Mexico with a prevalence of 17–41.3%, this condition is intricately linked to the country's rising rates of obesity, T2DM, and metabolic syndrome (4). Despite its impact, accurate diagnosis of MASLD remains limited due to diagnostic challenges (5). In 2021, the prevalence of CKD was reported at 9,184.9 cases per 100,000 inhabitants, largely driven by T2DM, the leading cause of CKD. T2DM contributed to 69,052 deaths (95% CI = 60,412–77,991) across all age groups in Mexico (6). Furthermore, the prevalence of T2DM was estimated at 18.3% among adults aged 20 years and older, equating to around 14.6 million individuals (7).

Unhealthy dietary habits, particularly the consumption of sugary drinks, processed meats, saturated fats, and general caloric imbalance, are the most significant modifiable factors associated with metabolic diseases, contributing to 27.3% of Disability-Adjusted Life Years (DALY) lost (8). Effective management of these diseases requires addressing dietary risk factors. Nutritional Medical Treatment (NMT) is a crucial component emphasized in various consensus statements for its integration into multidisciplinary teams managing metabolic conditions. Guidelines recommend implementing NMT through comprehensive nutritional education programs aimed at promoting self-care. This approach should be consistently reinforced across different life contexts to achieve metabolic control, reduce complications, and improve quality of life (3, 9). International guidelines advocate for nutrition professionals to utilize evidence-based NMT to address nutritional issues at both individual and population levels.

The Nutrition Care Process (NCP), introduced by the Academy of Nutrition and Dietetics in 2003, provides a valuable framework for implementing NMT across various clinical settings (10–13). Despite its potential, the NCP is underutilized in nutrition service centers, primarily due to barriers such as inefficient staffing, limited time for documentation, and the lack of necessary infrastructure, including supportive electronic health record systems (14–17). While the NCP has been shown to enhance nutritional care quality in chronic metabolic diseases (18–20). most studies focus on non-Latin American settings. This gap indicates different health systems, food cultures, accessibilities, and metabolic disease rates, such as those in Mexico. Research supports the effectiveness of culturally adapted programs to improve lifestyle intervention adherence among Latinos in the US (21), underscoring the need for tools that simplify the NCP's implementation in environments reflecting the unique characteristics of the Mexican population, especially concerning prevalent metabolic disorders, particularities of the health system and food culture. In this study, we aimed to describe the adaptation of the NCP for managing five metabolic diseases—Individuals with Obesity at Risk of Type 2 Diabetes (ORT2D), T2DM, CKD, MASLD, and dyslipidemia—in Mexican individuals. The objectives of the adaptation involved prioritizing specific evaluation items and nutritional diagnoses for each disease, creating educational materials, summarizing clinical guidelines for nutritional management, and recommending tailored monitoring tables for each pathology.

Methods

Adaptation team

The selection criteria for the adaptation team for each disease included extensive experience in the nutrition care of metabolic diseases and significant research involvement. Seven dietitians from one tier 3 hospital and another from a different tier 3 hospital were selected based on their diverse clinical expertise and perspectives. All chosen dietitians were required to have at least a master's degree and active participation in research protocols in their field, ensuring a rigorous evaluation of the quality of the evidence presented. Additionally, each dietitian had a minimum of five years of experience and was actively involved in their respective specialty departments. All members had also completed at least one training course on NCP methodology. The teams were organized by disease focus—ORT2D, T2DM, CKD, MASLD, and dyslipidemia—to optimize the adaptation process. The tier 3 hospitals function as referral centers, directing patients from various regions to specialized medical and nutritional care and also offering areas for non-specialized, general treatment. This structure accommodates a broad spectrum of the country's healthcare needs and ensures a wide representation of the population.

The adaptation was done in three steps: 1.- Literature review, 2.- Adaptation to Mexican population, 3.- Adaptation of NCP to metabolic diseases and development of educational materials (Figure 1).

Critical literature review

Each team gathered scientific literature pertinent to their specific pathology. We conducted a literature review to gather the most current information on the epidemiological status and clinical guidelines for the

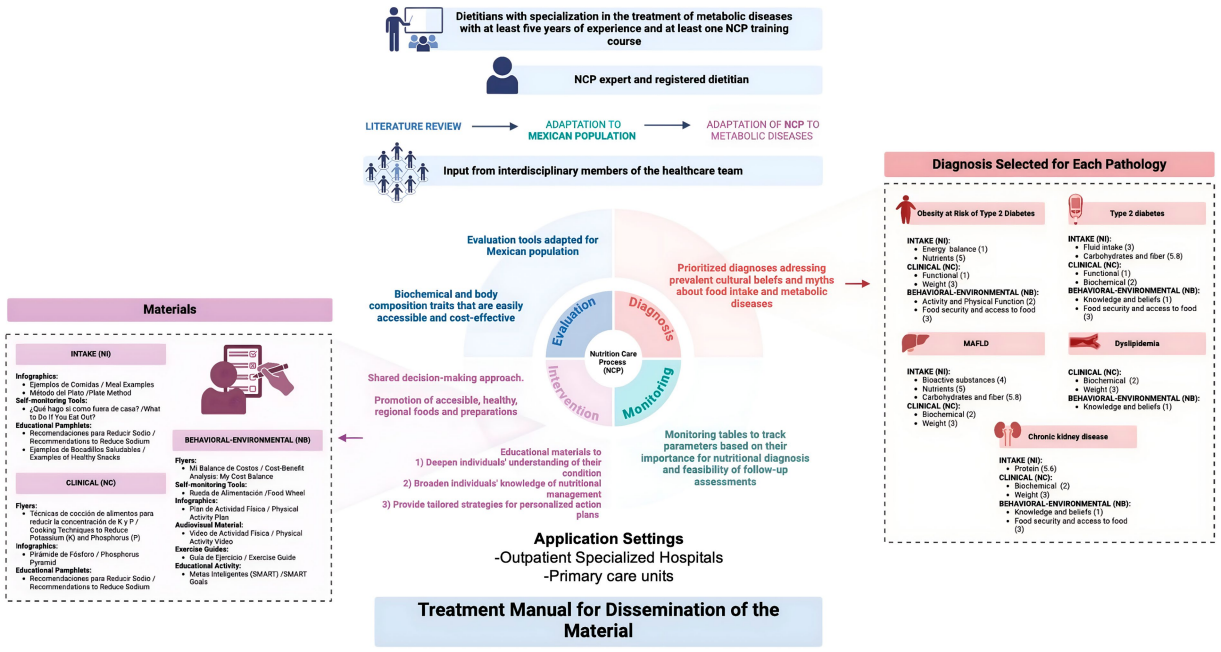

FIGURE 1
Summary of the adaptation of the nutrition care process in metabolic diseases in Mexican population. Created with BioRender.com.

nutritional management of five pathologies. Clinical guidelines were obtained from national and international medical societies, and we accessed relevant information through PubMed database. There was no restriction on the publication year for the literature search, although the most current clinical guidelines and research studies published more than five years ago were included, provided they were highly relevant to the topic. To standardize the literature search, each researcher used keywords and MeSH terms, excluding only reports and case series. We also prioritized studies focusing on the Mexican population.

Adapting nutrition guidelines for the Mexican population

Each team facilitated discussions with the aim to compare the recommendations outlined in the guidelines with their practical implementation in real clinical settings, identifying any discrepancies or gaps. This approach was designed to reveal potential deficiencies in the application of guidelines within real-world scenarios.

Adapting the NCP for metabolic diseases

We carefully reviewed the evaluation items, aligning them with relevant literature to include only those pertinent or most used in the treatment of metabolic diseases. Similarly, we prioritized common diagnoses observed in clinical practice for adaptation. Regarding interventions, each team documented guidelines-based suggestions tailored to our population. To facilitate the educational intervention, we assembled a toolbox of educational resources. This helped to simplifying the explanation of nutritional and disease concepts. Some of the adapted materials were piloted implemented in an interdisciplinary program for treating individuals with T2DM, as well as in nutrition clinics for patients with dyslipidemia, MASLD, and renal diseases. This implementation facilitated valuable feedback from both patients and dietitians. Lastly, we developed pathology-specific monitoring tables, incorporating suggested monitoring times from literature and clinical practice.

The implementation of the educational materials was fully approved by the Ethics and Research Committee of the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán and was registered at ClinicalTrials.gov (NCT02836808). Written informed consent was obtained from each participant. Research was conducted according to the tenets of the Helsinki Declaration of Human Studies principles.

Integrating interdisciplinary for adaptation

Following the framework of the NCP methodology, each adaptation team sought input from interdisciplinary team members, all of whom were part of the same clinical team within the institution. These team members offered valuable insights into the patient treatment context and provided tools to identify referral signals. This collaborative approach ensures a comprehensive overview of patient needs for an effective care coordination.

Expert consultation for NCP adaptation

Throughout the adaptation process, our team received invaluable support from an NCP expert—a registered dietitian with over a decade of experience in NCP methodology. With a robust background, including completion of courses at the Academy of Nutrition and Dietetics and years of experience conducting training sessions.

TABLE 1 Clinical guidelines used in the development of the adaptation of the NCP model in Mexican population.

Pathology	Guidelines
Obesity at risk of type 2 diabetes	1. Exercise Testing and Prescription; 2021 (22). 2. Obesity Treatment in Primary Care; 2016 (51).
Type 2 diabetes	3. AHA/ACC/TOS Management of Overweight and Obesity in Adults; 2014 (52). 4. Type 1 and Type 2 Diabetes in Adults; 2017 (53).
MASLD	5. JSGE. Nonalcoholic fatty liver disease/nonalcoholic steatohepatitis; 2015 (54). 6. Nonalcoholic fatty liver disease/nonalcoholic steatohepatitis; 2015 (54). 7. NAFLD; 2018 (55). 8. EASL, EASD, EASO. Management of non-alcoholic fatty liver disease; 2016 (56). 9. ESPEN Liver disease; 2019 (24).
Chronic kidney disease	10. K/DOQI Nutrition in chronic renal failure; 2001 (57). 11. EBPG Nutrition; 2007 (58). 12. KDIGO 2012 Evaluation and Management of Chronic Kidney Disease (59). 13. KDIGO 2020 Diabetes Management in Chronic Kidney Disease (60). 14. KDIGO 2021 Management of Blood Pressure in Chronic Kidney Disease (61). 15. KDOQI Nutrition in CKD: 2020 (62). 16. ESPEN Enteral nutrition: Adult renal failure; 2006 (25). 17. K/DOQI Chronic kidney disease: evaluation, classification, and stratification. 2002 (63, 64). 18. Dietary Guidelines for Americans; 2010 (64).
Dyslipidemia	19. AHA/ ACC Lifestyle management to reduce cardiovascular risk; 2013 (65). 20. AHA/ACC/TOS The Obesity Society; 2014 (52). 21. Management of Dyslipidemia and Prevention of Cardiovascular Disease; 2017 (66).
	22. ESC/EAS Management of dyslipidemias. 2011 (67). 23. Scientific report of the 2015 Dietary Guidelines Advisory Committee (68). 24. The 2015 US Dietary Guidelines (69). 25. Physical activity for adults; 2010 (23).

AHA; American Heart Association, ACC; American College of Cardiology, TOS; the Obesity Society, JSGE; Japanese Society of Gastroenterology, NAFLD; Non-alcoholic fatty liver disease, EASL; European Association for the Study of the Liver, EASD; European Association for the Study of Diabetes, EASO; European Association for the Study of Obesity, AASLD; American Association for the Study of Liver Diseases, ESPEN; European Society for Clinical Nutrition and Metabolism, K/DOQI; Kidney Disease Outcomes Quality Initiative, KDIGO; Kidney Disease Improving Global Outcomes, ESC; European Society of Cardiology, EAS and European Atherosclerosis Society.

Regular meetings were held with the expert to address queries and ensure clarity. The final report was reviewed and edited by the NCP expert, ensuring alignment with NCP standards. We documented our results and process in a document, which was published as a book.

Results

Our literature review encompassed 370 articles, including 25 clinical practice guidelines. Two of these guidelines specifically focused on exercise and physical activity [Guides 1 (22) and 24 (23), as detailed in Table 1] for managing obesity and dyslipidemia. The majority of the guidelines supported the implementation of the NCP across various settings, primarily in primary care for metabolically stable patients. They provided a framework for outpatient management, with limited recommendations for inpatient care [Guides 8 (24) and 15 (25) in Table 1].

Evaluation

In selecting evaluation items, we focused on the most commonly used and critical metrics for each pathology, prioritizing biochemical and body composition traits that are accessible and cost-effective. We developed medical histories in two formats—simplified and detailed—to accommodate diverse clinical settings and address the time constraints faced by dietitians in both primary care and tier 3 hospitals within the Mexican health system. Our aim was to streamline the evaluation process, enhancing efficiency and practicality for healthcare professionals. Furthermore, we incorporated Mexican-adapted evaluation tools, such as the Malnutrition Inflammation Score for CKD (26), vector analysis and body composition assessments in hemodialysis patients (27) and two formulas for estimating energy expenditure specific to the Mexican population (28, 29).

Diagnostics

For diagnostics, we identified the conditions most commonly observed in individuals with the specified metabolic pathologies. Special attention was given to addressing prevalent cultural beliefs and myths related to food intake that negatively impact the understanding and management of these diseases. Recognizing that individuals in this population can be at risk for metabolic diseases even at lower BMI values (30, 31), we emphasized the importance of considering alternative parameters beyond BMI for diagnosis. Where feasible (in-hospital or clinical research settings), more precise anthropometric and clinical measures like body fat percentage were utilized to provide a better assessment of health status. The most common diagnostics for each pathology are detailed in Table 2.

TABLE 2 Common nutritional care process diagnosis selected for each pathology.

Metabolic disease	Diagnosis	Code	Number
Intake (NI)			
ORT2D, MASLD	Energy balance (1)		
	Excessive energy intake	NI-1.3	10,635
ORT2D, T2DM	Fluid intake (3)		
	Excessive fluid intake	NI-3.2	10,650
ORT2D, T2DM, MASLD	Bioactive substances (4)		
	Excessive intake of food additives	NI-4.2.6	11,083
ORT2D, T2DM, MASLD	Nutrients (5)		
	Inadequate (suboptimal) energy-protein intake	NI-5.2	10,658
	Nutrient imbalance	NI-5.4	10,660
CKD, T2DM	Protein (5.6)		
	Inadequate protein intake	NI-5.6.1	10,666
	Excessive protein intake	NI-5.6.2	10,667
ORT2D, T2DM, MASLD	Carbohydrates and fiber (5.8)		
	Excessive carbohydrate intake	NI-5.8.2	10,671
	Deficient fiber intake	NI-5.8.5	10,675
Clinical (NC)			
ORT2D, T2DM	Functional (1)		
	Altered gastrointestinal function	NC-1.4	10,757
ORT2D, T2DM, MASLD, CKD	Biochemical (2)		
	Altered nutrition-related laboratory values (specify)	NC-2.2	10,760
ORT2D, T2DM, CKD, Dyslipidemia	Weight (3)		
	Overweight/obesity	NC-3.3	10,766
	Overweight, adult or pediatric	NC-3.3.1	10,767
	Type I obesity	NC-3.3.3	10,769
	Type II obesity	NC-3.3.4	10,818
	Type III obesity	NC-3.3.5	10,819
Behavioral-environmental (NB)			
ORT2D, T2DM, CKD, MASLD	Knowledge and beliefs (1)		
	Insufficient knowledge in food and nutrition topics	NB-1.1	10,773
	Not prepared for lifestyle/diet change	NB-1.3	10,775
	Deficit in self-monitoring	NB-1.4	10,776
	Insufficient adherence to nutritional recommendations	NB-1.6	10,778
	Undesirable food choices	NB-1.7	10,779
ORT2D, T2DM, CKD	Activity and Physical Function (2)		
	Physical inactivity	NB-2.1	10,782
	Poor nutritional quality of life	NB-2.5	10,786
ORT2D, T2DM, CKD	Food security and access to food (3)		
	Limited access to food	NB-3.2	10,790
	Others (NO)		
	No nutritional diagnosis at this time	NO-1.1	10,795

NI: Intake domain; NC: Clinical domain; NB: Behavioral-Environmental domain; ORT2D: Individuals with Obesity at Risk of Type 2 Diabetes; T2DM: Type 2 Diabetes Mellitus; CKD: kidney disease; MASLD: Metabolic Dysfunction-associated Steatotic Liver Disease.

Intervention

Dietetic

We tailored dietary modifications to consider the availability of regional foods and the specific nutritional needs of the Mexican population (32). Additionally, these modifications were integrated into dietary recommendations for outpatient nutritional counseling, ensuring they are practical and applicable in real-world settings. Key macronutrient adjustments were made in sources of carbohydrates, proteins, and fatty acids. In Mexico, corn is a primary carbohydrate source, while chicken, eggs and beans are significant protein sources (33–35). We developed strategies to highlight the availability and accessibility of healthy food options, challenging the prevailing belief that healthy eating is expensive and hard to reach (36). Our objective was to promote healthier versions of regional foods through nutritious preparations, positioning these healthier choices as the most convenient option.

Counseling

We adopted a shared decision-making framework, wherein health-related decisions are collaboratively made between the patient and a health professional (37, 38). Specifically, treatment options were discussed between dietitians and patients, with a strong emphasis on adapting these options to be more accessible for the patients. This approach enabled patients to choose the treatment strategies they found most suitable. Additionally, when setting goals, we utilized the SMART method (39) to ensure they were specific, measurable, achievable, relevant, and time-bound, thereby enhancing the effectiveness and achievability of the goals set during counseling.

Educational materials

Our educational resources were designed to address three critical areas: healthy eating, physical activity, and disease risk awareness. The materials aimed to enhance individual's awareness of disease risks, enhance their knowledge of nutritional management, and provide tailored strategies for personalized action plans. We ensured that all materials were written in clear, accessible language and featured engaging designs. They were produced in various formats, including infographics, educational pamphlets, recipes, exercise guides, and self-monitoring tools. Infographics and pamphlets provided concise, clear information on nutrition and health, offering guidelines for balanced diets and disease-specific advice. Interactive educational activities were incorporated to boost participant engagement and understanding of their conditions. Recipe books highlighted practical, balanced meal examples, focusing on regional recipes and locally accessible ingredients. Audiovisual materials were utilized in training sessions and workshops to reinforce learning. A summary of each educational material, its focus area, and its alignment with diagnoses from the NCP is detailed in Table 3.

Interdisciplinary

For the pathologies ORT2D and MASLD, we engaged with physicians specializing in these disorders to gain deeper insights into the integration of nutritional and medical treatments. Specifically, for ORT2D, feedback from a psychology expert was incorporated, detailing tools designed to enhance patient adherence to nutritional treatments. Recognizing the high demand for treatment among these patient populations, we also explored the implementation of electronic tools aimed at improving adherence to dietary recommendations, which could facilitate more efficient patient management and outcome tracking (40).

Monitoring

We developed monitoring tables to systematically track the most relevant clinical and behavioral parameters across subsequent visits. The selection of these parameters was based on their critical role in nutritional diagnosis and their feasibility for follow-up assessments in real world-settings. Given the logistical and economic challenges faced by this population, including limited appointment availability and transportation difficulties, we prioritized parameters that are practical and cost-effective to monitor. Additionally, considering the high costs of clinical tests for patients and institutions, optimizing these parameters is essential for resource management and effective monitoring. To address and mitigate barriers during treatment, we employed strategies derived from documented experiences of individuals with T2DM (41) in similar settings, facilitating improved adherence and outcomes.

Implementation of adapted NCP in diverse settings

The adapted NCP was implemented across various clinical and research settings, each tailored to meet specific needs and objectives. In research settings, the adaptation was primarily applied within lifestyle intervention protocols for individuals at risk of type 2 diabetes. These protocols utilized the adapted NCP to guide personalized nutritional interventions, emphasizing evaluation, nutrition diagnosis, and rigorous documentation and follow-up, as detailed in our recent studies (40, 42).

In contrast, the clinical implementation focused on comprehensive care programs at the National Institute of Medical Sciences and Nutrition Salvador Zubirán in Mexico City. Here, the adapted NCP was integrated into routine patient care for managing Type 2 Diabetes Mellitus (T2DM), supporting patients in achieving and maintaining health goals through structured nutritional interventions within a multidisciplinary team framework (11, 41, 43–45).

Additionally, departments specializing in dyslipidemia, gastroenterology, and renal diseases at the same institute adopted the adapted NCP materials, including educational resources and nutritional diagnostic processes, into their clinical practices. Evidence indicates feasibility of implementation and differences in the effectiveness of the adapted NCP across clinical and research settings. In research protocols, the adapted approach not only standardized lifestyle interventions among dietitians but also enhanced the monitoring of nutritional care. In clinical settings, the adaptation has contributed to identify the barriers to adherence to a nutritional plan and strategies to overcome them in patients with T2D (41). It also supported the stratification of individuals based on their nutritional diagnosis, enabling more tailored and effective nutritional treatment within an interdisciplinary program (11). These findings suggest that the implementation of culturally and disease-adapted nutritional interventions can significantly improve nutrition practice across diverse settings.

TABLE 3 Materials, learning goal, NCP diagnoses and type of material.

Material name (Spanish/ English)	Learning goal	NCP Diagnoses	Type of material
1) Healthy eating			
De la Idea a la Acción/From Idea to Action (Personalized Meal Planning)	Step-by-step guide to creating a personalized meal plan, including food group equivalents and ingredients.	Intake (NI): Excessive energy intake (NI-1.3), Nutrient imbalance (NI-5.4)	Infographics
¿Cuánta agua llevas?/How Much Water Have You Drunk?	Visual guide to help increases water intake.	Intake (NI): Inadequate fluid intake NI-3.1	Infographics
Plato Saludable y Uso de las Manos/Healthy Eating Plate and Using Hands to Measure	Visual guide for balanced meals using hands to measure portions.	Intake (NI): Excessive energy intake (NI-1.3), Nutrient imbalance (NI-5.4)	Infographics
Método del Plato/Plate Method	Visual guide for balanced meals focusing on appropriate portions of proteins, carbohydrates, and fats.	Intake (NI): Excessive energy intake (NI-1.3), Nutrient imbalance (NI-5.4)	Infographics
Ejemplos de Comidas/Meal Examples	Example menus for balanced daily meals, focusing on portion control and nutrient variety.	Intake (NI): Inconsistent carbohydrate intake (NI-5.8.4), Nutrient imbalance (NI-5.4)	Infographics
Consumo de Grasas Saludables/Consumption of Healthy Fats	Information on selecting healthy fats, such as monounsaturated and polyunsaturated fats, and avoiding trans and saturated fats.	Intake (NI): Deficient lipid intake (NI-5.5.1), Excessive lipid intake (NI-5.5.2)	Infographics
Semáforo de Productos/Product Traffic Light	Tool to classify foods based on their energy density, encouraging low-density options for better health.	Behavioral-Environmental (NB): Undesirable food choices (NB-1.7)	Flyers
Técnicas de cocción de alimentos para reducir la concentración de K y P/Cooking Techniques to Reduce Potassium (K) and Phosphorus (P)	Cooking Techniques to Reduce phosphorus and potassium.	Clinical (NC): Chronic kidney disease (NC-1.4)	Flyers
Rueda de Alimentación/Food Wheel	Tool to assess performance in different aspects of life that impact nutrition, such as emotional eating, exercise, and body image.	Behavioral-Environmental (NB): Disordered eating pattern (NB-1.5), Physical inactivity (NB-2.1)	Self-monitoring Tools
¿Qué hago si como fuera de casa?/What sould I do If I Eat Out?	Tips for choosing healthier options when dining out, including what to prefer and what to avoid.	Intake (NI): Excessive energy intake (NI-1.3). Behavioral-Environmental (NB): Undesirable food choices (NB-1.7)	Self-monitoring Tools
Talleres Interactivos/Interactive Workshops	Engaging sessions to educate about healthy eating habits, physical activity, and overall lifestyle changes.	Depending on specific NCP diagnoses	Educational Activity
Recomendaciones para Reducir Sodio/ Recommendations to Reduce Sodium	Guidelines on reducing sodium intake by choosing healthier alternatives and avoiding high-sodium products.	Intake (NI): Excessive sodium intake (NI-5.10.7). Clinical (NC): Hypertension	Educational Pamphlets
Ejemplos de Bocadillos Saludables/Examples of Healthy Snacks	Examples of balanced snacks that combine carbohydrates with proteins or fats for sustained energy and satiety.	Intake (NI): Inadequate (suboptimal) energy-protein intake (NI-5.2)	Educational Pamphlets
Ejemplos de Comidas/Meal Examples	Example menus for balanced daily meals, focusing on portion control and nutrient variety.	Intake (NI): Inconsistent carbohydrate intake (NI-5.8.4), Nutrient imbalance (NI-5.4)	Educational Pamphlets
2) Physical activity			
Plan de Actividad Física/Physical Activity Plan	Guidelines to incorporate physical activity into daily routines with tips on frequency, intensity, and types of exercises.	Behavioral-Environmental (NB): Physical inactivity (NB-2.1), Excessive physical activity (NB-2.2)	Infographics
Video de Actividad Física/Physical Activity Video	Demonstration of exercises and guidelines for incorporating physical activity into daily routines.	Behavioral-Environmental (NB): Physical inactivity (NB-2.1), Excessive physical activity (NB-2.2)	Audiovisual Material

(Continued)

TABLE 3 (Continued)

Material name (Spanish/ English)	Learning goal	NCP Diagnoses	Type of material
Guía de Ejercicio/Exercise Guide	Detailed guide on different exercises, their benefits, and how to perform them safely.	Behavioral-Environmental (NB): Physical inactivity (NB-2.1), Excessive physical activity (NB-2.2)	Exercise Guides
(3) Disease risk awareness			
Pirámide de Fósforo/Phosphorus Pyramid	Visual guide to managing phosphorus intake for kidney health.	Clinical (NC): Chronic kidney disease (NC-1.4)	Infographics
Mi Balance de Costos/Cost–Benefit Analysis: My Cost Balance	Tool to weigh the advantages and disadvantages of making lifestyle changes.	Behavioral-Environmental (NB): Not ready to make diet or lifestyle changes (NB-1.3)	Flyers
Comer por Ansiedad/Eating Due to Anxiety	Strategies to address emotional eating, including identifying triggers and replacing harmful habits with healthier actions.	Behavioral-Environmental (NB): Disordered eating pattern (NB-1.5), Emotional eating (NB-1.7)	Flyers
¿Cómo como?/Food Diary: How Do I Eat?	Food diary to record meals, hunger levels, and emotions associated with eating.	Intake (NI): Inconsistent carbohydrate intake (NI-5.8.4), Deficit in self-monitoring (NB-1.4)	Self-monitoring Tools
Metas Inteligentes (SMART)/SMART Goals	Framework to set specific, measurable, achievable, realistic, and time-bound goals.	Behavioral-Environmental (NB): Insufficient adherence to nutritional recommendations (NB-1.6)	Educational Activity
¿Sabes que te estas comiendo?/Do You Know What You Are Eating? Reading Labels	Information on how to read food labels to make healthier choices.	Behavioral-Environmental (NB): Undesirable food choices (NB-1.7)	Educational Pamphlets

NI: Intake domain; NC: Clinical domain; NB: Behavioral-Environmental domain; Infographics: Visual representations summarizing key information on nutrition and health topics. Flyers: Short, concise materials focusing on key health messages. Self-monitoring Tools: Tools for tracking dietary intake, physical activity, and other health metrics. Educational activity: Visual materials to reinforce key messages about healthy eating and lifestyles. Educational Pamphlets: Booklets and brief documents on specific healthy eating topics. Audiovisual Material: Videos and multimedia presentations used in workshops and training sessions. Exercise Guides: Instructions and tips for physical activity and exercise.

Development of a resource for disseminating the adapted material

To disseminate our findings, we compiled them into a comprehensive book. The book is structured into six chapters: the first chapter outlines the general principles of the NCP, while the subsequent chapters focus on its implementation for specific pathologies. Where applicable, subchapters on interdisciplinary treatment approaches are also included. Each chapter begins with an introduction to the disease, followed by a presentation of its global and regional epidemiology. The chapters detail how the steps of the NCP—evaluation, diagnosis, intervention, and monitoring—are tailored for each pathology. To enhance clarity and usability, abbreviated tables summarizing the most frequently used NCP terms for each pathology are included. A detailed checklist of the sections for each pathology can be found in Supplementary Table S1. Furthermore, we developed a comprehensive toolbox of educational resources to support the effective implementation of the NCP. Each chapter also features a clinical case example, demonstrating the practical application of the materials in real-world scenarios. The book is available as an online publication at the following link: https://www.amazon.com.mx/proceso-atencion-nutricia-enfermedades-metab%C3%B3licas-ebook/dp/B0BPJKNDHZ. The content of the book was reviewed and subsequently approved by the publications committee of the Mexican Society of Endocrinology and Nutrition, ensuring the integrity and accuracy of the information presented.

Discussion

We adapted the NCP to address five prevalent metabolic diseases in the Mexican population. The material provides a standardized framework for the various NCP steps—diagnosis, evaluation, nutritional intervention, and monitoring—to ensure consistent care across different settings and providers. Each step of the NCP was meticulously customized to these conditions, including the development of targeted educational materials designed to (1) increasing individuals' disease risk awareness, (2) broaden their knowledge of nutritional management, and (3) provide tailored strategies for developing personalized action plans. This tailored approach was successfully implemented in both research and clinical environments. The educational materials created are documented in an online book publication, serving as a valuable resource for health professionals.

The NCP has been adapted and successfully implemented in diverse settings and geographical locations, though several barriers to its adoption have been noted. In the Philippines, authors at a level 3 hospital emphasized the need for enhanced support from institutions, professional organizations, and policymakers to facilitate implementation (46). In Saudi Arabia, although most dietitians are familiar with the NCP and confident in its application, it has not yet been adopted as a standard practice in hospitals (47). Australian dietitians, prior to implementation, reported barriers including a lack of knowledge, support, training, and resources, while those already using the NCP identified heavy workloads and work status as obstacles

(48). Lövestam et al. stressed the necessity for context-specific strategies to address local challenges and improve dietetic support (16).

The primary barriers to NCP implementation have been identified as inefficient staffing, limited time for completing necessary documentation, and the lack of supportive infrastructure, such as electronic health record systems (16, 17). In Switzerland, the integration of NCP documentation into electronic patient records has helped strengthen the linkage between assessment and nutrition diagnosis, although the frequent selection of similar nutrition problems by dietitians' points to an ongoing challenge in adopting critical thinking (49). Additionally, Chen et al. explored mobile applications as a means to enhance the efficiency of the nutrition care process, potentially freeing up more time for dietetic counseling (50), found that apps could improve the efficiency of the nutrition care process, allowing more time for dietetic counseling. While these apps show promise in complementing dietetic care, they cannot replace direct practice. In Mexico, where the demand for healthcare services related to metabolic diseases is rapidly increasing, the adoption of electronic systems and tools that streamline healthcare management and reduce commute times to hospitals presents an attractive opportunity for further exploration.

Our study represents a pioneering effort in adapting the NCP for metabolic diseases within a Latin-American context, marking the first such implementation across diverse clinical and research settings in the region. This adaptation not only addresses a significant gap in the literature but also provides a practical framework for healthcare professionals in similar settings. However, several limitations warrant mention. First, the literature review that underpinned the adaptation process was conducted several years ago. While it incorporated the most relevant and up-to-date references available at that time, some of the references may now appear outdated, potentially overlooking recent advances in the management of metabolic diseases. Despite this, we have made efforts to update critical aspects, such as the nomenclature and clinical nutrition management of the diseases, to reflect current standards and practices. Second, the scope of the literature review was primarily confined to PubMed. This decision was made due to PubMed's comprehensive coverage of biomedical literature, which aligned well with our study's focus on metabolic diseases. However, this approach, while thorough within its specified domain, inevitably limited the breadth of our review by excluding potentially valuable insights from broader multidisciplinary sources available in other databases such as Web of Science or ScienceDirect. This limitation may have restricted our perspective and lessened the comprehensiveness of the adaptation process.

The effective implementation of the NCP in Mexican healthcare settings demands a well-established set of skills, robust institutional support, and specific practices to ensure its adoption, sustainability, and impact. Dietitians treating metabolic diseases often encounter significant challenges, including high workloads and budget constraints, which can impede the adoption of new strategies requiring additional training or resources. Moreover, the role of dietitians is not consistently defined within institutional decision-making processes, complicating the implementation of standardized care protocols. Successful implementation relies on allocating dedicated time for practitioners to familiarize themselves with the NCP, providing ongoing training to maintain and improve skills, and securing strong support and leadership from management and department leaders. These elements represent both challenges and opportunities for institutions to advocate for programs that demonstrate the benefits of such changes, thereby supporting the sustained impact of the NCP. The adapted NCP discussed in this study marks substantial progress in creating targeted tools to enhance nutritional counseling practices in populations severely affected by metabolic diseases. A standardized NCP framework not only promotes consistent practice but also provides a solid basis for evaluating the effects of nutrition care on patient health outcomes. Achieving this, however, requires active participation and commitment from both institutions and healthcare professionals. Future research should focus on validating the effectiveness of these tools in real-world settings exploring their implementation alongside electronic systems to optimize service delivery.

Conclusion

We adapted the NCP for five metabolic diseases, incorporating assessment tools, dietary recommendations, and educational materials specifically tailored to the Mexican population. This comprehensive framework is designed to enhance professional nutrition practice. The adaptation is particularly significant for the Mexican population, which faces disproportionately high rates of metabolic diseases and associated treatment challenges. Who face disproportionately high rates of metabolic diseases and related treatment challenges. Future research is needed to evaluate the effectiveness of this adapted NCP in clinical settings and to explore its integration with electronic health records and mobile apps to facilitate implementation within health systems.

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 and Research Committee of the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán. 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.

Author contributions

AG-O: Investigation, Validation, Writing – original draft. ML-A: Conceptualization, Investigation, Supervision, Validation, Writing – original draft, Writing – review & editing. MM-H: Conceptualization, Investigation, Supervision, Validation, Writing – original draft,

Writing – review & editing. AA-M: Visualization, Writing – review & editing. FDR-O: Investigation, Validation, Writing – original draft, Writing – review & editing. BR-C: Investigation, Validation, Writing – review & editing. AM-L: Validation, Visualization, Writing – review & editing. AM-V: Investigation, Validation, Writing – review & editing. KH-N: Investigation, Validation, Writing – review & editing. AE-C: Investigation, Validation, Writing – review & editing. MS-G: Conceptualization, Supervision, Investigation, Validation, Writing – original draft, 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.

Generative AI statement

The author(s) declare that Gen AI was used in the creation of this manuscript. During the preparation of this work the authors used ChatGPT in order to improve readability. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

Publisher's note

Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fnut.2025.1513747/full#supplementary-material

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Effectiveness of CONUT and NRI as nutritional risk screening tools in peritoneal dialysis: a multicenter study

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Background: Nutritional risk is a significant concern for patients undergoing peritoneal dialysis (PD), adversely affecting their quality of life and increasing the risk of infections and complications. Effective screening tools are needed to identify high-risk patients for targeted interventions. This study investigates whether different nutritional assessment methods, like the Controlling Nutritional Status (CONUT) score and Nutritional Risk Index (NRI), correlate with patient prognosis, highlighting the importance of selecting appropriate screening tools to improve clinical outcomes in PD patients.

Methods: This multicenter retrospective cohort study initially collected data from 2,427 patients across 10 centers, but ultimately included a cohort of 2,105 PD patients to evaluate the prevalence of malnutrition assessed using both the CONUT and NRI and its independent effects on all-cause mortality. Statistical analyses included log-rank tests, Cox regression models and the receiver operating characteristic curves to evaluate the association between nutritional risk and mortality.

Results: Our findings revealed that 76.58% of patients were classified as having nutritional risk according to the CONUT score, while 79.10% by the NRI. Patients with nutritional risk exhibited a significantly higher all-cause mortality rate (log-rank test, $p < 0.001$). Cox regression analysis demonstrated that severe nutritional risk was an independent predictor of all-cause mortality, with adjusted hazard ratios of 2.55 (95% CI, 1.34–4.85; $p = 0.007$) for the CONUT score and 2.64 (95% CI, 1.74–4.03; $p < 0.001$) for the NRI. Kaplan–Meier survival curves highlighted the correlation between nutritional risk and survival.

Conclusion: CONUT and NRI are effective for initial nutritional risk screening in PD patients, enabling clinicians to identify risk individuals who should undergo diagnostic assessments for a more comprehensive nutritional evaluation. Their

simplicity and ease of implementation support integration into routine practice, making it feasible for healthcare providers to conduct regular screenings. Future studies should validate dynamic monitoring approaches.

KEYWORDS

peritoneal dialysis, nutritional risk screening, controlling nutritional status score, nutritional risk index, GLIM criteria, all-cause mortality, multicenter study

Introduction

Nutritional risk is a prevalent complication among patients undergoing peritoneal dialysis (PD), significantly impacting their quality of life and overall health outcomes. The increasing utilization of PD as a replacement therapy for chronic kidney disease has underscored the urgent need to address nutritional risk stratification within this population. Despite recognizing this issue, there is a lack of standardized screening protocols in clinical practice.

While the Global Leadership Initiative on Malnutrition (GLIM) criteria provide a two-step diagnostic framework (screening followed by phenotypic/etiologic confirmation), traditional methods like the Subjective Global Assessment (SGA) require multidisciplinary expertise and advanced measurements (e.g., muscle mass quantification), limiting their feasibility in routine practice (1, 2). However, patients undergoing PD require routine nutritional risk assessments, making it vital to have simplified tools for initial screening. The Controlling Nutritional Status (CONUT) score and Nutritional Risk Index (NRI) offer simplified and cost-effective alternatives, utilizing readily available clinical data. While these tools have been widely used in assessing nutritional status in other diseases (3, 4), their application in PD patients remains underexplored.

This multicenter study aims to evaluate the utility of CONUT and NRI as nutritional risk screening tools in PD patients. First, we assessed the prevalence of different nutritional risk at baseline using both scores. Second, we examined their independent associations with long-term all-cause mortality, adjusting for confounders such as inflammation and residual renal function. Finally, we propose a stepped care model: CONUT/NRI for initial risk stratification followed by GLIM-based confirmation for high-risk cases. Through this approach, we aim to standardize nutritional risk monitoring in PD care, enabling timely interventions that may mitigate morbidity and mortality. Our findings underscore the importance of integrating simplified screening tools into routine practice while emphasizing the need for confirmatory diagnostics to address the multifactorial nature of malnutrition.

Materials and methods

Study populations

This multicenter, observational cohort study enrolled 2,427 patients on peritoneal dialysis (PD) from 10 Chinese peritoneal dialysis centers between March 1, 2005, and February 28, 2023. The study included patients who started PD and were at least 18 years old, with a minimum duration of PD of 3 months. Patients were excluded if they had acute inflammatory disease during the baseline period or a history of malignant tumors. Ultimately, 2,105 patients were included and followed up until May 31, 2023, or until reaching an endpoint (death, kidney transplantation, transfer to hemodialysis, transfer to other centers, or loss to follow-up) (Figure 1). All patients provided informed consent. This study was conducted in accordance with the ethical standards of the Declaration of Helsinki and its amendments, with approval from the Human Ethics Committee.

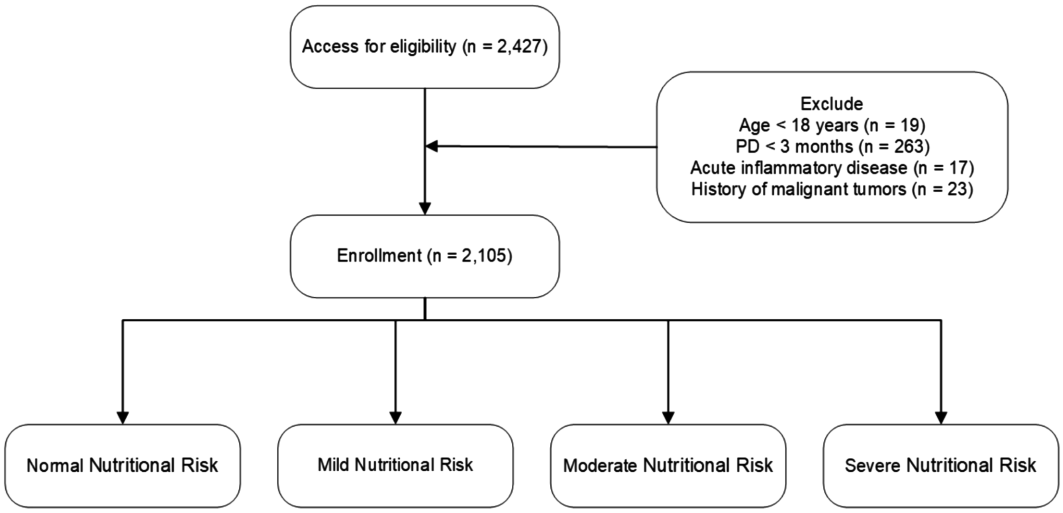

FIGURE 1
Flowchart of participant enrollment and exclusion criteria. Nutritional risk categories are defined as follows: CONUT score—Normal (0–1), Mild (2–4), Moderate (5–8), Severe (9–12); NRI—Normal (≥100), Mild (97.50–99.99), Moderate (83.50–97.49), Severe (<83.50).

Baseline investigations

Baseline demographic and clinical information was collected at the commencement of PD therapy. All baseline demographic and clinical data were collected within the first 3 months after PD initiation. The baseline data included demographic information, medical comorbidities, medications, and laboratory indicators obtained from electronic medical records. Demographic variables consisted of age, sex, body mass index (BMI), and medical history related to diabetes (ICD-10 E10-E14), hypertension (I10-I15), hyperlipidemia (E78), and cardiovascular disease (CVD). CVD was defined as documented coronary artery disease (I20-I25), heart failure (I50), cerebrovascular disease (I60-I69), or peripheral artery disease (I70-I79), with all diagnoses based on the International Classification of Diseases, Tenth Revision (ICD-10) codes and corroborated by physician assessment from medical records. Laboratory indicators included leukocyte count, hemoglobin levels, serum albumin, creatinine, blood urea nitrogen, triglycerides, total cholesterol, serum phosphorus, serum calcium, and serum potassium. These laboratory metrics were evaluated using standard measurement techniques employed by each PD center's laboratory.

Medical histories were recorded according to the initial page of the patients' medical records, while additional data were gathered from hospitalization records and physicians' orders. Clinicians at each PD center reviewed the patients' electronic medical records, and trained researchers entered the data into a database, which was subsequently verified by trained graduate students. Patients attended follow-up assessments at their respective centers every 1 to 3 months, and trained nurses conducted monthly phone interviews to monitor their overall health status.

Nutritional risk screening tools

Given the characteristic progression of malnutrition in patients with peritoneal dialysis (PD) due to factors such as inadequate nutrient intake, protein losses through dialysis, and chronic inflammation (5), we selected both the Controlling Nutritional Status (CONUT) score and the Nutritional Risk Index (NRI) to screen for nutritional risk in these patients.

The CONUT score is calculated based on serum albumin, total cholesterol, and lymphocyte count (6). The scoring ranges are categorized as normal (0–1), mild (2–4), moderate (5–8), or severe nutritional risk (9–12).

The NRI is calculated using the formula (7):

$$\mathrm{NRI} = \left(1.519 \times \text{serum albumin}\left(\mathrm{g/L}\right)\right) + \left(41.7 \times \left[\frac{\text{current body weight}\left(\mathrm{kg}\right)}{\text{usual body weight}\left(\mathrm{kg}\right)}\right]\right)$$

For our study, the usual body weight was replaced by the ideal body weight, following previous studies and using the Lorenz formulas:

For males:

$$\text{Ideal body weight}\left(\mathrm{kg}\right) = \text{height}\left(\mathrm{cm}\right) - 100 - \left[\frac{\text{height}\left(\mathrm{cm}\right) - 150}{4}\right]$$

For females:

$$\text{Ideal body weight}\left(\mathrm{kg}\right) = \text{height}\left(\mathrm{cm}\right) - 100 - \left[\frac{\text{height}\left(\mathrm{cm}\right) - 150}{2.5}\right]$$

When the current weight exceeds the ideal weight, we set the weight ratio as

$$\frac{\text{ideal weight}}{\text{current weight}} = 1$$

We classified patients into four nutritional risk categories based on the established NRI grading criteria: severe nutritional risk (NRI < 83.5), moderate (83.50 ≤ NRI < 97.49), mild (97.50 ≤ NRI < 100), and normal (NRI ≥ 100).

Outcome

The main outcome assessed was all-cause mortality. Each patient was monitored until one of the following events occurred: death, transition to hemodialysis, kidney transplantation, referral to other medical facilities, loss to follow-up, or until the end of the study on May 31, 2023.

Statistical analysis

All statistical analyses were performed by SPSS (version 25.0) and R (version R-4.4.1). All tests were two-sided, and $p < 0.05$ was considered statistically significant. The Kolmogorov–Smirnov normality test was used to determine whether variables conformed to a normal distribution. Continuous variables that conformed to a normal distribution were expressed as the mean ± standard deviation (SD), and non-normally distributed variables are expressed as the median and interquartile range (IQR). Categorical variables are expressed in terms of numbers and percentage (n, %).

Univariate and multivariate Cox regression analyses were performed to evaluate hazard ratios (HRs) and 95% confidence intervals (CIs) of significant risk predictors based on overall survival. Kaplan–Meier curves and log-rank tests were used to present time-to-event data and compare survival between groups, respectively. Time-area under the curve (AUC) were calculated to assess and compare the discrimination capacity of the three malnutrition indexes to predict mortality. For the subgroup analysis, patients were stratified by gender, age, and body mass index (BMI) to assess the impact of these variables on all-cause mortality. To test whether the pattern of association varied across stratifications, we estimated multiplicative interactions by including the product term (exposure × stratification variable) in the models.

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Results

Baseline characteristics of the patients

The final sample consisted of 2,105 patients who met the study's inclusion and exclusion criteria. At a mean follow-up of 94.62 months, 328 cases of deaths were recorded (Figure 1). The median albumin level was 36.00 g/L (35.79 ± 6.16 g/L), A significant portion of the PD patients had comorbid conditions: 23.09% of patients had diabetes, 77.67% had hypertension, 13.78% had a history of cardiovascular disease (CVD) events, and 10.21% had hyperlipidemia. Additional baseline characteristics data for the study population were detailed in Table 1.

Prevalence of nutritional risk

The prevalence of nutritional risk in the study population was 79.10% using the CONUT and 76.58% by used the NRI (Table 1) Notably, 67.7% of patients were classified as moderate-to-severe risk by CONUT (53.59% moderate, 14.11% severe), whereas 75.82% fell into mild-to-moderate risk categories by NRI (47.08% mild, 28.74% moderate) (Table 2). These discrepancies underscore the tool dependent variability in risk stratification.

Nutritional risk and mortality

The Kaplan–Meier survival curves indicated significantly higher all-cause mortality in patients with nutritional risk over the 10-year follow-up period, irrespective of whether the CONUT or NRI score was applied (log-rank test, $p < 0.001$; Figure 2).

The Cox proportional hazards regression analysis was conducted to evaluate the impact of nutritional risk on all-cause mortality. The analysis showed that the risk of all-cause mortality increased for each one-point increment in the CONUT score (aHR, 1.07; 95% CI, 1.02–1.12; $p = 0.008$) and decreased for each one-point increment in the NRI score (aHR, 0.97; 95% CI, 0.96–0.98; $p < 0.001$).

In the fully adjusted model (Model 3), compared with patients with normal nutritional status, the adjusted hazard ratio (aHR) for all-cause mortality was 1.87 (95% CI, 1.30–2.67; $p < 0.001$) for patients with mild nutritional risk screened by CONUT, and 1.84 (95% CI, 1.12–3.03; $p = 0.016$) for patients with mild nutritional risk screened by NRI. For severe nutritional risk, the aHRs for all-cause mortality were 2.55 (95% CI, 1.34–4.85; $p < 0.001$) and 2.64 (95% CI, 1.74–4.03; $p < 0.001$) according to CONUT and NRI, respectively (Table 3).

The Receiver Operating Characteristic (ROC) curves in Figure 3 show the time-dependent diagnostic performance of the Nutritional Risk Index (NRI) and CONUT. For the CONUT dataset (Figure 3A), the Area Under the Curve (AUC) values for 1-year, 2-year, and 5-year are 0.641, 0.605, and 0.579, respectively. For the NRI dataset (Figure 3B), the AUC values were 0.677 for 1-year, 0.640 for 2-year, and 0.618 for 5-year.

Subgroups analysis

We performed subgroup analysis in some subgroups that we were interested in and explored the interaction between the subgroups and

TABLE 1 Demographic and laboratory values of the study population.

Variables	Total (n = 2,105)
Age, Mean ± SD, years	51.07 ± 14.54
Gender, *n* (%)	
Male	1,125 (53.44)
Female	980 (46.56)
PD Vintage, Mean ± SD, Months	94.62 ± 45.55
BMI, M (Q_1, Q_3), kg/m^2	21.63 (19.67, 24.05)
Smoking History, *n* (%)	
No	2011 (95.53)
Yes	94 (4.47)
Drinking History, *n* (%)	
No	2077 (98.67)
Yes	28 (1.33)
Diabetes, *n* (%)	
No	1,619 (76.91)
Yes	486 (23.09)
Hypertension, *n* (%)	
No	470 (22.33)
Yes	1,635 (77.67)
CVD History, *n* (%)	
No	1815 (86.22)
Yes	290 (13.78)
Hyperlipidemia, *n* (%)	
No	1890 (89.79)
Yes	215 (10.21)
Total Kt/V, M (Q_1, Q_3)	2.21 (1.79, 2.71)
Serum Albumin, Mean ± SD, Months, g/L	35.79 ± 6.16
RRF, M (Q_1, Q_3), ml/min	3.54 (1.93, 6.45)
WBC, M (Q_1, Q_3), 10^9/L	6.31 (5.00, 7.78)
RBC, M (Q_1, Q_3), 10^{12}/L	3.16 (2.63, 3.80)
Hemoglobin, M (Q_1, Q_3), g/L	91.00 (76.00, 109.00)
FBG, M (Q_1, Q_3), mmol/L	4.70 (4.11, 5.60)
Serum Creatinine, M (Q_1, Q_3), μmol/L	743.00 (568.00, 966.00)
Calcium, M (Q_1, Q_3), mmol/L	2.13 (1.95, 2.30)
Phosphorus, M (Q_1, Q_3), mmol/L	1.65 (1.33, 2.01)
iPTH, M (Q_1, Q_3), pg./ml	190.50 (74.20, 355.00)
Total Cholesterol, M (Q_1, Q_3), mmol/L	4.50 (3.66–5.40)
Triglycerides, M (Q_1, Q_3), mmol/L	1.37 (0.96, 1.95)
Nutrition Risk	
Any degree of nutrition risk, *n* (%)	
COUNT	1,612 (76.58)
NRI	1,665 (79.10)

SD: standard deviation, M: Median, Q_1: 1st Quartile, Q_3: 3rd Quartile. BMI, body mass index; CVD, cardiovascular disease; RRF, residual renal function; WBC, white blood cell; RBC, red blood cell; FBG, fasting blood glucose; iPTH, intact parathyroid hormone.

TABLE 2 Prevalence of nutritional risk according to two different scoring systems.

Nutritional indices		Nutritional Risk			
		Normal	Mild	Moderate	Severe
CONUT, points		(0–1)	(2–4)	(5–8)	(9–12)
Formula	Albumin, g/dl (score)	≥3.5 (0)	3.0–3.4 (2)	2.5–2.9 (4)	<2.5 (6)
	Total cholesterol, mmol/L (score)	≥180 (0)	140–199 (1)	100–139 (2)	<100 (3)
	Lymphocyte count, × 10^9/L (score)	≥1.60 (0)	1.20–1.59 (1)	0.80–1.19 (2)	<0.80 (3)
Study population, *n* (%)		493 (23.42%)	187 (8.88%)	1,128 (53.59%)	297 (14.11%)
NRI, points		≥100	97.50–99.99	83.50–97.49	<83.50
Formula	1.519 albumin (g/L) + 41.7 [current body weight [kg]/ideal weight (kg)]				
Study population, *n* (%)		440 (20.9%)	991 (47.08%)	605 (28.74%)	69 (3.28%)

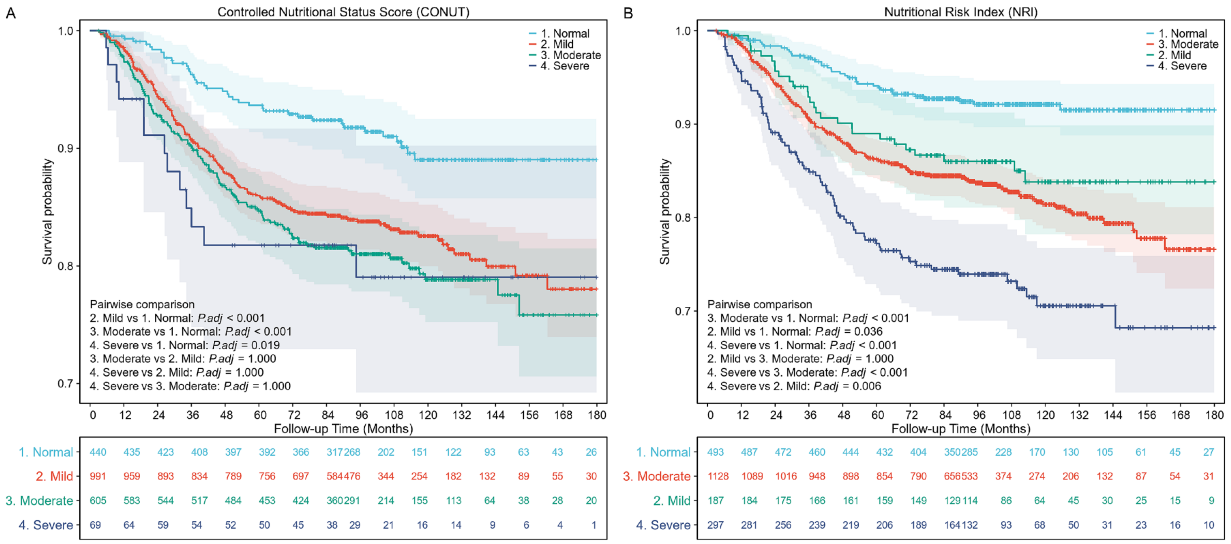

FIGURE 2
Kaplan–Meier (KM) survival curves stratified by different nutritional risk statuses. **(A)** KM curves according to the Controlled Nutritional Status Score (CONUT) (unweighted). Log-rank test, $p < 0.001$. **(B)** KM curves according to the Nutritional Risk Index (NRI) (unweighted). Log-rank test, $p < 0.001$.

nutritional risk. The forest plot showed no interaction between the subgroups (Figure 4).

Discussion

Nutritional risk is a critical issue among patients undergoing peritoneal dialysis (PD), significantly affecting their overall health and quality of life. This condition, often worsened by dialysis-related factors such as protein loss, inadequate intake, and inflammation, leads to adverse outcomes like increased hospitalization and mortality (8–10). Thus, effective and standardized nutritional risk screening protocols are crucial for optimizing patient care (11, 12).

Our multicenter retrospective study with 2,105 PD patients assessed nutritional risk prevalence and its impact on mortality using CONUT and NRI. Both scores revealed a high nutritional risk burden, with 76.58 and 79.10% of patients classified as high-risk by CONUT and NRI, respectively. Severe nutritional risk was independently associated with an increase in mortality hazard (CONUT-adjusted HR = 2.55; NRI-adjusted HR = 2.64). These findings highlight the necessity of integrating regular nutritional screening into PD patient care to improve outcomes (8, 13).

Current approaches to nutritional risk evaluation in PD patients predominantly rely on established frameworks such as the Global Leadership Initiative on Malnutrition (GLIM) and the Subjective Global Assessment (SGA). Notably, the development of GLIM was built upon earlier standards from the European Society for Clinical Nutrition and Metabolism (ESPEN) and the American Society for Parenteral and Enteral Nutrition (ASPEN). The ASPEN 2012 consensus established a comprehensive framework integrating both subjective assessments (e.g., Subjective Global Assessment) and objective tools (e.g., Malnutrition Universal Screening Tool) to standardize malnutrition diagnosis in hospitalized populations, emphasizing multidisciplinary collaboration and proactive nutritional interventions (14). Similarly, the ESPEN 2015 guidelines introduced multidimensional evaluations, combining anthropometric measurements, biochemical markers, and clinical

TABLE 3 All-cause mortality hazard ratios (HRs) for patients according to different nutritional risk status.

Risk factor	Model 1		Model 2		Model 3	
	HR (95% CI)	*p* value	HR (95% CI)	*p* value	HR (95% CI)	*p* value
CONUT, continuous						
Per 1-score increment	1.10 (1.05 ~ 1.15)	<0.001	1.08 (1.03 ~ 1.13)	<0.001	1.07 (1.02 ~ 1.12)	0.008
CONUT, categorical						
Normal	Ref					
Mild	2.00 (1.41 ~ 2.82)	<0.001	2.00 (1.41 ~ 2.83)	<0.001	1.87 (1.30 ~ 2.67)	<0.001
Moderate	2.32 (1.62 ~ 3.33)	<0.001	2.17 (1.51 ~ 3.12)	<0.001	1.87 (1.27 ~ 2.74)	0.001
Severe	2.46 (1.32 ~ 4.60)	0.005	2.13 (1.13 ~ 4.00)	0.019	2.55 (1.34 ~ 4.85)	0.004
NRI, continuous						
Per 1-score increment	0.96 (0.95 ~ 0.97)	<0.001	0.97 (0.95 ~ 0.98)	<0.001	0.97 (0.96 ~ 0.98)	<0.001
NRI, categorical						
Normal	Ref					
Mild	1.98 (1.20 ~ 3.25)	0.007	1.93 (1.18 ~ 3.18)	0.009	1.84 (1.12 ~ 3.03)	0.016
Moderate	2.46 (1.73 ~ 3.50)	<0.001	1.94 (1.35 ~ 2.79)	<0.001	1.66 (1.15 ~ 2.39)	0.007
Severe	4.11 (2.78 ~ 6.08)	<0.001	3.25 (2.15 ~ 4.90)	<0.001	2.64 (1.74 ~ 4.03)	<0.001

Model 1: No adjusted. Model 2: Adjusted by age, gender, BMI, hyperlipemia, diabetes, cardiovascular disease. Model 3: Model 2 plus serum uric acid, serum phosphorus, serum potassium, serum alkaline phosphatase, iPTH, FBG, CRP, HGB, Kt/V. CONUT, the Controlled Nutritional Status Score; NRI, the Nutritional Risk Index; BMI, body mass index; iPTH, intact parathyroid hormone; FBG, fasting blood glucose; CRP, C-reactive protein; HGB, hemoglobin; HR, hazard ratio; CI, confidence interval.

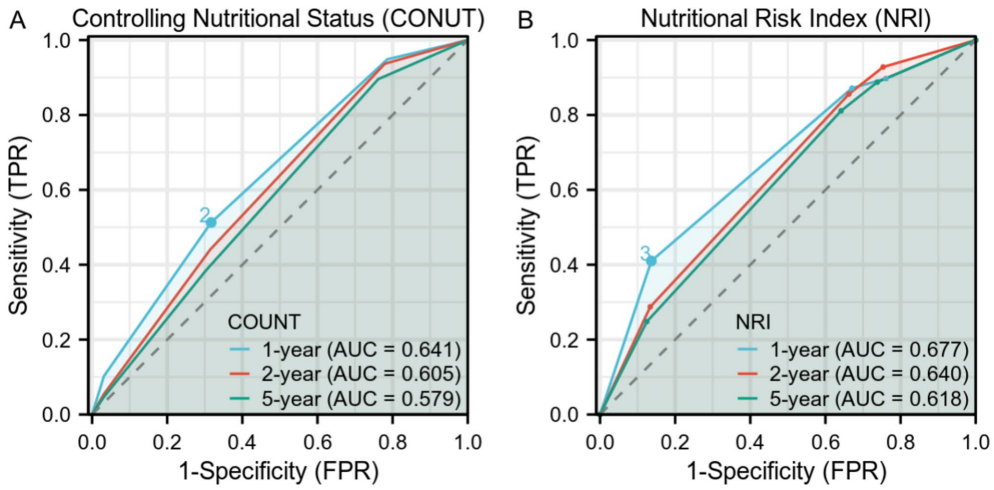

FIGURE 3
Time-Dependent Receiver Operating Characteristic (ROC) Curves for Controlling Nutritional Status (CONUT) and Nutritional Risk Index (NRI) over 1-year, 2-year, and 5-year intervals. **(A)** ROC curves for CONUT with Area Under Curve (AUC) values of0.641, 0.605, and 0.579 for 1-year, 2-year, and 5-year intervals, respectively. **(B)** ROC curves for NRI with AUC values of 0.677, 0.640, and 0.618 for 1-year, 2-year, and 5-year intervals, respectively.

assessments to enhance diagnostic accuracy, particularly in chronic disease and surgical patients (15). The GLIM criteria, formalized through a consensus by major societies including ESPEN and ASPEN, provide a two-step diagnostic framework: phenotypic criteria (e.g., weight loss >5%, low body mass index [BMI] < 18.5 kg/m^2, or reduced muscle mass—a hallmark of sarcopenia) and etiologic criteria (e.g., reduced dietary intake or chronic inflammation) (1). This framework explicitly recognizes sarcopenia-related muscle depletion as a central component of malnutrition risk stratification. In contrast, SGA, as the most widely used clinical tool, relies on subjective clinician assessments of weight changes, dietary intake, and physical signs of muscle or fat wasting (16, 17).

The simplicity of SGA allows for quick bedside evaluations but its reliance on clinician judgment can limit its sensitivity in fluid-overloaded PD patients, where fluid retention might be mistaken for improved nutrition (18). Advanced techniques like bioelectrical impedance analysis (BIA) can more accurately assess dry body weight by distinguishing fluid from lean and fat mass, providing clearer insights into nutritional status (19). BIA is crucial for early detection of sarcopenia

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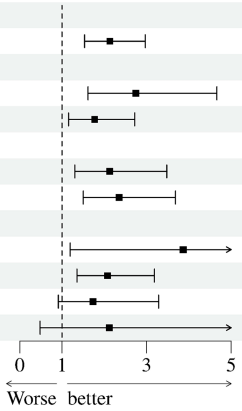
A **Controlled Nutritional Status Score (CONUT)**

Variables	n (%)	Normal	Malnutrition	HR (95%CI)	P	P for interaction
		No. of events/ No. of total				
All patients	2105 (100.00)	40/440	288/1665	2.13 (1.53 ~ 2.97)	<.001	
Sex						0.225
Male	1125 (53.44)	15/213	156/912	2.74 (1.61 ~ 4.66)	<.001	
Female	980 (46.56)	25/227	132/753	1.77 (1.16 ~ 2.72)	0.009	
Age						0.777
< 60	1432 (68.03)	18/287	139/1145	2.13 (1.30 ~ 3.48)	0.003	
≥ 60	673 (31.97)	22/153	149/520	2.35 (1.50 ~ 3.68)	<.001	
BMI						0.634
Underweight	299 (14.20)	3/66	37/233	3.86 (1.19 ~ 12.54)	0.024	
Normal	1267 (60.19)	24/261	170/1006	2.08 (1.35 ~ 3.18)	<.001	
Overweight	438 (20.81)	11/92	65/346	1.73 (0.91 ~ 3.28)	0.093	
Obese	101 (4.80)	2/21	16/80	2.12 (0.48 ~ 9.26)	0.320	



B **Nutritional Risk Index (NRI)**

Variables	n (%)	Normal	Malnutrition	HR (95%CI)	P	P for interaction
		No. of events/ No. of total				
All patients	2105 (100.00)	37/493	291/1612	2.69 (1.91 ~ 3.78)	<.001	
Sex						0.678
Male	1125 (53.44)	20/263	151/862	2.52 (1.58 ~ 4.02)	<.001	
Female	980 (46.56)	17/230	140/750	2.87 (1.73 ~ 4.75)	<.001	
Age						0.916
< 60	1432 (68.03)	21/373	136/1059	2.50 (1.58 ~ 3.96)	<.001	
≥ 60	673 (31.97)	16/120	155/553	2.42 (1.45 ~ 4.05)	<.001	
BMI						0.290
Underweight	299 (14.20)	0/21	40/278	27394035.95 (0.00 ~ Inf)	0.995	
Normal	1267 (60.19)	20/312	174/955	3.22 (2.03 ~ 5.11)	<.001	
Overweight	438 (20.81)	13/126	63/312	2.29 (1.26 ~ 4.18)	0.007	
Obese	101 (4.80)	4/34	14/67	1.85 (0.61 ~ 5.63)	0.280	

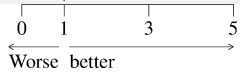


FIGURE 4
Cox proportional hazards regression models of different malnutrition status and all-cause mortality. **(A)** CONUT, the Controlled Nutritional Status Score; **(B)** NRI, the Nutritional Risk Index; BMI, body mass index.

in PD patients, where fluid can mask muscle loss, allowing for timely nutritional interventions to preserve muscle health (20). This method provides a more precise evaluation by differentiating between the water weight and actual body composition, offering a clearer insight into the patient's nutritional state (21).

Although these diagnostic frameworks are methodologically thorough, their implementation often requires specialized resources (e.g., imaging for muscle mass quantification, multidisciplinary coordination), which challenges routine use in PD practice. In this context, CONUT and NRI offer a streamlined alternative for rapid screening. The CONUT score integrates three routinely measured parameters—serum albumin, lymphocyte count, and total cholesterol—to generate a risk score ranging from 0 to 12 (7). The NRI calculates risk using current weight/ideal weight and albumin levels (6). Both tools enable efficient risk stratification, with CONUT identifying 67.7% of patients with moderate-to-severe risk and NRI classifying 75.82% as mild-to-moderate risk. These differences highlight their complementary roles: CONUT's emphasis on inflammation may prioritize patients needing anti-inflammatory interventions, while NRI's focus on energy-protein balance could guide dietary support.

ROC curve analysis provides insights into how well NRI and CONUT perform as diagnostic tools for predicting mortality in PD patients over different time periods. Although AUC values suggest an acceptable but lower predictive ability, NRI generally shows slightly better. The decline in AUC values over time highlights challenges in long-term prognostication. Our findings suggest a two-step nutritional care pathway: first, CONUT/NRI can assist in screening to identify high-risk patients, followed by a confirmatory evaluation using GLIM criteria to diagnose and grade malnutrition.

Study limitations include reliance on retrospective data, which may introduce biases and limit causality. Our sample, though substantial, is from multiple centers within a single country, affecting external validity. Additionally, the lack of clinical validation raises concerns about applicability in practice, necessitating future prospective studies incorporating diverse demographics and rigorous validation.

In conclusion, this study suggests that the Controlling Nutritional Status (CONUT) score and the Nutritional Risk Index (NRI) can assist in screening for nutritional risk in PD populations. Their ability to capture both inflammatory and catabolic pathways enables targeted interventions that address multifactorial nutritional deterioration.

While these tools incorporate into PD care protocols represent an important step towards reducing morbidity. Future studies should focus on validating dynamic monitoring approaches, including the frequency of re-evaluation and the integration of additional parameters, to enhance the accuracy and comprehensiveness of nutritional assessments in this population.

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 Ethics Committee of the General Hospital of Ningxia Medical University (application ID: 2022-410-01). 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

WQ: Conceptualization, Data curation, Formal analysis, Investigation, Software, Validation, Writing – original draft. RC: Data curation, Investigation, Methodology, Validation, Writing – original draft. YM: Conceptualization, Investigation, Writing – review & editing. JX: Conceptualization, Formal analysis, Investigation, Writing – review & editing. QX: Resources, Writing – review & editing. YW: Resources, Writing – review & editing. XZ: Resources, Writing – review & editing. FP: Resources, Writing – review & editing. XWa: Resources, Writing – review & editing. JW: Resources, Writing – review & editing. NS: Resources, Writing – review & editing. XF: Resources, Writing – review & editing. XT: Resources, Writing – review & editing. XWu: Resources, Writing – review & editing. QZ: Methodology, Writing – review & editing. NT: Data curation, Funding acquisition, Project administration, Supervision, 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.

Generative AI statement

The author(s) declare that no Gen AI was used in the creation of this manuscript.

Publisher's note

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Association between body composition in early pregnancy and the risk of gestational diabetes mellitus

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Background: Gestational diabetes mellitus (GDM) is a common complication during pregnancy that poses serious health risks to both mothers and their offspring. Risk factors for GDM, such as obesity, have been extensively reported. However, the association between body composition and GDM risk remains unclear. Therefore, we conducted a retrospective cohort study to investigate the relationship between body composition in early pregnancy and the risk of developing GDM.

Methods: A total of 3,159 pregnant women were enrolled between June 2020 and December 2021, with 280 (10.43%) diagnosed with GDM. Bioelectrical impedance analysis (BIA) was used to measure the percentage of body fat (PBF), fat mass (FM), fat-free mass (FFM), and lean mass (LM). Logistic regression and restricted cubic spline (RCS) analyses were performed to examine the associations between body composition and GDM risk.

Results: Compared with the bottom tertile, the top tertile levels of PBF and FM were significantly associated with an increased risk of GDM, with adjusted odds ratios (ORs) and corresponding 95% confidence intervals (95% CI) of 1.77 (1.13, 2.77) and 1.99 (1.23, 3.20), respectively. Each standard deviation (SD) increase in PBF and FM was associated with a 31% (95% CI: 1.07–1.60) and 27% (95% CI: 1.03–1.57) increased risk of GDM, respectively. RCS analysis indicated that the risk of GDM continuously increased with higher levels of PBF and FM, whereas it decreased with FFM and LM (p-overall < 0.001, p-non-linear range: 0.073–0.924). These findings provide important threshold values in predicting GDM risk, specifically 24.74% for PBF, 13.13 kg for FM, 39.81 kg for FFM, and 36.74 kg for LM.

Conclusion: The risk of GDM is positively associated with PBF and FM whereas negatively associated with FFM and LM.

KEYWORDS

gestational diabetes mellitus, body composition, body fat percentage, fat mass, fat free mass

Introduction

Gestational diabetes mellitus (GDM) is a common complication characterized by impaired glucose metabolism during pregnancy, and it can adversely affect the health of both mothers and their offspring (1). GDM elevates the risk of adverse pregnancy outcomes, including fetal dysplasia, neonatal hypoglycemia, and preterm birth (2, 3), and is also associated with an elevated risk of long-term insulin resistance and type 2 diabetes (4, 5). However, the etiology of GDM is complex and remains incompletely understood. Further research is urgently needed to identify the potential risk factors for GDM.

Pre-pregnancy obesity has been demonstrated to play a significant role in the development of GDM through multiple pathways (1). Body mass index (BMI) is commonly used to identify women at risk of developing GDM during pregnancy; however, it cannot provide accurately distinguish between fat mass and lean mass (6). Studies have shown that both adipose and muscle tissues contribute to insulin sensitivity (7). During pregnancy, maternal metabolism accelerates to support the rapid growth and development of the fetus, and maternal intestinal fat absorption capacity increases, resulting in a greater accumulation of visceral and subcutaneous fat compared to pre-pregnancy levels (8). A cohort study involving 627 women indicated that visceral adipose tissue in early pregnancy was a better predictor of GDM risk than the traditionally used BMI (9).

Body composition, consisting of muscle, fat, and bone mass, can be easily measured using bioelectric impedance analysis (BIA). Excessive fat accumulation may induce chronic inflammation in adipose tissue, dysfunction of pancreatic β-cells, and ultimately, systemic insulin resistance (10). Evidence has shown that individuals with normal weight but a high body fat percentage have a greater risk of cardiovascular disease and metabolic syndrome compared to those with both normal weight and normal body fat percentage (11, 12). A 15-year follow-up cohort study conducted in the Japanese population found that leg fat percentage was negatively associated with diabetes risk in both men and women (13). Additionally, pregnancy complications such as preeclampsia (14) and gestational hypertension (15) are also associated with body composition. However, only a few studies have explored the association between body composition and GDM risk (6). The role of body composition in early pregnancy in predicting GDM during the second trimester remains unclear.

Body composition distribution also changes with age, characterized by an increase in total fat content (especially abdominal fat), along with a decrease in lean mass and bone density (16). Additionally, certain medical conditions (such as hypothyroidism and polycystic ovary syndrome) may contribute to increased fat accumulation (17, 18). Unhealthy body composition can be effectively improved through lifestyle management. Evidence suggests that interventions such as reducing energy intake and increasing physical activity levels can positively influence body composition (19). Early identification of associations between abnormal body composition and GDM can facilitate its prevention. Therefore, the aim of our study was to explore the relationship between body composition in early pregnancy and the risk of developing GDM.

Methods

Study design

This retrospective cohort study recruited women in early pregnancy (6–13 weeks of gestation) who registered and delivered at Chengdu Shuangliu District Maternal and Child Health Care Hospital (Sichuan Province, China) between June 2020 and December 2021. Written informed consent was obtained from all participants. The study was approved by the Ethics Committee of Chengdu Shuangliu District Maternal and Child Health Care Hospital (Approval No. ky202404) and conducted in accordance with the Declaration of Helsinki of the World Medical Association.

Participants

A total of 3,249 eligible pregnant women aged 18–45 years at 6–13 weeks of gestation were initially recruited. Among these participants, 90 pregnant women were excluded due to the following conditions: (1) chronic metabolic diseases diagnosed before pregnancy, including previous GDM or other types of diabetes ($n = 4$), polycystic ovary syndrome (PCOS) ($n = 17$), thyroid dysfunction ($n = 16$), chronic nephritis ($n = 5$), and heart disease ($n = 1$); (2) infectious diseases ($n = 33$), such as acquired immune deficiency syndrome (AIDS) ($n = 2$), syphilis ($n = 5$), hepatitis ($n = 22$), severe pneumonia ($n = 2$), pulmonary tuberculosis ($n = 1$), and myocarditis ($n = 1$); and (3) incomplete body composition information ($n = 14$). Ultimately, 3,159 women were included in the study. All participants underwent an oral glucose tolerance test between 24 and 28 weeks of gestation.

Collection of basic information

The collection of basic information and measurement of physical parameters were performed by trained medical professionals, including doctors and nurses. The demographic characteristics and medical histories of pregnant women were obtained through face-to-face interviews during the first prenatal visit. Collected data included maternal age, education level (junior, senior, college), ethnicity (Han, other), household registration type (rural, urban), gravidity (<3, ≥3), parity (primiparity, multiparity), last menstrual period, and a previous disease history. Height and weight were measured using an electronic scale with an accuracy of 0.1 cm and 0.1 kg, respectively. BMI was calculated as early pregnancy weight (kg) divided by height squared (m^2) and classified into three categories: underweight (<18.5 kg/m^2), normal (18.5–23.9 kg/m^2), and overweight/obesity (≥24 kg/m^2). Maternal age was categorized into two groups: <35 years and ≥35 years.

Collection of body composition data

Body composition in early pregnancy was assessed using BIA (NAQ-P, Si Hai Hua Chen, Inc., China). Before measurement, participants were instructed to wear light clothing without any metal

accessories and stand barefoot on the metal plates of the instrument. They were then asked to lightly hold the metal electrodes with both hands. Data were recorded once the measurement was completed. Body fat mass (FM), fat-free mass (FFM), lean mass (LM), percentage of body fat (PBF), and basal metabolic rate (BMR) were recorded. PBF was calculated as the ratio of FM to total weight multiplied by 100%.

Diagnosis of GDM

The diagnosis of GDM followed the guidelines established by the International Association of Diabetes and Pregnancy Study Groups (20). An oral glucose tolerance test was performed at 24–28 weeks of gestation, for which the participants were instructed to fast overnight for 8–12 h and then consume 300 mL of glucose solution containing 75 g glucose within 5 min before 9:00 AM. Blood samples were collected at fasting and 1 h and 2 h after glucose loading. GDM was diagnosed if any of the fasting, 1-h, or 2-h post-load blood glucose values reached or exceeded 5.1, 10.0, or 8.5 mmol/L, respectively.

Statistical analysis

Data processing and analysis were performed using RStudio software, version 4.3.0 (RStudio, Inc., United States).

Continuous variables with normal distribution are expressed as means with standard errors (SE), while categorical variables are presented as frequencies with percentages (%). Non-normally distributed data are displayed as medians (interquartile ranges, IQR). Between-group differences in continuous and categorical variables were assessed using the independent samples t-test and chi-square test, respectively. Given the skewed distribution of the data, Spearman's correlation coefficients were calculated to assess correlations between early-pregnancy body composition and blood glucose values at different time points. Additionally, the continuous body composition variables (PBF, FM, FFM, and LM) were divided into tertiles, with the first tertile serving as the reference group. Binary logistic regression analysis was subsequently conducted to estimate odds ratios (ORs) and corresponding 95% confidence intervals (95% CIs) for the risk of GDM associated with these body composition variables in early pregnancy. Restricted cubic spline (RCS) with three knots was conducted to assess dose–response relationships between body composition parameters and GDM risk. A two-tailed p-value < 0.05 was considered statistically significant. Model 1 represented unadjusted univariate analysis, whereas Model 2 was adjusted for potential confounding variables, including maternal age, education level, ethnicity, household registration type, early-pregnancy BMI, gestational weight gain, gravidity, and parity.

Results

This study included 3,159 pregnant women with a mean age of 27.77 ± 3.99 years, among whom 280 (10.43%) were diagnosed with GDM (Table 1). Pregnant women with GDM had significantly higher maternal age (29.58 ± 4.43 vs. 27.59 ± 3.90 years, $p < 0.001$), early-pregnancy BMI (22.72 ± 2.91 vs. 21.72 ± 2.76 kg/m^2, $p < 0.001$), and gravidity (≥3 pregnancies: 44.34% vs. 32.78%, $p < 0.001$) compared with normal pregnant women. However, the gestational weight gain in the GDM group was significantly lower than that in the normal group (5.01 ± 3.11 vs. 7.04 ± 3.79 kg, $p < 0.001$). No significant differences were observed in the baseline gestational weeks, ethnicity, household registration type, education level, or parity between the GDM and normal groups (all $p > 0.05$).

Table 2 shows the comparison of early pregnancy body composition parameters between the GDM and normal groups. Pregnant women with GDM had significantly higher levels of PBF, FM, FFM, and LM compared with normal pregnant women (all $p < 0.005$).

Normality tests indicated that blood glucose values and body composition indicators were skewed in distribution (Supplementary Table 1 and Supplementary Figure 1). Therefore, Spearman correlation analyses were conducted. As shown in Table 3, Spearman's correlation analysis revealed positive correlations between early pregnancy PBF, FM, FFM, and LM levels and blood glucose values measured during the oral glucose tolerance test at 24–28 weeks of pregnancy (r: 0.07–0.18, all $p < 0.001$).

Generally, a tolerance value of <0.2 or a variance inflation factor (VIF) of >5 indicates multicollinearity among independent variables. Based on these criteria, the collinearity between BMI and body composition parameters (PBF, FM, FFM, LM) was considered acceptable (Supplementary Table 2). Table 4 presents the ORs and corresponding 95% CIs for GDM risk according to early-pregnancy levels of PBF, FM, FFM, and LM. When modeling one body composition measurement (e.g., PBF), other measurements were not included simultaneously. Compared with the lowest tertile, the multivariable-adjusted ORs (95% CIs) for GDM in the highest tertile were 1.77 (1.13, 2.77) for PBF and 1.99 (1.23, 3.20) for FM (both p for trend < 0.001). Additionally, each one-standard deviation increase in early-pregnancy PBF and FM was associated with a 31% (OR = 1.31, 95% CI: 1.07–1.60) and 27% (OR = 1.27, 95% CI: 1.03–1.57) higher risk of GDM, respectively.

The RCS analysis demonstrated that early-pregnancy PBF and FM levels were positively and linearly associated with GDM risk, with threshold values identified as 24.74% for PBF and 13.13 kg for FM. In contrast, early-pregnancy FFM and LM levels were negatively and linearly associated with GDM risk, with threshold values of 39.81 kg and 36.74 kg, respectively (p-overall < 0.001, p-non-linear range: 0.073–0.924) (Figure 1).

Discussion

This large-scale cohort study (3,159 pregnant women) investigated the relationship between maternal body composition at 6–13 weeks of gestation and the risk of maternal GDM. Our findings revealed that elevated PBF and FM were independently associated with an increased risk of GDM, whereas elevated FFM and LM showed protective effects against the development of GDM.

In the literature, the association between obesity and GDM risk has mainly been assessed using traditional BMI (21, 22). In our study, the proportion of pregnant women with an early-pregnancy BMI ≥ 24 kg/m^2 was higher in the GDM group than in the control group (29.29% vs. 19.66%), which aligns with previous findings (21, 22). Although BMI is a widely used parameter for assessing obesity, it cannot provide accurate information on fat distribution (23). In

TABLE 1 Basic information among 3,159 participants according to GDM status.

Variables	Overall (*N* = 3,159)	None-GDM (n1 = 2,879)	GDM (n2 = 280)	*p*-values
Gestational weeks	10.43 (1.91)	10.43 (1.93)	10.48 (1.73)	0.684
Maternal age, years	27.77 (3.99)	27.59 (3.90)	29.58 (4.43)	**<0.001**
Maternal age, *n* (%)				**<0.001**
≤35	3,049 (96.52)	2,796 (97.12)	253 (90.36)	
>35	110 (3.48)	83 (2.88)	27 (9.64)	
Nation (Han), *n* (%)	3,104 (98.26)	2,828 (98.23)	276 (98.57)	0.858
Education level, *n* (%)				
Junior	639 (20.35)	559 (19.54)	80 (28.67)	
Senior	2014 (64.14)	1868 (65.29)	146 (52.33)	**<0.001**
College	487 (15.51)	434 (15.17)	53 (19.00)	
Account (Rural), *n* (%)	2,141 (67.77)	1935 (67.21)	206 (73.57)	**0.035**
Gravidity, *n* (%)				
<3	2,393 (66.14)	2,207 (67.22)	186 (45.66)	**0.001**
≥3	766 (33.86)	672 (32.78)	94 (44.34)	
Parity, *n* (%)				
Primiparity	2,192 (57.25)	2012 (57.71)	180 (52.83)	0.196
Multiparity	967 (42.75)	867 (42.29)	100 (47.17)	
Early pregnancy BMI, kg/m2	21.81 (2.79)	21.72 (2.76)	22.72 (2.91)	**<0.001**
Early pregnancy BMI, kg/m^2				**<0.001**
<18.5	250 (7.91)	234 (8.13)	16 (5.71)	
18.5 ~ 23.9	2,261 (71.57)	2079 (72.21)	182 (65.00)	
≥24	648 (20.51)	566 (19.66)	82 (29.29)	
Gestational weight gain, kg	6.78 (3.78)	7.04 (3.79)	5.01 (3.11)	**<0.001**
FBG, mmol/L	4.03 (0.38)	3.99 (0.32)	4.48 (0.59)	**<0.001**
OGTT-1 h, mmol/L	7.23 (1.67)	6.94 (1.39)	10.19 (1.37)	**<0.001**
OGTT-2 h, mmol/L	6.29 (1.37)	6.04 (1.08)	8.90 (1.35)	**<0.001**

Data are presented as mean ± standard deviation (SD) for continuous variables and frequency (%) for categorical variables.
GDM, gestational diabetes mellitus; N/n, numbers of subjects; BMI, body mass index; OGTT, oral glucose tolerance test; SD, standard deviation. Bold values represent statistical significance.

TABLE 2 Comparison of body composition between GDM group and None-GDM group.

Variables	Overall (*N* = 3,159)	None-GDM (n1 = 2,879)	GDM (n2 = 280)	*P*-values
PBF, %	25.16 (4.49)	25.03 (4.45)	26.47 (4.72)	**<0.001**
FM, kg	13.87 (4.18)	13.76 (4.14)	15.03 (4.41)	**<0.001**
FFM, kg	40.24 (3.94)	40.19 (3.94)	40.74 (3.85)	**0.026**
LM, kg	36.94 (4.46)	36.88 (4.48)	37.51 (4.30)	**0.024**

Data are presented as mean (SD).
N/n, numbers of subjects; GDM, gestational diabetes mellitus; n, numbers of subjects; PBF: percentage of body fat; FM, body fat mass; FFM, fat free mass; LM, lean mass. Bold values represent statistical significance.

TABLE 3 Correlation between body composition index and glucose values in OGTT.

Body composition markers	OGTT-fasting		OGTT-1 h		OGTT-2 h	
	β (95% CI)	*P*-values	β (95% CI)	*P*-values	β (95% CI)	*P*-values
PBF, %	0.18 (0.16, 0.23)	**<0.001**	0.13 (0.11, 0.18)	**<0.001**	0.15 (0.11, 0.18)	**<0.001**
FM, kg	0.18 (0.16, 0.23)	**<0.001**	0.14 (0.11, 0.18)	**<0.001**	0.15 (0.11, 0.18)	**<0.001**
FFM, kg	0.10 (0.09, 0.15)	**<0.001**	0.09 (0.06, 0.13)	**<0.001**	0.07 (0.04, 0.10)	**<0.001**
LM, kg	0.11 (0.09, 0.16)	**<0.001**	0.10 (0.07, 014)	**<0.001**	0.08 (0.05, 0.12)	**<0.001**

Data are presented as β with 95% confidence intervals.
OGTT, oral glucose tolerance test; PBF, percentage of body fat; FM, body fat mass; FFM, fat free mass; LM, lean mass. Bold values represent statistical significance.

TABLE 4 Odds ratios and corresponding 95% confidence intervals for GDM according to tertiles of body composition in early pregnancy.

Variable	ORs (95% CIs) for GDM			Per 1 SD increase	*P* for Trend
	Tertile 1	Tertile 2	Tertile 3		
PBF, %	<22.60	22.60–27.20	≥27.30		
Case/total (%)	68/1036 (6.56)	89/1172 (7.59)	123/951 (12.93)		–
Model 1	Reference	1.17 (0.84, 1.63)	**2.11 (1.56, 2.90)**	**1.37 (1.21, 1.54)**	**<0.001**
Model 2	Reference	0.90 (0.6, 1.37)	**1.77 (1.13, 2.77)**	**1.31 (1.07, 1.60)**	**<0.001**
FM, kg	<11.50	11.50–15.30	≥15.40		
Case/total (%)	66/1017 (6.49)	97/1205 (8.05)	117/937 (12.49)		–
Model 1	Reference	1.26 (0.91, 1.75)	**2.06 (1.50, 2.83)**	**1.33 (1.18, 1.49)**	**<0.001**
Model 2	Reference	1.08 (0.72, 1.66)	**1.99 (1.23, 3.20)**	**1.27 (1.03, 1.57)**	**<0.001**
FFM, kg	<38.50	38.50–41.50	≥41.60		
Case/total (%)	75/1049 (7.15)	112/1138 (9.84)	93/972 (9.57)		–
Model 1	Reference	1.42 (1.05, 1.93)	**1.37 (1.00, 1.89)**	**1.14 (1.01, 1.29)**	**<0.001**
Model 2	Reference	1.12 (0.78, 1.64)	0.98 (0.64, 1.50)	0.99 (0.83, 1.18)	**<0.001**
LM, kg	<35.00	35.00–38.60	≥38.70		
Case/total (%)	87/1071 (8.12)	105/1105 (9.50)	88/983 (8.95)		–
Model 1	Reference	1.19 (0.88, 1.60)	1.11 (0.82, 1.52)	**1.15 (1.02, 1.30)**	**<0.001**
Model 2	Reference	0.88 (0.61, 1.26)	0.70 (0.46, 1.07)	0.99 (0.82, 1.19)	**<0.001**

Data are presented as odds ratios with corresponding 95% confidence intervals. "Per 1 SD Increase" represents the effect value of GDM risk corresponding to each standard deviation increase in body composition; while "*P* for trend" is the trend effect value obtained by including body composition tertiles as ordinal variables in the regression model.
GDM, gestational diabetes mellitus; OR, odds ratio; CI, confidence intervals; SD, standard deviation; PBF, percentage of body fat; FM, body fat mass; FFM, fat free mass; LM, lean mass.
Model 1: without adjustment.
Model 2: adjusted for maternal age, early pregnancy body mass index, nationality, household registration type, education level, gravidity, parity, gestational weight gain. Bold values represent statistical significance.

overweight individuals, BMI is highly correlated with the FM (24); however, some women with normal weight are also prone to abnormal body fat accumulation, a condition known as normal-weight obesity. A Korean study identified normal-weight obesity as an early predictive biomarker of metabolic syndrome (25). A prospective cohort study from China on the general population also showed that individuals with normal-weight obesity had a significantly increased risk of diabetes after 9 years (26). Moreover, evidence from the National Health and Nutrition Examination Survey indicates that within each BMI category, higher body fat levels are associated with increased homeostatic model assessment-insulin resistance (27). This suggests that even at a normal body weight, fat accumulation can induce changes in glucose metabolism, affecting health.

Positive associations between first-trimester PBF and FM levels and GDM risk were observed in our research. A retrospective study by Zhang et al. (28) similarly reported that elevated early-pregnancy PBF was an independent risk factor for GDM. Rahnemaei et al. (29) conducted a meta-analysis (29 studies, 56,438 participants) and found that FM, especially visceral fat, significantly contributes to GDM progression, consistent with our findings. Additionally, our study showed that for each standard deviation increase in first-trimester PBF and FM, the odds of developing GDM increased by 31 and 27%, respectively. This discovery fills a knowledge gap regarding dose–response relationships. Unlike previous studies, we verified the independence between BMI and body composition measurements, enhancing the reliability of risk assessment. This strengthens the validity of our findings and indicates that body composition parameters may provide greater value than traditional BMI in early pregnancy GDM risk assessment.

Restricted cubic spline analysis provided important thresholds for body composition parameters in predicting GDM risk. Skeletal muscle may protect against GDM by improving insulin sensitivity and regulating glucose metabolism (10, 30). The identification of specific thresholds (PBF: 24.74%, FM: 13.13 kg, FFM: 39.81 kg, LM: 36.74 kg) provides valuable clinical reference points. Notably, our determined PBF threshold (24.74%) was considerably lower than the typical lean obesity thresholds (30–35% body fat) for women cited in previous definitions (31). This lower threshold suggests that even a moderate elevation in early-pregnancy PBF may substantially impact GDM risk. A previous study (32) reported an average PBF of 33.18% ± 5.94% (our study: 25.16% ± 4.49%) among subjects aged 30.20 ± 3.98 years (our study: 27.77 ± 3.99 years). Age may influence PBF levels, and studying younger populations could help establish lower PBF thresholds.

A metabolic characteristic of GDM is relative insulin deficiency, wherein maternal β-cell insulin secretion cannot compensate adequately for the gradual increase in insulin resistance during pregnancy (33). Elevated circulating placental hormones, including estrogen, progesterone, and growth hormone, decrease insulin sensitivity, prompting β-cells to secrete more insulin and contributing to insulin resistance (34). Obesity before or early in pregnancy exacerbates insulin resistance. The complex mechanisms by which obesity induces metabolic disorders have been widely reported (35, 36). Adipose tissue is an active endocrine organ that can secrete various adipokines and cytokines, which induce chronic

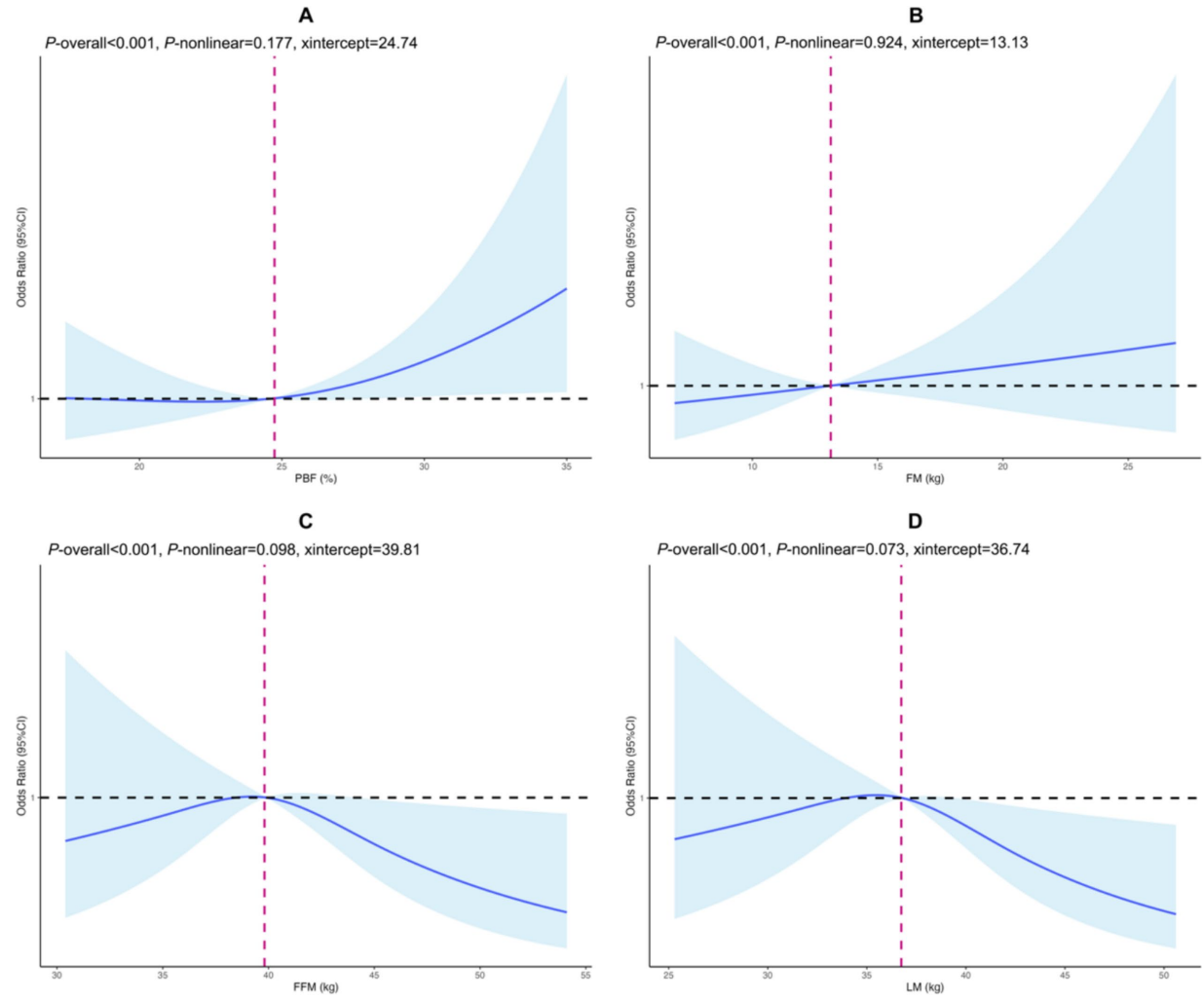

FIGURE 1
Cubic spline regression of body composition in early pregnancy and gestational diabetes mellitus. **(A)** PBF, **(B)** FM, **(C)** FFM, **(D)** LM. The horizontal axis represents the body component value (continuity variable), and the vertical axis is the odds ratio corresponding to GDM risk. The black horizontal dashed line is the reference line for the odds ratio, while the fuchsia vertical dashed line indicates the value of the body composition when OR is 1. Solid blue lines and shadows are point estimates with corresponding 95% confidence intervals of GDM risk. PBF, percentage of body fat; FM, body fat mass; FFM, fat free mass; LM, lean mass. Adjusted for early pregnancy BMI, maternal age, ethnicity, household registration type, education level, gravidity, parity, gestational weight gain.

low-grade inflammation and insulin resistance, impairing glucose uptake in peripheral tissues (37, 38). High FM levels may further exacerbate insulin resistance (39, 40), leading to hyperglycemia and GDM.

Identifying PBF and FM as important predictors of GDM risk holds crucial clinical value. Early assessment of body composition helps identify women at a high risk of GDM before significant metabolic disorders occur. Early identification facilitates timely interventions, including personalized nutrition management (41), physical activity plans (42), and closer blood glucose monitoring (43), potentially reducing GDM risk or severity. We recommend incorporating body composition measurements into routine prenatal care to enhance GDM risk stratification and prevention.

This large-scale study assessed obesity's impact on GDM using body composition rather than BMI, providing more accurate results than previous BMI-based studies. However, several limitations remain. First, using BMI measured at the first obstetric visit instead of pre-pregnancy BMI may not accurately reflect pre-pregnancy condition, potentially causing information bias. Second, confounding bias may still exist due to unmeasured or unknown variables. For instance, previous evidence suggests correlations between GDM incidence and dietary nutrition (fiber intake, vitamin D, sugar-sweetened beverages) (42, 44–46), physical activity (42), socioeconomic status (47), sleep duration (48), and mental health factors such as anxiety or depression (49). Additionally, we only collected body composition data in early pregnancy, thus, changes during pregnancy might have greater impacts on GDM risk. Finally, all participants were from southwestern China, limiting the generalizability of our findings to other populations. Further research is urgently needed to explore the mechanisms underlying the non-linear relationship between lean body mass and GDM risk.

Conclusion

GDM risk is positively associated with PBF and FM but negatively correlated with FFM and LM. Body composition measurements should be incorporated into routine prenatal care to facilitate the early identification and prevention of GDM.

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 study was approved by the Ethics Committee of Chengdu Shuangliu District Maternal and Child Health Care Hospital (No. ky202404). Written informed consent was obtained from all participants.

Author contributions

YanL: Conceptualization, Formal analysis, Funding acquisition, Writing – original draft, Writing – review & editing. BZ: Project administration, Supervision, Writing – review & editing. YT: Data curation, Formal analysis, Writing – review & editing. YangL: Data curation, Investigation, Writing – review & editing. XL: Data curation, Investigation, Writing – review & editing. HG: Data curation, Investigation, Writing – review & editing. LX: Data curation, Investigation, Writing – review & editing. JY: Conceptualization, Methodology, 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.

Generative AI statement

The authors declare that no Gen AI was used in the creation of this manuscript.

Publisher's note

Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fnut.2025.1565986/full#supplementary-material

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An observational study on non-communicable disease risk factors among healthcare workers in high-stress environments

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Introduction: Non-communicable diseases (NCDs) account for 74% of global mortality and place significant socioeconomic burdens on healthcare systems. Despite their knowledge and awareness, healthcare workers (HCWs) often struggle to adopt preventive measures due to demanding work conditions and high-stress environments.

Methods: This observational study aimed to evaluate the prevalence of NCD risk factors among HCWs at the University Hospital "Paolo Giaccone" in Palermo, Italy. An online questionnaire, based on the WHO's STEPS approach, was administered to 390 HCWs. Data from 273 responses were analyzed using SPSS software.

Results: The sample comprised 57.9% women, predominantly nurses (35.9%).

Discussion: Key findings revealed that 56.8% consumed alcohol, 42.1% used tobacco, and 86.1% frequently skipped meals due to work. Lifestyle factors, such as fruit and vegetable consumption, salt intake, and physical activity, were assessed alongside metabolic risk factors like blood pressure, glycemia, and triglycerides. Despite their expertise in NCD prevention, HCWs often failed to implement healthy behaviors. While evening shift work showed limited correlation with lifestyle changes, results underscored the need for targeted health promotion programs for HCWs. Healthcare institutions should actively support their workforce in adopting healthier lifestyles to mitigate NCD risks and improve public health outcomes.

KEYWORDS

non-communicable diseases, healthcare workers, lifestyle risk factors, health promotion programs, occupational health

1 Introduction

Non-communicable diseases (NCDs), are long-lasting conditions not caused by infectious agents triggered by various risk factors, and marked by slow progression and/gradual deterioration of organ or tissue function. To date, NCDs represent the leading cause of death and disability worldwide. The estimates produced by the World Health Organization (1), called Global Health Estimates (GHE) between 2000 and 2019 speak clearly: NCDs with 74% of total deaths (72% in males and 75% in females) are the main cause of death worldwide and, in Italy, it has been estimated that they were the main cause of mortality in 91% of cases (90% in males and 91% in females) (2).

The most widespread NCDs globally are currently grouped into four main groups: cardiovascular diseases, tumors, chronic respiratory diseases and diabetes; together they constitute almost 80% of all causes of death globally (3). In the population of individuals aged 30 to 69 years, nearly half (49%) of NCDs are considered preventable through appropriate public health interventions, lifestyle modifications, and access to timely healthcare. This staggering statistic translates to approximately 2.4 million deaths each year that could be avoided, along with the prevention of 93.8 million disability-adjusted life-years (DALYs)—a measure reflecting years of healthy life lost due to illness or premature mortality (4).

In Italy, NCDs impact approximately 24 million individuals, significantly influencing both life expectancy and quality of life. While these conditions can affect people at all life stages, they are most prevalent among the older adult—over 85% of individuals aged 75 and above are affected—and among women, particularly those over the age of 55 (5). Data observed at global and national level align with those recorded in Sicily where, in 2020, the statistics provided by ISTAT (6) confirm 19,078 deaths from cardiovascular diseases, 13,067 from tumor pathologies, 2,053 from chronic diseases of the respiratory system, 3,014 for diabetes mellitus.

One of the main characteristics of NCDs is, undoubtedly, the etiological multifactorial nature. Modifiable risk factors include tobacco and alcohol consumption, lack of physical activity, overweight and obesity, increased fat and salt consumption, low fruit and vegetable consumption, increased blood pressure, increased glucose levels and cholesterol that predispose to the development of NCD (1).

Healthcare workers (HCWs)are not exempt from the risk of NCDs and represent a critical population for examining individual health behaviors. This is due to their heightened awareness of health-related choices compared to the general population and their pivotal role in advising patients while modeling and promoting healthy lifestyles and behaviors. The World Health Organization (WHO) broadly defines HCWs as all people engaged in actions whose primary intent is to enhance health. This therefore includes doctors, nurses, obstetricians, public health professionals, laboratory, personal care workers, community workers, paramedical staff, as well as non-medical staff who carry out assistance-related activities, such as support staff ranging from rescue drivers to company managers (7).

Those who are employed in the provision of healthcare are exposed to numerous risks to their health daily, including biological risk, chemical risk, physical risk, ergonomic risk and psychosocial risk (8).

All the factors listed above are already widely known, studied and find their recognition in the implementation of mandatory preventive strategies, not only by the employer, but primarily for the worker himself and included in the current legislation which corresponds to the D.lgs. 81/08, the Consolidated Law on the health and safety of workers (9).

The healthcare sector is among the most dangerous working environment from the point of view of health and well-being with less than 1/6 of countries that have issued a national-level policy for the health and safety of workers in the healthcare sector (10), with an ever-increasing number of HCWs contracting infections, occupational diseases and injuries every day at work, who are subjected to strong psychological and emotional stress which can degenerate into burnout. All these factors if not timely identified and managed, may cause significant distress and increased risk for the development of long-term consequences.

This situation could lead to absenteeism, long periods of illness, personal and professional dissatisfaction, high turnover of operators, instability in the work organization, poor relationships between colleagues and numerous other problems that significantly affect the quality of the work environment and its general performance (11).

As far as NCDs and related risk factors are concerned, although they are increasingly relevant and in-depth topics in the literature, there is still very little evidence that focuses on individual work environments, particularly healthcare and health professionals. Healthcare workers face unique occupational challenges, including high levels of stress, long working hours, irregular schedules, and exposure to demanding clinical or administrative conditions. These factors may significantly influence health behaviors and amplify certain risk factors such as physical inactivity, unhealthy diets, smoking, or stress-related conditions (12).

Understanding the interplay between occupational settings and individual health choices is crucial, as healthcare workers are not only at risk themselves but also serve as role models and advisors for patients.

The objective of this study is to assess among HCWs, the prevalence of risk factors contributing to the development of NCDs, while also exploring the role of the work environment in shaping these risks. Moreover, this study aims to identify workplace dynamics that may contribute to the risk of NCDs, thereby providing insights into targeted interventions to improve occupational health and promote healthier behaviors in this critical workforce.

2 Materials and methods

An analytical cross-sectional survey-based study was carried out from 20th June until 31st July 2023. The study included HCWs of the University Hospital "Paolo Giaccone." – Palermo (Italy) of both sexes, aged between 18 and 70 years, working at the University Hospital "P. Giaccone," who voluntarily decided to complete the administered questionnaire. Data collection was conducted using a structured questionnaire designed to assess key variables related to NCDs and associated risk factors. The questionnaire was distributed digitally using the "Google Form" platform, ensuring accessibility and ease of response for participants. The structured format of the questionnaire enabled the systematic collection of data, allowing for the evaluation of health behaviors, risk factors, and the potential influence of occupational environments on the prevalence of NCD-related risk factors among healthcare workers.

The questions were extrapolated from the questionnaire used to implement the WHO "STEPS" approach (STEPwise approach to NCD risk factor surveillance).

The WHO STEPwise Approach to Surveillance (STEPS) is an internationally comparable, standardized and integrated surveillance tool through which countries can collect, analyze and disseminate key information on non-communicable diseases (13).

The questionnaire comprises three main sections, beginning with an introductory segment that clearly outlines the objectives and methodology of the study in a concise and comprehensive manner. This section also includes essential information regarding data privacy and the handling of personal and sensitive data, in compliance with the provisions of D. lgs 101/2018. This introductory section also informed participants on the anonymity of the data collection and analysis as well as the possibility that the research results may

be published in medical journals or presented at conferences to advance scientific knowledge.

The first section focuses on collecting basic demographic and personal information. The second section is structured into thematic subsections and contains a total of 26 multiple-choice questions designed to assess common risk factors for non-communicable diseases (NCDs). These include queries on alcohol and tobacco use, dietary habits, salt intake, physical activity levels, vital signs, and any prior diagnoses of risk factors associated with chronic conditions.

We evaluated two groups of main risk factors: behavioral and metabolic.

The assessment of the key variables was conducted as follows:

- Alcohol consumption was estimated based on the intake of alcoholic beverages in the previous 30 days and based on the frequency of intake in the given period.
- Tobacco use was calculated on those who declared having smoked in the last 30 days and based on the frequency of smoking cigarettes and similar products.
- For the "eating habits" variable, was asked about the weekly frequency of "eating fruit and vegetable meals" and the "habit of consuming meals related to working hours."
- The consumption of salt and products with a high sodium content was estimated based on the habitual addition of salt to food and the frequency with which this occurs.
- For physical activity, work-related information was collected, in terms of 3 factors: a consistent and/or moderate increase in heart rate and/or breathing; activity practiced habitually over a week for at least 20–30 min; the methods of traveling for short distances and a personal opinion on the perception of one's own level of physical activity.
- For risk factors, questions regarding the variables "measurement of blood pressure, blood sugar and cholesterol/triglyceridemia" were included with the help of a qualified operator.
- For chronic diseases, previous history of arterial hypertension, diabetes, hypercholesterolemia/hypertriglyceridemia and adherence to therapy in relation to working hours were evaluated.

The final segment comprises two additional concise multiple-choice subsections aimed at evaluating potential behavioral changes that could either reduce or increase the risk of developing NCDs. This structured approach ensures a comprehensive evaluation of participants' health behaviors and their potential modifiability in relation to NCD prevention. The questionnaire was proposed to all HCWs and was completed voluntarily and anonymously, involving almost all levels of the organization outlined by Henry Mintzberg, except for the strategic top management. Nurses and doctors represented the largest sample followed by administrative staff and the IT staff. To ensure the widest dissemination, the invitation to fill up the questionnaire was published on the Intranet of the University Hospital, prior to authorization from the "Palermo 1" ethics Committee.

2.1 Statistical analysis

The required minimum sample size for this investigation was calculated using Epi InfoTM version 7.2.5 (CDC, Atlanta, GA, USA, 2021) and was 335 subjects with a potential drop-out of 25%. The sample size was calculated to provide 80% power with $\alpha = 0.05$.

The data are expressed as a mean ±SD, or frequency (%). Differences between gender and age were assessed by a chi-square test or Fisher's exact test, as needed for categorical variables, and by univariate analysis of variance (ANOVA) for parametric variables. Characteristics of the habits and lifestyle of the HCWs (dependent variables) correlated with evening/night shift work activity (independent variable) were evaluated by univariable (Crude OR) and multivariable (Adjusted OR) regression analysis.

The data were analysed using IBM SPSS Software version 24 (IBM Corp., Armonk, NY, USA). All p values were two-tailed, and $p \leq 0.05$ was considered to indicate statistical significance.

3 Results

A total of 273 healthcare workers (around 80% of the study population) at the University Hospital "Paolo Giaccone" filled the questionnaire, out of approximately 335 HCWs to whom the questionnaire was proposed.

The sample obtained was then classified, using the Sturges rule, within the following age classes:

- I class: 23–29 years.
- II class: 30–50 years.
- II class: 51–64 years.
- IV class: 65–70 years.

Table 1 reports the characteristics of the study population, represented mostly by females (57.9%), and with average age 47.0 (±11.9) years. The most represented age group was the 53–58 years (17.9%). The various health professionals were represented as follows: nurses (35.9%), physicians/residents (25.6%), healthcare support workers (9.5%), health technicians (9.2%), other HCWs (19.8%) More than a half (55.7%) of the respondents reported working evening/night shifts.

Table 2 summarizes the results related to the habits and lifestyle of those interviewed, investigating the prevalence of the various behavioral risk factors. More than half of the respondents (56.8%) reported having consumed alcohol in the last 30 days, and the most frequent group (38.7%) reported consumption 1–2 times per week. No differences emerged between sexes in alcohol consumption ($p = 0.09$), while younger individuals tended to consume significantly more alcohol ($p < 0.0005$).

To evaluate smoking habits, the questionnaire investigated those who smoked tobacco products at least once, resulting in 42.1% positive response. The most represented group was those who smoked fewer than 5 (35.7%) and 10 (30.4%) cigarettes per day. No significant differences emerged between sexes in smoking habits ($p = 0.258$); smokers were also more frequent in the younger age group ($p = 0.012$).

Overall, 66.6% ($N = 182$) and 51.3% ($N = 140$) of respondents reported consuming fruit and vegetables daily or 5–6 times per week, respectively, with a higher fruit consumption among males ($p = 0.030$) and a higher vegetable consumption among females ($p < 0.0005$). Older individuals reported consuming more fruits ($p < 0.0005$), while no age differences were observed in vegetable consumption.

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TABLE 1 Characteristics of the study population.

	N (%)
Age classes	
23–28	19 (7.0)
29–34	33 (12.1)
35–40	41 (15.0)
41–46	32 (11.7)
47–52	43 (15.8)
53–58	49 (17.9)
59–64	42 (15.4)
65–70	14 (5.1)
Gender	
Male	115 (42.1)
Female	158 (57.9)
Work	
Nurses	98 (35.9)
Physicians/residents	70 (25.6)
Healthcare support workers	26 (9.5)
Health technicians	25 (9.2)
Others	54 (19.8)
Shift work	
Yes	152 (55.7)
No	121 (44.3)

The consumption of salt and the intake of processed foods with a high sodium content appeared to be moderate in both sexes and for all age groups.

It also emerged that 235 interviewed (86.1%) had skipped (often/sometimes) a meal due to working hours.

Regarding physical activity in the workplace, 71.4% versus 28.6% responded that their work does not involve high intensity activities that can cause a significant increase in heart rate and/or breathing; while 56% versus 44% said that their work involves moderate intensity activity, which can cause modest changes in heart rate and/or breathing.

The questionnaire included also behavioral questions such as the mode of travel for short distances. The majority of those interviewed, 44.7%, seemed to prefer moving on foot, while the second most used means of transport are the car and public transport (37%) and, in modest percentages, motor vehicles (12.8%).

Physical activity was further investigated, and it was found that only 42.1% practiced a high/medium intensity sporting, physical activity or hobby for at least 20–30 min, however, with a weekly frequency of 1–2 times or less.

Table 3 includes the results related to the prevalence of metabolic risk factors. The presence of any NCDs in the anamnesis and the relationship with any related therapy were also investigated.

For the hypertension factor, 94.9% of those interviewed had their blood pressure measured at least once; furthermore, 31.5% had received a diagnosis of hypertension. 22% of women and 44% of men had values above the average and/or received a diagnosis of hypertension ($p < 0.0005$). The diagnosis of hypertension was

TABLE 2 Characteristics of the habits and lifestyle of the HCWs interviewed.

Alcohol and tobacco consumption	
Have you drink alcoholic beverages in the 30 days after?	
Yes	155 (56.8%)
No	118 (43.2%)
If yes, how often	
Every day	3 (1.9%)
5–6 times a week	4 (2.6%)
3–4 times a week	10 (6.5%)
1–2 times a week	60 (38.7%)
1–3 times a month	49 (31.6%)
Less than 1 a month	29 (18.7%)
Have you ever smoked/do you smoke cigarettes or other products with tobacco?	
Yes	115 (42.1%)
No	158 (57.9%)
If yes, how many cigarettes do you smoke daily?	
More than 20	9 (7.8%)
11–20	30 (26.1%)
6–10	35 (30.4%)
1–5	41 (35.7%)
How often do you eat fruits?	
Every day	165 (60.4%)
5–6 times a week	17 (6.2%)
3–4 times a week	35 (12.8%)
1–2 times a week	32 (11.7%)
Less than 1 a week	24 (8.8%)
How often do you eat vegetables?	
Every day	103 (37.7%)
5–6 times a week	37 (13.6%)
3–4 times a week	66 (24.2%)
1–2 times a week	48 (17.6%)
Less than 1 a week	19 (7.0%)
How often do you add salt or high-sodium condiments (e.g., bouillon cubes, ketchup, soy sauce, etc.) to your meals?	
Always	24 (8.8%)
Often	41 (15.0%)
Sometimes	82 (30.0%)
Rarely	93 (34.1%)
Never	33 (12.1%)
How often do you consume processed foods with a high salt content? (e.g., packaged savory snacks, cheese, processed meat, fast food, canned foods).	
Always	7 (2.6%)
Often	50 (18.3%)
Sometimes	124 (45.4%)

(Continued)

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TABLE 2 (Continued)

Alcohol and tobacco consumption	
Rarely	80 (29.3%)
Never	12 (4.4%)
Have you ever skipped a meal because of your work shifts?	
Yes	235 (86.1%)
No	38 (13.9%)
If yes, how often?	
Always	12 (5.1%)
Often	80 (34.0%)
Sometimes	106 (45.1%)
Rarely	37 (15.8%)
Does your job involve high-intensity physical activities that can cause a significant increase in heart rate and/or breathing?	
Yes	78 (28.6%)
No	195 (71.4%)
Does your job include moderate intensity physical activities that may cause modest changes in heart rate and/or breathing?	
Yes	153 (56%)
No	120 (44%)
During the week, do you practice a high/medium intensity sporting or physical activity or hobby for at least 20–30 min?	
Yes	115 (42.1%)
No	158 (57.9%)
If yes, how often?	
Every day	6 (5.2%)
5–6 times a week	5 (4.3%)
3–4 times a week	38 (33.0%)
1–2 times a week	58 (50.5%)
Less than 1 a week	8 (7.0%)

associated with an older age ($p < 0.0005$), and the frequency increases with age, reaching 88% among those over 55.

In terms of diabetes secondary prevention, 90.5% of those interviewed had their blood sugar measured with the help of a professional. Overall, 14.7% of the respondents reported elevated blood glucose levels without sex differences but associated with a higher average age ($p = 0.006$), with 80% of the cases occurring in individuals over 40 years of age. For the metabolic risk factor "dyslipidemia," 94.5% carried out this measurement with the help of a professional. Among those who measured hypercholesterolemia and triglyceridemia, 49.1% of both women and men found values above the physiological threshold, with a significant association with a higher average age ($p < 0.0005$) and 68% of the cases occurring in individuals over 45 years of age. Finally, respondents diagnosed with NCD were asked whether they were able to take medications regularly for their condition, and only 30.8% said they took medications regularly.

Ultimately, the attitude of the interviewees toward a possible change of their lifestyle in order to improve their health was observed

TABLE 3 Characteristics of the NCDs and metabolic risk factors of the HCWs interviewed.

Non-communicable disease	Yes	No
Have you ever measured your blood pressure, at least once, with the help of a professional?	259 (94.9%)	14 (5.1%)
Have you ever had blood pressure readings above average and/or been diagnosed with hypertension?	86 (31.5%)	187 (68.5%)
Have you ever measured your glycemic values, at least once, with the help of a professional?	247 (90.5%)	26 (9.5%)
Have you ever had blood sugar levels above average or been diagnosed with diabetes?	40 (14.7%)	233 (85.3%)
Have you ever measured, at least once, your cholesterol levels (HDL, LDL) and/or triglycerides?	258 (94.5%)	15 (5.5%)
Have you ever experienced high cholesterol and/or triglycerides?	134 (49.1%)	139 (50.9%)
If you have ever been diagnosed with a chronic disease (e.g., hypertension, diabetes) do you regularly take medications for your condition?	84 (30.8%)	156 (57.2%)

From a univariate analysis, evening shift resulted significantly associated with younger age ($p < 0.0005$), alcohol consumption ($p = 0.043$), impact of shifts on the quality/quantity of meals ($p < 0.0005$), salt consumption ($p = 0.002$), and inversely correlated with the possibility of high blood pressure ($p = 0.040$), high blood sugar ($p = 0.005$), and high cholesterol ($p = 0.036$).
In a multivariable model, the evening shift resulted significantly associated with younger age, salt consumption, and the impact of shifts on the quality of meals, while hyperglycemia was inversely associated with evening shifts.

and the results were the following: 26.4% thought about quitting smoking, but only 13.9% actually implemented this behavior; 33.7% thought about increasing their weekly fruit and vegetable intake and 27.5% implemented this decision; again, 27.5, 42.1 and 38.8% thought of reducing the daily intake of salt, fat and sugar in their diet, respectively, and 24.2, 38.5 and 34.1% paid attention to implementing this indication.

Finally, for the physical activity factor, 57.5% thought at least once about starting or carrying out more physical activity and 62.6% thought it appropriate to pay attention to achieving and maintaining an optimal weight, but only 40.7 and 52% carried out this choice (Table 4).

4 Discussion

The aim of our study was to determine the prevalence of NCD risk factors and their association with shift work among HCWs at a University teaching hospital.

Our study reveals a complex interplay between lifestyle habits, occupational patterns, and NCD risk. The findings show that over half of respondents reported alcohol consumption in the past 30 days (56.8%) and 42.1% reported a history of smoking, with both behaviors significantly more common among younger individuals. Although the majority consumed fruits daily or almost daily, and 51.3% reported similar frequency for vegetables, only a minority engaged in regular physical activity of moderate-to-high intensity (42.1%), and a striking 86.1% reported skipping meals due to work-related constraints. In

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TABLE 4 Factors associated with evening/night shift work activity at uni (Crude OR) and multivariable (Adjusted OR) regression analysis (95% CI: 95% confidence interval).

	Evening/night shift work activity			
	Crude OR (95% CI)	*p*-value	Adj-OR (95% CI)	*p*-value
Age				
	Ref.	<0.0005	Ref.	<0.0005
	0.943 (0.922–0.964)		0.947 (0.920–0.974)	
Sex				
Female	Ref.	0.137	Ref.	0.224
Male	0.693 (0.427–1.124)		0.689 (0.378–1.257)	
Fruit consumption (5–6 times a week or more)				
Yes	Ref.	0.169	Ref.	0.781
No	1.433 (0.858–2.394)		0.906 (0.452–1.817)	
Vegetable consumption (5–6 times a week or more)				
Yes	Ref.	0.990	Ref.	0.856
No	0.997 (0.618–1.608)		0.943 (0.500–1.780)	
Consumed alcohol in the last 30 days (5–6 times a week or more)				
No	Ref.	0.043	Ref.	0.509
Yes	1.648 (1.016–2.673)		1.211 (0.686–2.139)	
Smoking tobacco products (10 cigarettes or more)				
No	Ref.	0.108	Ref.	0.309
Yes	1.494 (0.916–2.436)		1.338 (0.7642.343)	
Salt consumption (Often/sometimes)				
No	Ref.	0.002	Ref.	0.040
Yes	1.538 (1.177–2.010)		1.352 (1.010–1.823)	
Skipped meals (Often/simetimes)				
No	Ref.	0.684	Ref.	0.858
Yes	1.153 (0.580–2.293)		1.073 (0.496–2.320)	
Physical activity (3–4 times a week)				
Yes	Ref.	0.627	Ref.	0.515
No	0.887 (0.546–1.439)		1.216 (0.676–2.188)	
Diagnosis of hypertension				
No	Ref.	0.040	Ref.	0.238
Yes	0.582 (0.348–0.974)		1.489 (0.768–2.888)	
Hyperglycemia				
No	Ref.	0.005	Ref.	0.030
Yes	0.371 (0.184–0.747)		0.405 (0.179–0.918)	
Hypercholesterolemia/hypertriglyceridemia				
No	Ref.	0.036	Ref.	0.435
Yes	0.598 (0.370–0.968)		0.802 (0.461–1.395)	
On a scale of 1–5, do you think work hours affect the quality of your meals?				
No	Ref.	<0.0005	Ref.	<0.0005
Yes	1.755 (1.403–2.196)		1.682 (1.300–2.175)	

terms of metabolic risk factors, 31.5% had been diagnosed with hypertension (with prevalence increasing to 88% in those over 55), 14.7% had elevated blood glucose (primarily over age 40), and 49.1% reported dyslipidemia, with a strong age association (68% over age 45). Despite these health risks, adherence to medical therapy was low, with only 30.8% of those diagnosed with an NCD reporting regular medication intake. Interestingly, evening shift work was associated with greater behavioral risks (e.g., alcohol and salt consumption), but inversely correlated with the presence of hyperglycemia, hypertension, and dyslipidemia. These findings underscore the dual burden of behavioral and occupational factors influencing health among HCWs and highlight both age- and shift-related vulnerabilities that warrant targeted intervention.

Several studies have investigated the development of NCDs in the category of shift workers, yet relatively few have focused specifically on HCWs, despite their high exposure to rotating schedules and occupational stress. A notable Norwegian cross-sectional study (14) involving over 23,000 HCWs found a significant association between shift work and musculoskeletal disorders, particularly affecting the cervical and dorsal-lumbar spine, conditions frequently leading to chronic disabilities. This association was hypothesized to stem from shift work-induced disturbances, which elevate inflammatory markers such as C-reactive protein (CRP). Emerging evidence suggests that these systemic inflammation can mediate the link between irregular work hours and chronic musculoskeletal pain, though the study acknowledged limitations and called for further longitudinal research. Complementing these findings, a Scandinavian cohort study (15) compared two groups of HCWs - those engaged in regular shifts versus those assigned to fixed evening or night shifts.

One year after the baseline survey, individuals working with fixed evening and/or night shifts, exhibited higher risk of obesity, greater tobacco consumption and reduced or absent physical activity during free time, underscoring the multifaceted impact of shift work on behavioral and metabolic risk factors.

Some studies have suggested that rotating shift work may be associated with adaptive lifestyle changes or reduced perceived stress over time. For instance, a cross-sectional study by Chiang et al. (16) investigated the impact of shift patterns on lifestyle and stress among hospital nurses, revealing important associations between work schedules and health-related behaviors. The study found that nurses on fixed day shifts reported significantly lower levels of perceived stress compared to those working rotating shifts. Moreover, among rotating-shift nurses, those on fixed evening or night schedules experienced longer sleep duration than those on variable rotating schedules. Interestingly, longer duration of rotating shift work was positively associated with healthier dietary behavior, improved sleep quality, and reduced perceived stress, although it also correlated with slightly shorter sleep duration. These findings suggest that both the type and consistency of shift schedules influence nurses' ability to adapt lifestyle habits, with fixed shifts offering potential benefits in mitigating stress and supporting healthier routines.

Also, data from the Sixth European Working Conditions Survey (17) have shown that shift workers, including those in healthcare, are more likely to experience work-related stress, irregular sleep, and poor work–life balance, which are recognized contributors to long-term health risks. However, specific lifestyle-related behaviors were not directly assessed.

Given the scarce evidence regarding the effects of shift work on health-related behaviors, our decision to focus on healthcare workers (HCWs) was further supported by their unique position at the intersection of occupational vulnerability and public health responsibility. Choosing HCWs as our target population was also motivated by their dual role as caregivers and health models. Despite their heightened awareness compared to the general population, many HCWs still struggle to adhere to recommended strategies for NCD prevention, highlighting a critical disconnect between knowledge and practice. This points to the urgent need for institutional health promotion strategies tailored to this population. Policy interventions—such as the integration of physical activity zones within healthcare facilities and structured, protected mealtimes for shift workers—could significantly enhance both individual health outcomes and the broader sustainability of the healthcare system.

While certain risk factors appear to be associated with shift work, our findings suggest that lifestyle behaviors may play a more significant mediating role than work schedules alone. In most of cases, rather than the mere presence of night or evening shifts, it is often the behavioral adaptations individuals make in response to their working routines - such as increased tobacco use or irregular eating patterns - which may or may not lead to the development of cardiovascular and metabolic diseases. For instance, similar observations were made in a cross-sectional study conducted on railway network workers, which found significantly higher levels of total and LDL cholesterol levels among shift workers compared to their day-working counterparts (18). However, the limited number of scientific studies specifically targeting healthcare professionals poses a limitation, underscoring the need for more tailored investigations within this occupational group, to be able to make meaningful comparisons. Our study aimed to address this gap by focusing on healthcare workers (HCWs) as a unique subgroup of shift workers who are simultaneously exposed to occupational strain and elevated health risks. Despite being predominantly younger, those working evening shifts reported compromised dietary patterns, with a substantial proportion (86.1%) indicating they frequently skipped meals due to work demands. Importantly, most respondents reported having undergone objective assessments of key health indicators—including blood pressure, blood glucose, cholesterol, and triglycerides—demonstrating a relatively high level of health awareness. This was further reflected in their self-reported intentions to improve lifestyle behaviors, such as increasing fruit and vegetable intake, reducing salt and fat consumption, and enhancing physical activity levels, even if the actual implementation of these changes remained suboptimal.

Several limitations must be acknowledged. First, the lack of a control group limits causal inference and reduces the ability to generalize findings beyond the study population. While our cross-sectional design provides important insights into current health patterns among HCWs, longitudinal studies with appropriate comparison groups are needed to better understand temporal trends and causal relationships. Second, reliance on self-reported data introduces the potential for recall bias and social desirability bias, particularly in reporting behaviors such as alcohol and tobacco use or adherence to healthy practices. While the use of a structured, anonymous questionnaire may have mitigated some of these concerns, future studies could benefit from integrating objective measurements and clinical assessments. Lastly, while our sample was substantial relative to the population size, it represents a single institution, and

broader multi-center studies would strengthen the external validity of the findings. Another limitation of this study is the use of a shortened physical activity assessment tool consisting of questions that did not capture active commuting. This choice was intentional to reduce respondent burden. Additionally, Palermo's urban setting reduces the relevance of commuting-related physical activity in this population. However, this omission may have led to an underestimation of total physical activity which should be considered when interpreting the findings.

On the other hand, the added value of our study, in addition to being one of the first to be conducted at a University teaching hospital, is to be able to represent not only a stepping stone for developing other studies on the matter, but also to encourage policy makers to understand that the best strategy to safeguard the national healthcare system is the prevention of NCDs in every work, healthcare sector and not.

The findings of this study carry several practical implications for occupational health policy and preventive strategies in healthcare settings. The high prevalence of modifiable risk behaviors—such as alcohol consumption, irregular eating patterns, and physical inactivity—among HCWs underscores the need for workplace-centered interventions. Structured health promotion programs, including on-site fitness facilities, nutrition education, and scheduled protected meal breaks, could be especially beneficial. Moreover, given that many respondents expressed a willingness to adopt healthier behaviors, institutional support may bridge the gap between intention and sustained lifestyle change. As HCWs serve as role models for patient populations, investing in their well-being not only improves individual health outcomes but also has the potential to reinforce public health messaging through more credible, lived experiences.

From this perspective, it is easy to understand how effective strategies in matters of health promotion and prevention can bring significant benefits for optimal management of resources (19), both human and economic, as well as an improvement in terms of effectiveness, efficiency and performance of the Italian healthcare system.

5 Conclusion

In this observational study, we analyzed the characteristics of HCWs, focusing on the prevalence of the most common risk factors predisposing for NCDs and it was observed that their distribution changes significantly based on the sex, age and profession of the individual subject. It is necessary, however, to underline that the data collected regarding the correlation of these with shift work, both in this study and at an international level are still few and inconclusive. For this reason, it is still difficult to make a significant comparison of the association of risk factors with the different professional categories and respective shifts. However, from the analysis it emerges that, despite greater awareness compared to the general population, a large part of workers in the healthcare sector do not adhere to primary prevention strategies for NCDs and therefore they do not implement behaviors which can limit the risk of these pathologies. The data collected is currently insufficient and requires further investigation to clarify the correlation between these NCDs and shift work. Aside from the limitations, this is the first study of this type conducted at the University Hospital "P. Giaccone" and aims to provide a starting point to stimulate research on a larger scale. In conclusion, the prevalence of risk factors for NCD among healthcare workers require greater attention to ensure *ad hoc* prevention strategies, which include simple but highly effective actions, such as creating greater awareness and educating the population of reference to guarantee a high-quality health service, which cannot ignore a good state of physical, psychological and social health of those called upon to provide it.

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 protocol of this study complies with the European Union's Good Clinical Practice standards and the latest revision of the Declaration of Helsinki. It was approved on 19 April 2023 by the Palermo 1 Ethics Committee. Ethical approval number 04/2023. 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

AP: Methodology, Writing – review & editing, Writing – original draft, Investigation. DM: Writing – review & editing. CP: Writing – review & editing. AI: Validation, Writing – review & editing. VM: Writing – review & editing, Investigation. FT: Writing – review & editing. AC: Formal analysis, Writing – review & editing. PI: Writing – review & editing, Supervision, Project administration, Conceptualization.

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Healthcare professionals' perception of the ketogenic diet among patients with chronic obstructive pulmonary disease: a cross-sectional study

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Background: Chronic obstructive pulmonary disease (COPD) is a progressive respiratory disorder characterized by persistent inflammation and airflow limitation. The ketogenic diet (KD), recognized for its anti-inflammatory properties, has potential therapeutic benefits for COPD management. However, healthcare professionals' perceptions of KD's efficacy and applicability in COPD care remain underexplored, particularly in Saudi Arabia.

Methods: A cross-sectional online survey was conducted between June and September 2024, targeting healthcare professionals involved in COPD management. The survey evaluated perceptions of KD's benefits, limitations, and current nutritional practices. Descriptive statistics and logistic regression analyses were performed using JASP to identify predictors of KD training uptake and the likelihood of discussing dietary interventions with COPD patients.

Results: A total of 1,068 healthcare professionals participated in the survey. Of these, 58% believed KD could improve quality of life in COPD patients, and 61% acknowledged its potential to reduce inflammation. Logistic regression identified familiarity with KD as significant predictor for receiving KD training ($p < 0.001$). Concerns regarding KD's adverse effects, such as constipation and dehydration, were noted by 76% of respondents. Only 14% reported recommending KD, citing insufficient evidence and lack of professional training as primary barriers. Additionally, 74% highlighted patient adherence challenges due to KD's restrictive nature and potential side effects.

Conclusion: KD shows promise as a complementary therapy for COPD by modulating inflammation and improving symptom management. Addressing barriers such as limited evidence and inadequate professional training is essential. Further research is required to establish the efficacy and safety of KD in COPD care.

KEYWORDS

pulmonary disease, inflammation, ketogenic diet, healthcare professionals, nutrition

1 Introduction

Chronic obstructive pulmonary disease (COPD) is a progressive and debilitating respiratory condition that ranks as the fourth leading cause of death globally, affecting over 300 million individuals worldwide (1, 2). The progression of COPD is largely driven by persistent inflammation, marked by increased immune cell activity (e.g., macrophages, neutrophils, and lymphocytes) and overproduction of pro-inflammatory cytokines (e.g., TNF-α, IL-1β, IL-6), which contribute to resistance to standard therapies, such as corticosteroids (3, 4). These inflammatory processes also drive chronic airflow limitations caused by lung tissue destruction and airway obstruction, resulting in severe symptoms such as dyspnea, fatigue, and reduced physical capacity (5).

Despite significant advancements in COPD management, existing therapeutic strategies primarily target symptom relief, with limited focus on addressing the underlying inflammatory mechanisms. Resistance to corticosteroids, along with the limited success of other targeted therapies, underscores the urgent need for innovative approaches that offer broader anti-inflammatory effects (6, 7). One such promising approach is the ketogenic diet (KD), a high-fat, low-carbohydrate dietary regimen with known anti-inflammatory properties (8, 9). The various formulation of KD and their macronutrient compositions are illustrated in Figure 1. The KD, which has been used for nearly a century to manage and reduce seizure frequency in pediatric epilepsy (10), is now being explored for its therapeutic potential in a range of chronic conditions. Research has demonstrated that KD can reduce inflammatory markers and improve metabolic efficiency in diseases such as cardiovascular risk factors (11), Parkinson's disease (12), type II diabetes (13, 14), polycystic ovarian syndrome (15), metabolic syndrome (16), lipedema (17, 18), Alzheimer's disease (19), and several mental health disorders (20). Although the KD has demonstrated therapeutic benefits in various conditions, it is not without potential side effects, particularly during the initial adaptation phase. Common short-term symptoms include "keto flu," which may include headaches, fatigue, nausea, dizziness, and irritability due to sudden changes in electrolyte and glucose balance (21). Gastrointestinal disturbances such as constipation and bloating are also common, potentially related to low fiber intake (22). In some cases, prolonged adherence to the KD may lead to increased low-density lipoprotein cholesterol (23), and an increased risk of kidney stones (24). Therefore, medical supervision and individualized planning are highly recommended when starting or continuing a KD.

Emerging evidence suggests that KD may benefit COPD management by targeting inflammation. For instance, a recent case report documented a 37.5% improvement in forced expiratory volume (FEV1) and normalization of inflammatory markers in a COPD patient following a KD (25). Additionally, a controlled trial involving 60 COPD patients found significant improvements in lung function with a low-carbohydrate diet, highlighting the potential of dietary interventions in managing COPD (26).

Recent studies have also begun to unravel the biological mechanisms underlying these benefits, particularly the role of β-hydroxybutyrate (BHB), a ketone body produced during KD. BHB inhibits the NLRP3 inflammasome, a key component in the inflammatory response associated with COPD exacerbations (27, 28). Elevated levels of NLRP3 and associated markers (Asc, caspase-1 mRNAs) have been observed in active COPD cases, making this pathway a promising target for therapeutic intervention (29). By inhibiting NLRP3, BHB may reduce systemic inflammation, as seen in other inflammatory conditions like gout (30). Emerging evidence also indicates that specific microRNAs are involved in the regulation of inflammation during KD, potentially contributing to the therapeutic effects observed in inflammatory diseases (31, 32). The proposed mechanism by which the KD exerts anti-inflammatory effects in COPD is illustrated in Figure 2. While these findings are promising, further research is needed to establish the long-term safety, efficacy, and clinical applicability of KD in COPD management.

This study seeks to explore the perceptions of healthcare professionals in Saudi Arabia regarding the potential therapeutic role of the KD in COPD management. Specifically, the study aims to identify the benefits, challenges, and barriers to adopting KD as part of COPD treatment protocols. Additionally, it examines predictors of KD training uptake and the likelihood of discussing dietary interventions with COPD patients through logistic regression analysis.

2 Methods

2.1 Ethical consideration

Ethical approval was obtained from an independent research committee at King Faisal University (ID: ETHICS2220).

2.2 Study design and participants

This study used an online survey to explore healthcare professionals' perceptions of the KD among patients with COPD. The survey was conducted from June 1, 2024, to September 30, 2024. Healthcare practitioners were recruited using a convenience sampling method. The target population included health professionals likely to be involved in the care of patients with COPD, such as nurses, dietitians, family physicians, respiratory therapists, and general practitioners. Before participating, all potential respondents were informed about the study's objectives. Participation was entirely voluntary, and respondents were assured they could withdraw at any time without consequences. Confidentiality of the collected data was guaranteed, and no personal information was shared. Participants provided consent by responding "yes" to the question, "Do you agree to participate in the study?". Completing the survey required ~4–5 min.

To maximize participant reach, the researchers collaborated with professional committees, including the Saudi Society for Clinical Nutrition, the Saudi Society for Respiratory Care, and the Saudi Society for Family and Community Medicine. These organizations distributed the questionnaire via email to their members. In addition, the survey link was shared on social media platforms, including X (formerly Twitter), WhatsApp, and Telegram, to enhance participation and diversify the sample.

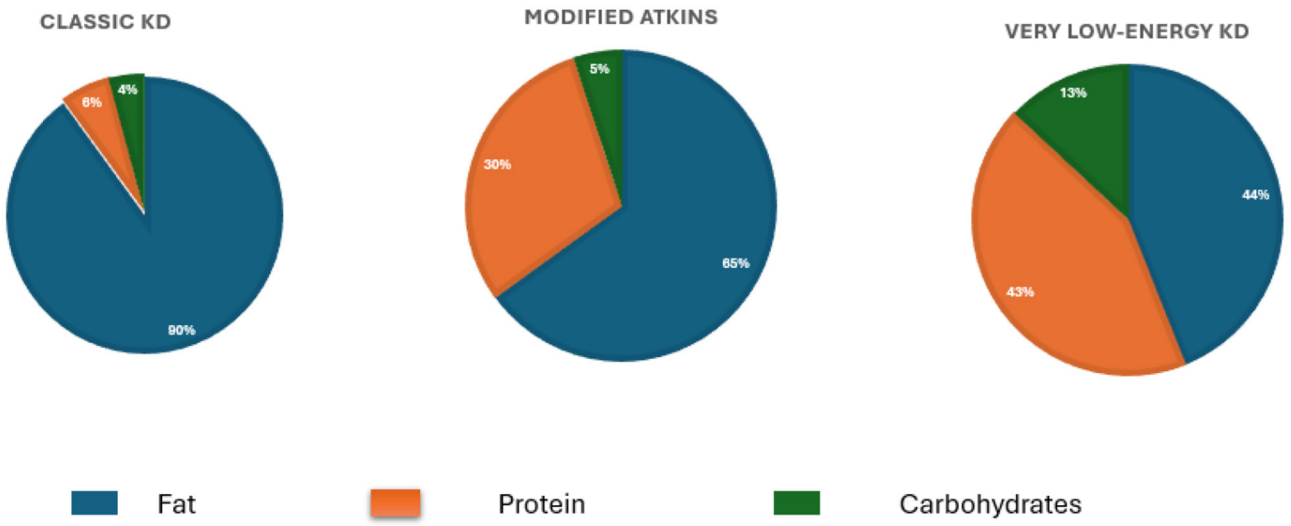

FIGURE 1
Macronutrient distribution across three types of ketogenic diets. The Classic Ketogenic Diet (KD) consists of ~90% fat, 6% protein, and 4% carbohydrates and is traditionally used in epilepsy management. The Modified Atkins Diet, introduced as a more flexible approach, includes 65% fat, 30% protein, and 5% carbohydrates. The Very Low-Energy Ketogenic Diet (VLEKD) mimics the metabolic effects of fasting and consists of 44% fat, 43% protein, and 13% carbohydrates, with a total daily energy intake typically below 800 kcal.

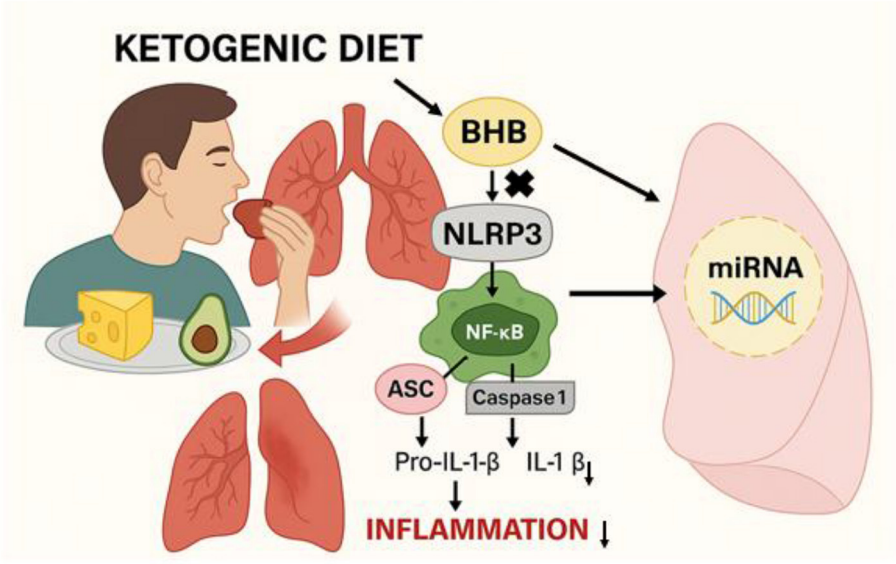

FIGURE 2
Illustration of the proposed mechanism by which the ketogenic diet modulates inflammation in COPD. A high-fat, low-carbohydrate intake induces β-hydroxybutyrate (BHB) production, which inhibits the NLRP3 inflammasome pathway. This results in reduced activation of NF-κB and decreased IL-1β production, ultimately lowering inflammation. Additionally, BHB may influence the expression of specific microRNAs (miRNAs) involved in immune regulation, contributing to improved lung function.

2.3 Questionnaire tool

The questionnaire consisted of four sections with closed-ended questions and optional free-text responses. It was developed by an independent researcher (SA) and reviewed by another researcher (EEA). A pilot study involving 50 healthcare practitioners (family physicians, pulmonologists, general practitioners, nurses, and dietitians) was conducted to validate the tool. Pilot participants were excluded from the final analysis.

1. **Section 1**: collected demographic and professional information, including gender, age, geographic location, specialty, clinical experience (in years), average number of COPD patients seen per month, prior training on the KD, and knowledge of the KD.

2. **Section 2**: contained 10 Likert-scale statements (1 = strongly disagree, 5 = strongly agree) to evaluate participants' opinions on prescribing the KD for COPD patients.
3. **Section 3**: focused on current practices in managing COPD patients, addressing dietary discussions, their frequency, common dietary recommendations, and factors influencing decisions to recommend or not recommend the KD.
4. **Section 4**: included two questions exploring perceived facilitators and barriers to prescribing the KD for COPD patients.

2.4 Statistical analysis

Data analysis was performed using JASP version 0.17.2. Descriptive statistical methods, including frequencies and percentages for categorical variables, were used to summarize the survey responses. Additionally, logistic regression analysis was conducted to identify predictors of receiving KD training and discussing dietary interventions with COPD patients. This analysis evaluated relationships between multiple independent variables, such as familiarity with KD, age, and professional background, and the dependent outcomes. GraphPad Prism (GraphPad Software, San Diego, CA, USA) was used to generate graphs.

3 Results

3.1 Characteristics of the respondents

A total of 1,068 healthcare professionals completed the online survey. The majority of respondents (64%) worked in government hospitals. They were categorized by specialty as follows: dietitians (27%), registered nurses (17%), pulmonologists (16%), family medicine practitioners (14%), general practitioners (16%), and pharmacists (10%). In terms of clinical experience, 37% of respondents reported having 1 to 4 years of experience in COPD care, with most seeing an average of 1 to 3 COPD patients per month. Notably, 68% of participants indicated they had no formal education or training on the KD. Despite this, 76% of respondents reported being somewhat familiar with the KD. A detailed summary of respondent characteristics is provided in Table 1.

TABLE 1 Demographics and professional background of study respondents (n = 1,068).

Characteristics	Frequency (%)
Gender	
Male	544 (51)
Female	524 (49)
Geographical region	
Central region	168 (16)
Eastern region	186 (17)
North region	256 (24)
South region	215 (20)
Western region	243 (23)
Profession	
Dietitian	286 (27)
Family medicine	151 (14)
General practitioner GP	168 (16)
Pharmacist	111 (10)
Pulmonologist/respiratory medicine	171 (16)
Registered nurse	181 (17)
Primary place of work	
Governmental hospital	688 (64)
Private hospital	380 (36)
Years of clinical experience with COPD	
≤ 1 year	204 (19)
1–4 years	394 (37)
5–9 years	325 (30)
≥ 10 years	145 (14)
The average number of COPD patients seen per month	
0	104 (10)
1–3	548 (51)
4–6	281 (26)
7–9	86 (8)
≥ 10	49 (5)
Received specific formal education or training on the ketogenic diet	
No	725 (68)
Yes	343 (32)
Familiarity with the ketogenic diet	
Not familiar	55 (5)
Somewhat familiar	807 (76)
Very familiar	206 (19)

COPD, Chronic obstructive pulmonary disease; KD, ketogenic diet.

3.2 Healthcare professional' views on the KD in COPD patients

Among the 1,068 respondents, 58% believed that the KD could improve the quality of life in COPD patients. Similarly, 61% agreed that the KD may exert anti-inflammatory effects, potentially benefiting COPD patients with lung inflammation. Moreover, 61% believed that the KD could help alleviate specific COPD symptoms, such as dyspnoea and fatigue.

In addition, 73% agreed that the KD might aid in weight management for COPD patients, which is critical, as obesity can exacerbate symptoms and increase the risk of complications. However, 66% expressed concern that the high-fat content of the KD might lead to increased carbon dioxide

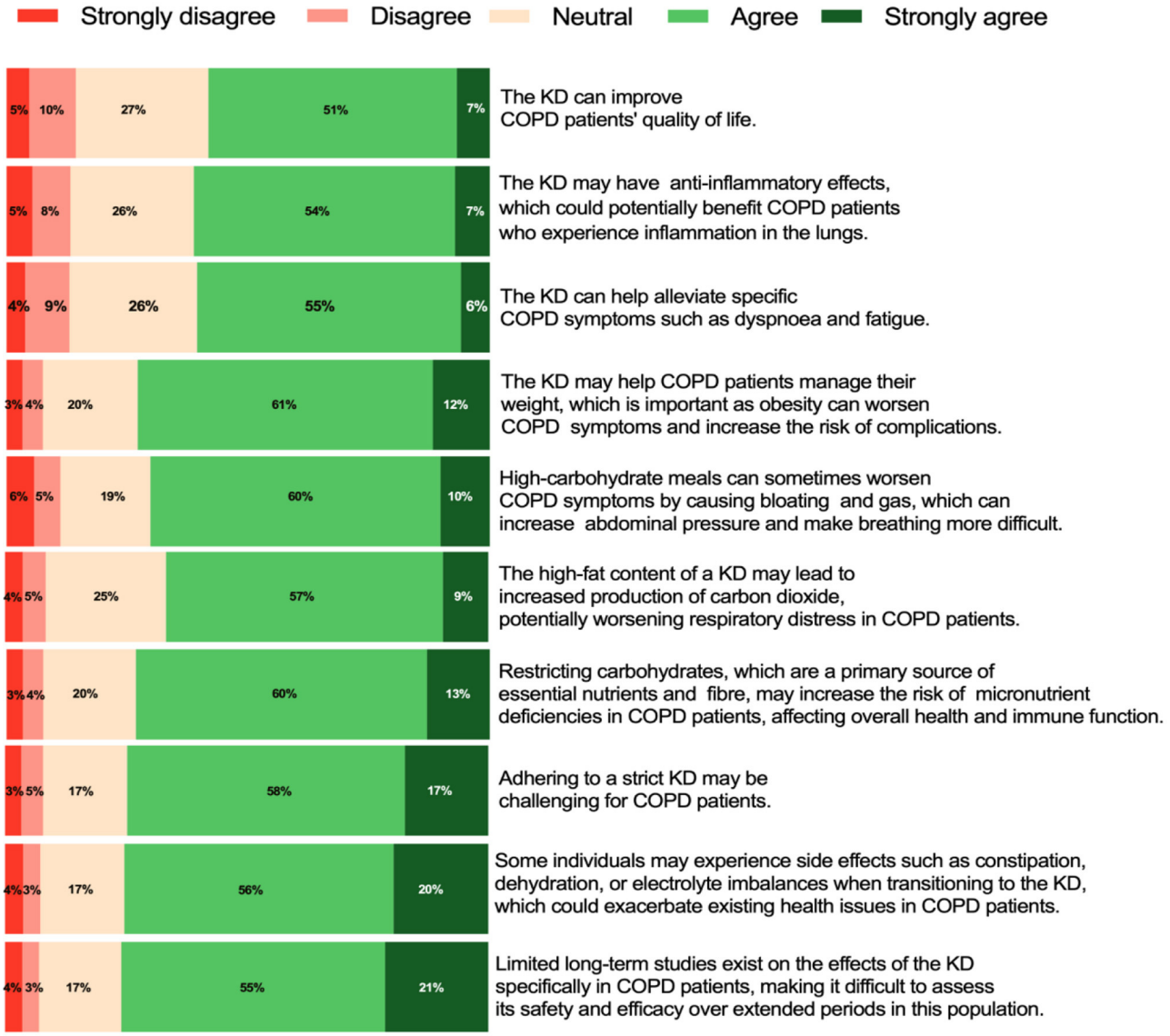

FIGURE 3
Health professionals' views on the ketogenic diet in patients COPD (n = 1,068).

production, potentially worsening respiratory symptoms in COPD patients.

Furthermore, 76% agreed with the potential side effects of the KD, such as constipation, dehydration, or electrolyte imbalances, which could exacerbate pre-existing health issues in COPD patients. Meanwhile, 73% believed that restricting carbohydrates, a primary source of essential nutrients and fiber, may increase the risk of micronutrient deficiencies in COPD patients, potentially affecting overall health and immune function.

Conversely, 70% agreed that high-carbohydrate meals could worsen COPD symptoms by causing bloating and gas, which may increase abdominal pressure and make breathing more difficult. Additionally, 74% agreed that adhering to the strict requirements of the KD might be challenging for COPD patients. Finally, 76% agreed that the lack of long-term studies on the effects of the KD in COPD patients makes it difficult to assess its safety and efficacy over extended periods for this population. Figure 3 provides a summary of healthcare professionals' views on the KD in COPD patients.

3.3 Current practices and attitudes toward recommending the KD to COPD patients

Only 51% of respondents reported discussing dietary interventions with COPD patients, and among these, the KD was recommended by only 14%. Most respondents (67%) prioritized a balanced diet, while smaller proportions advocated for high-protein (11%) or Mediterranean diets (8%). These results suggest that despite growing awareness of the KD, it remains underutilized in clinical practice for COPD patients. This could be due to limited evidence or insufficient professional training. Table 2 provides an overview of dietary practices and attitudes.

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TABLE 2 Current practices and attitudes toward recommending the KD to COPD patients ($n = 1,068$).

Practices	Frequency (%)
Discusses dietary intervention with COPD patients	
No	522 (49)
Yes	546 (51)
Frequency of dietary discussions with COPD patients	
Never discuss dietary interventions and always transfer patients to a dietitian	320 (30)
Never, dietary interventions are not typically discussed	147 (14)
Occasionally, based on patient interest or need	302 (28)
Rarely, only if specifically requested by the patient	215 (20)
Routinely, during every patient visit	84 (8)
Primary dietary recommendations for COPD patients	
Balanced diet	720 (67)
High protein diet	115 (11)
Ketogenic diet	147 (14)
Mediterranean diet	86 (8)

Definitions used in this study: a balanced diet provides moderate proportions of macronutrients based on general guidelines; a high-protein diet includes ≥20% of total energy from protein; the ketogenic diet is characterized by very low carbohydrates (≤10%) and high fat; the Mediterranean diet emphasizes unsaturated fats, plant-based foods, and moderate protein/carbohydrate intake. COPD, Chronic obstructive pulmonary disease; KD, ketogenic diet.

3.4 Barriers to implementing the KD in COPD care

Respondents were asked to select all applicable barriers to implementing the KD in COPD care from a predefined list. The most commonly selected barrier was the lack of evidence regarding the efficacy and safety of the KD in COPD patients (50%). This was followed by concerns about potential nutritional deficiencies associated with the KD (46%), a lack of healthcare professional knowledge and training (44%), limited patient adherence and compliance (44%), and difficulties in monitoring patient progress and dietary intake (42%). Figure 4 illustrates the distribution of these selected barriers.

3.5 Factors that facilitate the integration of the KD into COPD management

The most selected factor was the availability of educational resources for both healthcare professionals and patients (95%). This was followed by clear evidence supporting the efficacy and safety of the KD in COPD patients (90%), the inclusion of the KD in COPD treatment guidelines (89%), collaboration between healthcare professionals and dietitians (88%), and supportive dietary counseling and guidance for patients (86%). Figure 5 provides the percentages of these selected facilitating factors.

3.6 Predictors of receiving formal education or training on the KD

As shown in Table 3, logistic regression analysis indicates that familiarity with the KD emerged as a significant predictor. Professionals who reported familiarity with the KD were 21 times more likely to have received formal training (odds ratio = 21.159, $p < 0.001$).

3.7 Predictors of dietary intervention discussions in COPD care

As shown in Table 4, logistic regression analysis showed statistically significant effects of some factors associated with discussing dietary interventions with COPD patients. Nutrition professionals were more likely to discuss dietary interventions than GPs, with an odds ratio (OR) of 1.418 (95% CI: 1.106–1.730, $p < 0.001$). In contrast, respiratory professionals were less likely to discuss, with an OR of 0.618 (95% CI: 0.502–0.731, $p < 0.001$). Knowledge of the KD showed a significant positive effect, with the likelihood of discussion increasing with knowledge, with an OR of 1.402 (95% CI: 1.207–1.627, $p< 0.001$). Similarly, previous experience with COPD patients was associated with an increased likelihood of discussing dietary interventions, with an odds ratio of 1.522 (95% CI: 1.187–1.948, $p < 0.001$).

4 Discussion

This study aimed to evaluate healthcare professionals' perceptions regarding the KD as a potential therapeutic approach for managing COPD. The findings offer valuable insights into the perceived benefits, concerns, and barriers associated with KD implementation in COPD care. These perspectives highlight both the promise of KD and the challenges that need to be addressed for effective integration into clinical practice.

A significant portion of respondents (58%) acknowledged the potential of KD to enhance COPD patients' quality of life, primarily due to its anti-inflammatory effects. This perception aligns with emerging evidence suggesting that beta-hydroxybutyrate (BHB), a key ketone body produced during ketosis, can inhibit the NLRP3 inflammasome—a critical component of chronic inflammation in COPD pathophysiology (33, 34). Additionally, KD has been shown to suppress the NF-κB signaling pathway, reducing pro-inflammatory cytokines such as IL-1β, TNF-α, and IL-6 (34, 35). These mechanisms provide a plausible rationale for the anti-inflammatory benefits of KD in COPD management.

Further clinical evidence supports KD's role in improving mitochondrial efficiency, reducing oxidative stress, and enhancing respiratory function (33, 35). These combined effects suggest that KD could address multiple aspects of COPD pathology, including inflammation, energy metabolism, and respiratory efficiency. However, while these findings are promising, they underscore the necessity for well-designed, long-term clinical trials to confirm the efficacy and safety of KD in COPD management and determine its impact on patient-reported outcomes.

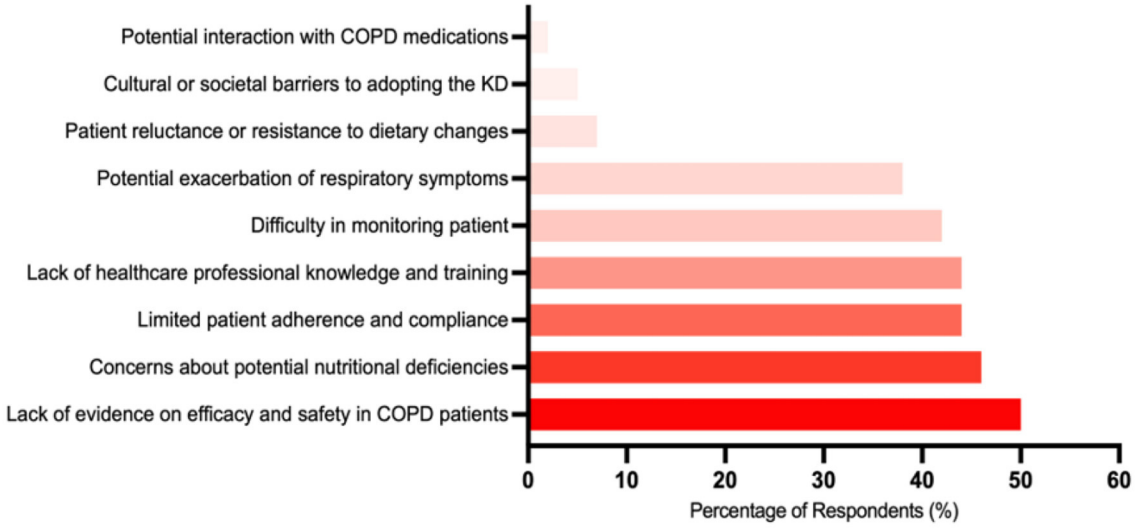

FIGURE 4
The most common barriers to implementing the ketogenic diet in COPD care (n = 1,068).

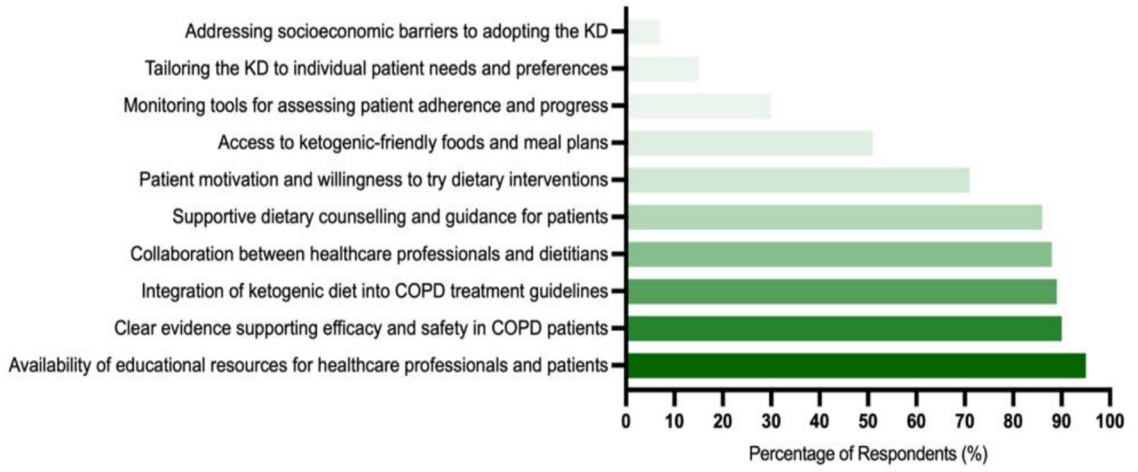

FIGURE 5
The most common factors that facilitate the integration of the ketogenic diet into COPD management (n = 1,068).

Despite the perceived benefits, 66% of respondents expressed concerns about KD's high-fat content and its potential to increase carbon dioxide (CO_2) production, which could worsen respiratory distress. While such concerns are theoretically valid, evidence indicates that a low-carbohydrate, high-fat diet may reduce CO_2 production due to a lower respiratory quotient (RQ) associated with fat metabolism (36–38). This discrepancy highlights a critical need for more robust research and clear guidelines to reconcile differing viewpoints and provide definitive recommendations for clinical practice.

Several barriers to adopting KD in COPD care were identified. The most frequently cited challenge was patient adherence (74% of respondents). KD's restrictive nature, coupled with side effects such as fatigue, gastrointestinal discomfort, and social limitations, presents significant hurdles to long-term compliance (21, 39). These challenges necessitate the development of personalized dietary plans and ongoing support mechanisms to improve adherence and mitigate side effects.

Another notable barrier was the lack of professional training in KD implementation (44% of respondents). This knowledge gap limits healthcare providers' ability to educate and guide patients effectively. Furthermore, 76% of respondents highlighted the absence of long-term studies on KD's safety and efficacy in COPD management, emphasizing the urgent need for further clinical research to build a comprehensive evidence base.

To address these barriers, several facilitators must be prioritized. A majority (95%) of respondents stressed the importance of comprehensive educational programs for both healthcare professionals and patients. These programs should focus on the practical aspects of KD implementation, the potential

TABLE 3 Logistic regression results for predictors of receiving KD training or education.

Variable	Estimate	Standard error	Odds ratio	z	Wald test			95% Confidence interval	
					Wald statistic	df	p	Lower bound	Upper bound
Professional background (general practitioner GP)	−0.124	0.307	0.883	−0.406	0.165	1	0.685	0.725	0.477
Professional background (pulmonologist/respiratory medicine)	−0.007	0.319	0.993	−0.021	4.621×10^{-4}	1	0.983	0.633	0.619
Professional background (dietitian)	0.848	0.294	2.335	2.883	8.309	1	0.004	0.271	1.424
Professional background (registered nurse)	0.454	0.305	1.574	1.486	2.209	1	0.137	0.145	1.052
Professional background (family medicine)	0.282	0.331	1.326	0.853	0.728	1	0.393	0.366	0.931
Workplace (private hospital)	−0.035	0.178	0.966	−0.194	0.038	1	0.846	0.384	0.315
Geographical region (North region)	0.658	0.264	1.931	2.491	6.206	1	0.013	0.140	1.176
Geographical region (central region)	0.396	0.274	1.486	1.443	2.083	1	0.149	0.142	0.934
Geographical region (south region)	0.466	0.266	1.593	1.747	3.054	1	0.081	0.057	0.988
Geographical region (western region)	0.035	0.245	1.035	0.141	0.020	1	0.888	0.446	0.515
Gender (female)	−0.260	0.161	0.771	−1.617	2.613	1	0.106	0.575	0.055
Familiarity with KD (somewhat familiar)	3.077	0.217	21.690	14.204	201.752	1	**<0.001**	2.652	3.501
Familiarity with KD (not familiar)	2.793	0.365	16.327	7.652	58.551	1	**<0.001**	2.077	3.508
Experience with COPD	0.144	0.095	1.155	1.523	2.319	1	0.128	0.041	0.330

"No" was used as the reference category in the regression model for the variable "Received specific formal education or training on the ketogenic diet." Bold values indicate statistically significant results at $p < 0.05$.

benefits, and strategies to manage side effects. Effective education can empower healthcare providers to deliver evidence-based dietary advice and support patients through the challenges of adhering to KD.

Additionally, robust scientific evidence was identified as critical by 90% of respondents. Collaborative efforts among clinicians, researchers, and policymakers are essential to generate high-quality evidence and develop standardized clinical guidelines for KD use in COPD management. This will help bridge the gap between theoretical knowledge and clinical application, fostering greater confidence in KD as a therapeutic option.

Logistic regression analysis identified familiarity with the KD as a key factor in determining interest in training, with results showing that participants with partial knowledge of the diet were 21 times more likely to receive training than those without ($p < 0.001$). This strong association suggests that awareness of the KD should be raised among healthcare professionals to enhance training opportunities and increase implementation of this strategy in clinical care. Previous studies confirm that targeted nutrition education enhances healthcare professionals' confidence and competence in implementing nutritional interventions (40). Therefore, incorporating experiential learning and interactive training modules into professional education could facilitate the adoption of the KD in clinical practice.

Furthermore, logistic regression analysis highlighted the role of healthcare professionals' backgrounds in determining the likelihood of discussing nutritional interventions. Dietitians were significantly more likely to engage in discussions about the KD with COPD patients compared to general practitioners ($p < 0.001$). Conversely, respiratory specialists were less likely to discuss nutritional interventions, which may reflect their greater focus on lung-specific treatments rather than holistic approaches, including nutrition. This disparity underscores the need for multidisciplinary education and training programs to bridge the knowledge gap between respiratory care and medical nutrition, and thus promote collaborative approaches to COPD management.

5 Strengths and limitations

This study presents several strengths. Firstly, it offers novel insights into healthcare professionals' perceptions of the KD as a therapeutic strategy for COPD management, addressing a

TABLE 4 Logistic regression results for predictors of dietary intervention discussion in COPD patients.

Variable	Estimate	Standard error	Odds ratio	z	Wald test			95% confidence interval	
					Wald statistic	df	*p*	Lower bound	Upper bound
Workplace (private hospital)	0.337	0.166	1.401	2.032	4.130	1	0.042	0.012	0.662
Professional background (general practitioner GP)	−0.618	0.266	0.539	−2.320	5.384	1	0.020	−1.140	−0.096
Professional background (pulmonologist/respiratory medicine)	−0.152	0.281	0.859	−0.539	0.291	1	0.590	−0.703	0.400
Professional background (Dietitian)	−2.837	0.290	0.059	−9.787	95.782	1	**<0.001**	−3.405	−2.269
Professional background (registered nurse)	0.112	0.261	1.118	0.429	0.184	1	0.668	−0.399	0.623
Professional background (family medicine)	0.339	0.291	1.404	1.163	1.353	1	0.245	−0.232	0.910
Geographical region (north region)	0.237	0.239	1.268	0.991	0.983	1	0.322	−0.232	0.706
Geographical region (central region)	0.632	0.253	1.882	2.496	6.232	1	0.013	0.136	1.129
Geographical region (south region)	0.289	0.245	1.335	1.179	1.391	1	0.238	−0.191	0.770
Geographical region (western region)	0.275	0.234	1.317	1.176	1.383	1	0.240	−0.184	0.735
Familiarity with KD (somewhat familiar)	0.777	0.190	2.175	4.100	16.810	1	**<0.001**	0.406	1.148
Familiarity with KD (not familiar)	0.747	0.338	2.111	2.211	4.889	1	0.027	0.085	1.410
Experience with COPD	0.420	0.086	1.522	4.872	23.738	1	**<0.001**	0.251	0.589

"No" was used as the reference category in the regression model for the variable "Discusses dietary intervention with COPD patients." Bold values indicate statistically significant results at $p < 0.05$.

critical gap in the literature—particularly within the Saudi Arabian healthcare context. Secondly, the application of logistic regression analysis enabled a robust evaluation of associations between participants' familiarity, professional training, and demographic characteristics, thereby enhancing analytical rigor. Thirdly, the relatively large sample size ($n = 1{,}068$) strengthens the reliability and validity of the findings, offering a representative view of prevailing attitudes toward KD. Finally, the inclusion of a broad range of healthcare professionals—such as general practitioners, dietitians, and nurses—provides a multidimensional perspective on the perceived barriers and facilitators to implementing KD in clinical settings.

Nonetheless, this study has limitations. The cross-sectional design limits causal inference regarding KD's impact on COPD outcomes. Longitudinal studies and randomized controlled trials are required to establish long-term safety and efficacy. Additionally, the use of self-reported data introduces potential biases, including recall, response, and social desirability bias, which may affect data accuracy. The sample was confined to healthcare professionals in Saudi Arabia, which may limit the generalizability of results to broader international contexts. Differences in healthcare infrastructure, nutritional practices, and cultural perceptions may affect the external applicability of the findings. Future research in diverse populations is essential to validate and extend these insights. Moreover, the study focused on perceptions rather than clinical outcomes, precluding definitive conclusions about KD's effectiveness in COPD symptom management. Finally, insufficient training and knowledge among respondents may have influenced their responses. These limitations underscore the need for comprehensive educational programs, rigorous clinical trials, and diverse participant cohorts in future investigations.

6 Conclusion

This study highlights the therapeutic potential of the ketogenic diet in the context of COPD management, particularly with regard to its anti-inflammatory and symptom-modifying effects. However, several practical challenges remain, including patient adherence, potential side effects, and gaps in professional training. It is also essential to distinguish between healthcare professionals who might suggest the ketogenic diet as a nutritional approach and those—such as registered dietitians—qualified to prescribe and supervise individualized diets.

These findings have practical implications for clinical practice, forming the basis for developing context-sensitive guidelines and multidisciplinary educational initiatives. Strengthening evidence-based knowledge and improving competency among healthcare

providers could support the safe and effective integration of the ketogenic diet into the care of patients with COPD. Furthermore, international studies are needed to assess the consistency of the patterns identified in this study across different health systems and cultural settings. As nutritional strategies grow in popularity in chronic disease management, attention to healthcare provider readiness and system-wide implementation barriers will be critical to bridging the gap between evidence and practice.

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 obtained from an Independent Research Committee at King Faisal University (ID: ETHICS2220). The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent for participation in this study was provided by the participants' legal guardians/next of kin.

Author contributions

SA: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. EA: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. RS: Data curation, Formal analysis, Methodology, Supervision, Writing – original draft, Writing – review & editing. YA: Data curation, Supervision, Writing – original draft, Writing – review & editing. AA: Data curation, Methodology, Supervision, Writing – original draft, 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.

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Association between prognostic nutritional index and all-cause mortality among intestinal obstruction patients in the intensive care unit: a retrospective study

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Background: Intestinal obstruction (IO) is a common surgical emergency associated with significant morbidity and mortality, particularly in critically ill ICU patients. The Prognostic Nutritional Index (PNI), calculated using serum albumin levels and total lymphocyte counts, has demonstrated prognostic value in various conditions. However, its role in critically ill IO patients remains unexplored.

Methods: We conducted a retrospective cohort study using the MIMIC-IV database. Critically ill patients with IO were identified, and their PNI values on the first day of ICU admission were recorded. Patients were stratified into quartiles based on PNI and analyzed for 30-day, 60-day, and 90-day all-cause mortality. Multivariable Cox regression models adjusted for potential confounders, and restricted cubic splines examined the relationship between PNI and mortality risk.

Results: A total of 701 patients were included in the analysis. Patients in the highest PNI quartile had significantly lower 30-day, 60-day, and 90-day all-cause mortality rates compared to those in the lowest quartile. After adjusting for covariates, higher PNI remained an independent predictor of reduced mortality (30-day HR 0.96, 95% CI: 0.93–0.98, $p < 0.001$; 60-day HR 0.96, 95% CI: 0.94–0.98, $p < 0.001$; 90-day HR 0.97, 95% CI: 0.95–0.99, $p = 0.002$).

Conclusion: PNI is independently associated with lower mortality in critically ill IO patients, supporting its utility as a risk stratification tool in this population. These findings underscore the importance of early nutritional assessment and intervention, and highlight PNI's potential to guide clinical decision-making in the ICU setting.

KEYWORDS

prognostic nutritional index, intestinal obstruction, ICU, mortality, MIMIC-IV, nutritional status, critical care

1 Introduction

Intestinal obstruction (IO) is a common surgical emergency, associated with high morbidity and healthcare costs (1). It involves either partial or complete blockage of the intestinal lumen, disrupting the normal gastrointestinal flow (2). This condition presents considerable risks, including bowel ischemia, perforation, sepsis, and an increased mortality rate among critically ill patients (3). Managing intestinal obstruction in the ICU is particularly challenging due to the compromised baseline health of these patients, which heightens their susceptibility to rapid clinical decline.

The Prognostic Nutritional Index (PNI), calculated using serum albumin levels and total lymphocyte counts, provides a quick and straightforward measure of a patient's nutritional and immune status (4). PNI was initially developed as a preoperative risk assessment tool for surgical patients, but it has also shown prognostic value in various conditions such as cardiovascular diseases and chronic inflammatory disorders (5, 6). Furthermore, while many studies of IO mortality have focused on inflammatory markers such as red cell distribution width (RDW) (7), C-reactive protein (CRP) (8), and neutrophil-to-lymphocyte ratio (NLR) (9), there is a growing recognition of the critical role that nutritional status plays in influencing patient outcomes. By reflecting both protein reserves and immune competence, PNI offers an integrated assessment of a patient's resilience, which is particularly crucial for those admitted to intensive care units, where metabolic stress and nutritional depletion can exacerbate the risk of adverse outcomes (10).

This study aims to evaluate the prognostic value of PNI in critically ill patients with IO using the MIMIC-IV database. By analyzing PNI values obtained on the first day of ICU admission, we aim to establish a reliable tool for early risk stratification in IO patients. Early identification of high-risk patients may allow clinicians to implement timely, targeted interventions that improve survival outcomes and optimize the use of ICU resources. This research underscores the critical role of incorporating nutritional and immune assessments into the management of IO and provides a foundation for future investigations that could inform clinical guidelines and practice standards.

2 Materials and methods

2.1 Research design

This research utilized the MIMIC-IV dataset (version 2.2), which consists of de-identified intensive care unit records from Beth Israel Deaconess Medical Center, spanning from 2008 to 2019. The dataset provides detailed information on patient demographics, laboratory test results, physiological indicators, therapeutic interventions, and clinical outcomes. To access the data, a data use agreement had to be completed, and certification in human research ethics was required. One of the authors (Ge ID: 13547277) met these conditions and carried out the data extraction and initial processing steps.

Initially, a total of 9,069 patients with IO admissions were identified. Among these, 2,928 patients were admitted to the ICU. After applying the exclusion criteria, 2,227 patients were excluded from the analysis. The exclusion criteria included: age less than 18 years ($n = 0$), non-first ICU admission ($n = 664$), ICU stays shorter than 24 h ($n = 280$), and patients without albumin or lymphocytes measured at admission ($n = 1,283$). This resulted in 701 patients being included in the final analysis. These patients were then stratified according to the quartiles of the PNI (Prognostic Nutritional Index) into four groups: Quartile 1 ($n = 154$), Quartile 2 ($n = 196$), Quartile 3 ($n = 165$), and Quartile 4 ($n = 186$) (Figure 1).

2.2 Data collection

Patient data were extracted from the MIMIC-IV (version 2.2) database using PostgreSQL, focusing on the first 24 h after ICU admission. Demographic variables included age, gender, race, weight, and insurance type. Clinical severity was measured by Charlson comorbidity index, Sequential Organ Failure Assessment (SOFA), and Acute Physiology Score III (APS III). Vital signs included heart rate, systolic blood pressure (SBP), respiratory rate, and oxygen saturation (SpO2). Comorbidities were recorded for diabetes, renal disease, malignant cancer, sepsis, and hypertension. Laboratory data included hemoglobin, white blood cell count (WBC), platelet count, albumin, lymphocytes, anion gap, sodium, potassium, international normalized ratio (INR), and total bilirubin. Treatment data included the use of mechanical ventilation, continuous renal replacement therapy

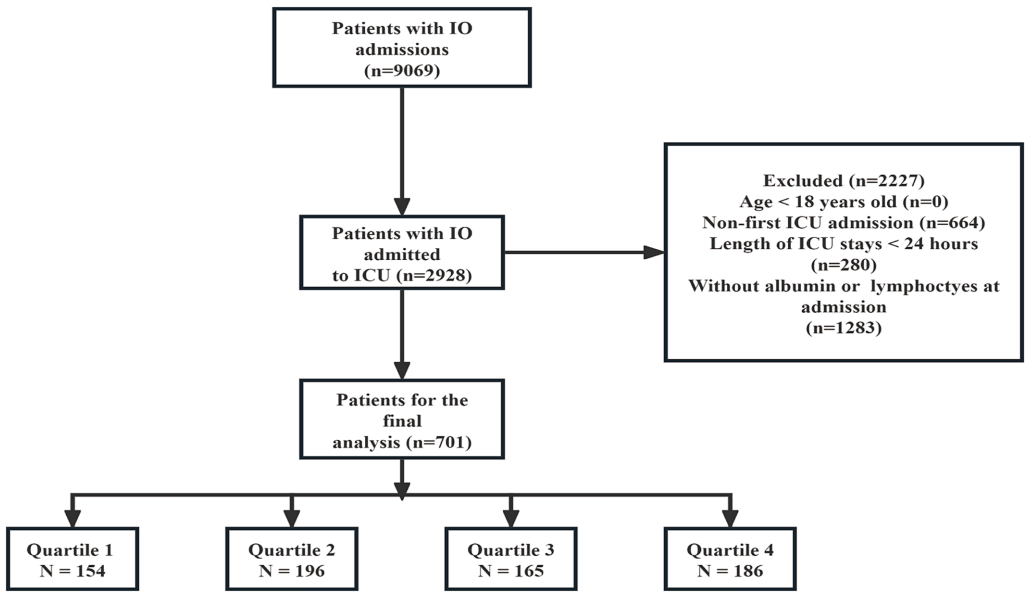

FIGURE 1
Patient flow through the trial. IO, Intestinal obstruction; ICU, Intensive Care Unit.

(CRRT), and octreotide. Outcomes assessed were hospital length of stay, ICU length of stay, and hospital mortality at 30, 60, and 90 days.

2.3 Definition and clinical results

The primary outcome was all-cause mortality within 30 days after hospital admission, while secondary outcomes included all-cause mortality within 60 and 90 days after admission. The PNI is calculated using the formula: PNI = 10 × serum albumin level (g/dL) + 5 × total lymphocyte count (10^9/L) (6). Both serum albumin and lymphocyte counts were obtained from routine venous blood samples analyzed by the hospital's central clinical laboratory.

2.4 Statistical analysis

Continuous variables were summarized as mean ± SD or median based on distribution, and categorical variables as percentages. Normality was assessed using the Kolmogorov–Smirnov test. For normally distributed variables, t-tests or ANOVA were used for group comparisons; non-normally distributed variables were compared with the Mann–Whitney U test or Kruskal-Wallis test. Kaplan–Meier curves analyzed the association between PNI quartiles and 30-day, 60-day, and 90-day mortality, using log-rank tests for group comparisons. Variables with >20% missing data were excluded. For variables with ≤20% missingness, multiple imputation was performed using the multivariate imputation by chained equations method, implemented via the *mice* package in R, under the assumption of missing at random. Details of the variables with missing data and their respective proportions are provided in Supplementary Table S1. Cox proportional hazards models estimated HRs and 95% CIs for the associations between PNI and clinical outcomes, with PNI analyzed both as a continuous variable and in quartiles, using the lowest quartile as the reference and adjusting for relevant covariates. Confounders were selected based on univariate analysis ($p < 0.05$) and clinical relevance. Multivariable models included: Model 1 (unadjusted); Model 2 (adjusted for age, sex, race, and weight); and Model 3 (further adjusted for hemoglobin, anion gap, INR, total bilirubin, Charlson comorbidity index, SOFA, APSIII, and sepsis). To assess potential multicollinearity among covariates, we calculated variance inflation factors, including generalized VIF for categorical variables. A restricted cubic spline (RCS) regression model with three knots assessed the nonlinear relationship between baseline PNI and 30-, 60-, and 90-day mortality. To evaluate whether combining PNI with a commonly used disease severity score could improve prognostic performance, we conducted a joint analysis using the PNI and the SOFA, and calculated the area under the receiver operating characteristic (ROC) curve (AUC). In addition, the optimal cutoff value for the combined model was determined using the Youden Index. Interaction tests evaluated the prognostic impact of PNI across subgroups defined by sex, age (<65 and ≥65 years), cancer status, and sepsis. Robustness analyses were performed to assess the stability of our primary findings. First, the multivariable Cox regression was repeated using the original (non-imputed) dataset. Second, patients with ICU stays less than 24 h—excluded from the main analysis—were included and analyzed using the same covariate adjustments as Model 3. Both analyses were conducted for the primary outcome of 30-day all-cause mortality. In addition, to explore long-term prognostic value, we performed a separate Cox regression analysis for 360-day all-cause mortality. Statistical significance was defined as $p < 0.05$. All analyses were conducted using R software (version 4.4.2).

3 Results

3.1 Baseline characteristics

Table 1 presents the baseline characteristics of the cohort stratified by PNI quartiles. Quartile 4 had a significantly higher proportion of male patients ($p = 0.010$). SOFA and APS III scores were lower in Quartile 4 compared to Quartile 1 ($p < 0.001$ for both). Heart rate decreased while SBP increased in Quartile 4 ($p < 0.001$ for both). The occurrence of malignant cancer and sepsis was lower in Quartile 4 ($p = 0.001$ and $p = 0.019$, respectively). Laboratory results showed higher albumin, lymphocyte counts, and total bilirubin levels ($p < 0.001$, $p = 0.005$, $p = 0.009$, respectively) as well as lower INR values in Quartile 4 ($p = 0.004$). Mortality rates at 30, 60, and 90 days were significantly reduced in Quartile 4 compared to Quartile 1 ($p < 0.001$ for all).

3.2 Kaplan–Meier survival curve

The Kaplan–Meier curves for 30, 60, and 90 days show statistically significant differences in survival probabilities between the PNI quartiles (log-rank p-values < 0.0001 at all time points). The fourth quartile consistently exhibits the highest survival probability across all follow-up periods (Figure 2).

3.3 Association between PNI and risk of mortality

The variables included in the multivariable Cox regression (Table 2) were selected based on univariable Cox regression analysis (Supplementary Table S2) and recommendations from clinical experts. In the fully adjusted model (Model 3), higher PNI as a continuous variable was associated with lower all-cause mortality risk at 30 days (HR 0.96, 95% CI: 0.93–0.98, $p < 0.001$), 60 days (HR 0.96, 95% CI: 0.94–0.98, $p < 0.001$), and 90 days (HR 0.97, 95% CI: 0.95–0.99, $p = 0.002$). When analyzed as a categorical variable, Quartile 4 of PNI showed significantly reduced mortality risk compared to Quartile 1 at 30 days (HR 0.47, 95% CI: 0.29–0.74, $p = 0.001$), 60 days (HR 0.54, 95% CI: 0.26–0.57, $p = 0.003$), and 90 days (HR 0.61, 95% CI: 0.42–0.90, $p = 0.012$). Trend tests for PNI quartiles were statistically significant at all three time points ($p = 0.001$, $p = 0.002$, and $p = 0.005$, respectively). RCS regression indicated a linear decrease in 30-, 60-, and 90-day mortality risk with increasing PNI (non-linearity p-values: 30-day 0.305, 60-day 0.196, 90-day 0.153) (Figure 3). To ensure model stability, multicollinearity among covariates was assessed using variance inflation factors. All adjusted GVIF values were <2, suggesting no significant multicollinearity in the fully adjusted model (Supplementary Table S3). For the primary outcome of 30-day all-cause mortality, the AUC for SOFA alone was 0.68, while the combined SOFA/PNI model yielded an AUC of 0.71. The optimal cutoff value for the SOFA/PNI model was 0.34 (Supplementary Table S4).

TABLE 1 Baseline characteristics stratified by PNI quartiles.

Characteristic	Overall *N* = 701	Quartile 1 *N* = 154	Quartile 2 *N* = 196	Quartile 3 *N* = 165	Quartile 4 *N* = 186	*p*-value
Demographics						
Age (years)	64.15 (53.45, 73.75)	63.16 (52.19, 72.73)	64.43 (54.97, 74.02)	64.51 (54.01, 74.61)	63.26 (50.89, 73.26)	0.661
Gender, male (%)	447 (64%)	86 (56%)	119 (61%)	107 (65%)	135 (73%)	**0.010**
Race, white (%)	484 (69%)	107 (69%)	142 (72%)	114 (69%)	121 (65%)	0.482
weight (Kg)	80.00 (67.90, 97.40)	78.20 (66.20, 96.30)	78.15 (68.00, 97.35)	82.50 (67.00, 97.70)	83.40 (68.60, 98.00)	0.634
Insurance, *n* (%)						0.732
Medicaid	130 (19%)	26 (17%)	38 (19%)	31 (19%)	35 (19%)	
Medicare	363 (52%)	75 (49%)	97 (49%)	93 (56%)	98 (53%)	
Other	32 (5%)	8 (5%)	7 (4%)	6 (4%)	11 (6%)	
Private	176 (25%)	45 (29%)	54 (28%)	35 (21%)	42 (23%)	
Clinical scores						
Charlson comorbidity index	5.00 (3.00, 7.00)	5.00 (3.00, 8.00)	5.00 (3.00, 7.00)	5.00 (3.00, 8.00)	5.00 (3.00, 7.00)	0.144
SOFA	7.00 (4.00, 10.00)	8.00 (5.00, 11.00)	7.00 (5.00, 11.00)	6.00 (3.00, 9.00)	5.50 (3.00, 9.00)	**<0.001**
APS III	57.00 (44.00, 76.00)	71.00 (56.00, 88.00)	59.00 (44.00, 73.00)	51.00 (41.00, 69.00)	50.00 (37.00, 65.00)	**<0.001**
Vital signs						
Heart rate (bpm)	78.00 (67.00, 91.00)	84.00 (72.00, 95.00)	78.00 (69.50, 89.50)	79.00 (68.00, 93.00)	73.00 (64.00, 87.00)	**<0.001**
SBP (mmHg)	85.00 (77.00, 96.00)	83.00 (73.00, 90.00)	83.50 (76.00, 92.00)	86.00 (78.00, 98.00)	90.00 (80.00, 101.00)	**<0.001**
Respiratory rate (bpm)	13.00 (10.00, 16.00)	13.00 (10.00, 16.00)	12.00 (10.00, 16.00)	14.00 (11.00, 16.00)	13.00 (10.00, 15.00)	0.062
SpO2 (%)	96.92 (95.38, 98.41)	97.11 (95.50, 98.12)	97.02 (95.27, 98.53)	96.67 (95.12, 98.44)	96.90 (95.57, 98.64)	0.721
Comorbidities (%)						
Diabetes, *n* (%)	183 (26%)	35 (23%)	51 (26%)	51 (31%)	46 (25%)	0.381
Renal Disease, *n* (%)	144 (21%)	31 (20%)	32 (16%)	36 (22%)	45 (24%)	0.280
Malignant Cancer, *n* (%)	142 (20%)	40 (26%)	50 (26%)	31 (19%)	21 (11%)	0.001
Sepsis, *n* (%)	573 (82%)	131 (85%)	171 (87%)	128 (78%)	143 (77%)	**0.019**
Hypertension, *n* (%)	234 (33%)	53 (34%)	67 (34%)	47 (28%)	67 (36%)	0.477
Laboratory test						
Hemoglobin (g/L)	9.40 (7.90, 11.00)	8.60 (7.30, 10.00)	8.95 (7.85, 10.10)	9.80 (8.40, 11.50)	10.50 (8.80, 11.90)	**<0.001**
Platelets (10^9/L)	165.00 (101.00, 251.00)	151.50 (72.00, 249.00)	155.50 (87.00, 266.00)	188.00 (119.00, 269.00)	167.00 (117.00, 223.00)	0.063
WBC (10^9/L)	9.60 (6.20, 14.50)	11.15 (6.90, 16.40)	9.70 (5.80, 15.30)	9.40 (6.00, 12.80)	9.20 (6.40, 12.20)	0.062
Albumin (g/dL)	2.80 (2.40, 3.30)	2.05 (1.90, 2.20)	2.60 (2.50, 2.70)	3.00 (2.90, 3.10)	3.65 (3.40, 3.90)	**<0.001**

(Continued)

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TABLE 1 (Continued)

Characteristic	Overall *N* = 701	Quartile 1 *N* = 154	Quartile 2 *N* = 196	Quartile 3 *N* = 165	Quartile 4 *N* = 186	*p*-value
Lymphocytes (10^9/L)	0.77 (0.46, 1.31)	0.74 (0.43, 1.18)	0.70 (0.41, 1.21)	0.86 (0.49, 1.35)	0.87 (0.56, 1.48)	**0.005**
PNI	28.02 (24.00, 33.00)	20.51 (19.00, 22.01)	26.00 (25.00, 27.01)	30.01 (29.01, 31.01)	36.51 (34.01, 39.01)	**<0.001**
Anion gap (m q/L)	13.00 (11.00, 16.00)	13.00 (10.00, 15.00)	13.00 (10.00, 16.00)	13.00 (11.00, 16.00)	14.00 (11.00, 16.00)	0.132
Sodium (mmol/L)	136.00 (132.00, 139.00)	136.00 (132.00, 138.00)	135.00 (132.00, 139.00)	137.00 (133.00, 140.00)	136.00 (131.00, 139.00)	**0.113**
Potassium (mmol/L)	3.80 (3.40, 4.20)	3.75 (3.40, 4.20)	3.80 (3.40, 4.20)	3.90 (3.50, 4.30)	3.80 (3.40, 4.20)	0.153
INR	1.30 (1.10, 1.60)	1.30 (1.20, 1.60)	1.40 (1.20, 1.70)	1.30 (1.10, 1.50)	1.20 (1.10, 1.50)	**0.004**
Total Bilirubin (umol/L)	0.80 (0.40, 1.90)	0.95 (0.40, 2.10)	1.00 (0.50, 2.60)	0.70 (0.40, 1.80)	0.60 (0.40, 1.30)	**0.009**
Treatments						
Mechanical Ventilation, *n* (%)	435 (62%)	103 (67%)	127 (65%)	95 (58%)	110 (59%)	0.238
CRRT, *n* (%)	75 (11%)	21 (14%)	17 (9%)	21 (13%)	16 (9%)	0.284
Octreotide, *n* (%)	75 (11%)	17 (11%)	24 (12%)	16 (10%)	18 (10%)	0.829
Events						
Los of Hospital (day)	15.59 (9.17, 24.80)	17.66 (8.94, 28.05)	15.68 (9.36, 27.40)	14.62 (9.98, 22.75)	14.46 (8.48, 22.18)	0.296
Los of ICU (day)	4.15 (2.18, 9.75)	4.30 (2.07, 10.14)	4.30 (2.30, 9.30)	4.01 (2.23, 9.05)	4.16 (1.99, 10.85)	0.965
30-day hospital Mortality (%)	183 (26%)	58 (38%)	53 (27%)	41 (25%)	31 (17%)	**<0.001**
60-day hospital Mortality (%)	233 (33%)	71 (46%)	70 (36%)	50 (30%)	42 (23%)	**<0.001**
90-day hospital Mortality (%)	255 (36%)	73 (47%)	78 (40%)	53 (32%)	51 (27%)	**<0.001**
360-day hospital Mortality (%)	289 (41.23)	78 (50.65)	87 (44.39)	62 (37.58)	62 (33.33)	**0.007**

PNI, Quartile 1 (9.00–24.00), Quartile 2 (24.00–28.02), Quartile 3 (28.02–33.00), Quartile 4 (33.00–55.01). PNI, prognostic nutritional index; SBP, Systolic blood pressure; WBC, White blood cell count; RBC, Red blood cell count; Platelet, Platelet count; SOFA, Sequential organ failure assessment; APS III, Acute Physiology Score III; SpO2, Oxygen saturation; INR, International normalized ratio; CRRT, Continuous renal replacement therapy. The variables with bold *p*-values are statistically significant.

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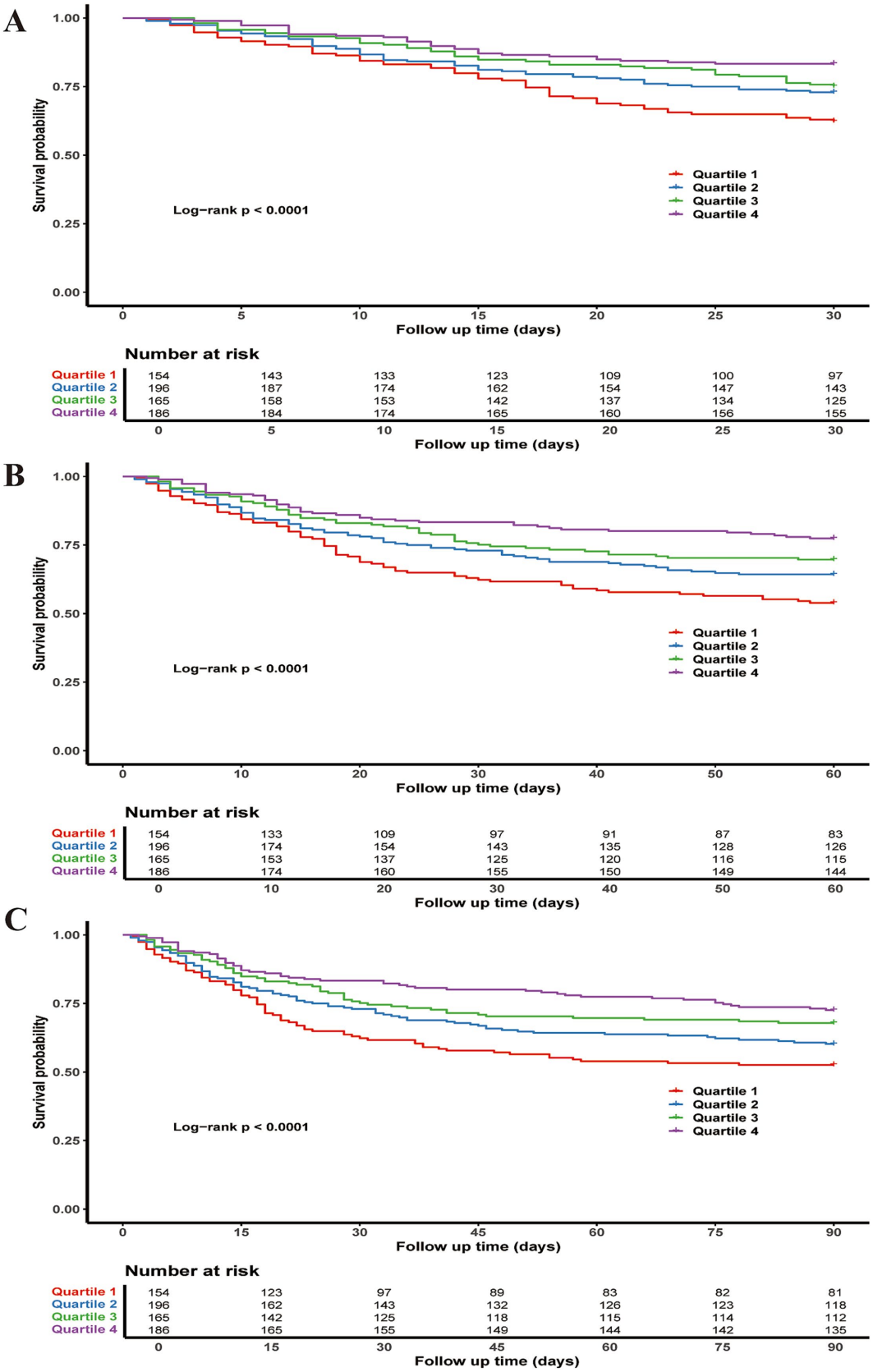

FIGURE 2
Kaplan–Meier survival curves for all-cause mortality: **(A)** 30-day, **(B)** 60-day, and **(C)** 90-day.

TABLE 2 Multivariable cox regression analysis of PNI and all-cause mortality.

Variables	Model 1		Model 2		Model 3	
	HR (95%CI)	*p*	HR (95%CI)	*p*	HR (95%CI)	*p*
30-day						
Continuous variable	0.96 (0.94, 0.98)	**<0.001**	0.95 (0.93, 0.97)	**<0.001**	0.96 (0.93, 0.98)	**<0.001**
PNI quartiles						
Quartile 1	—		—		—	
Quartile 2	0.68 (0.47, 0.99)	**0.042**	0.64 (0.44, 0.93)	**0.020**	0.70 (0.47, 1.02)	0.066
Quartile 3	0.60 (0.40, 0.90)	**0.013**	0.55 (0.23, 0.55)	**0.004**	0.58 (0.38, 0.89)	**0.013**
Quartile 4	0.39 (0.25, 0.61)	**<0.001**	0.36 (0.23, 0.55)	**<0.001**	0.47 (0.29, 0.74)	**0.001**
P for trend		**<0.001**		**<0.001**		**0.001**
60-day						
Continuous variable	0.96 (0.94, 0.98)	**<0.001**	0.95 (0.93, 0.97)	**<0.001**	0.96 (0.94, 0.98)	**<0.001**
PNI quartiles						
Quartile 1	—		—		—	
Quartile 2	0.72 (0.52, 1.00)	0.051	0.68 (0.49, 0.95)	**0.025**	0.77 (0.55, 1.09)	0.139
Quartile 3	0.58 (0.41, 0.84)	**0.004**	0.55 (0.38, 0.79)	**0.001**	0.62 (0.42, 0.92)	**0.017**
Quartile 4	0.42 (0.28, 0.61)	**<0.001**	0.39 (0.26, 0.57)	**<0.001**	0.54 (0.26, 0.57)	**0.003**
P for trend		**<0.001**		**<0.001**		**0.002**
90-day						
Continuous variable	0.96 (0.94, 0.98)	**<0.001**	0.96 (0.94, 0.97)	**<0.001**	0.97 (0.95, 0.99)	**0.002**
PNI quartiles						
Quartile 1	—		—		—	
Quartile 2	0.77 (0.56, 1.07)	0.117	0.74 (0.54, 1.02)	0.062	0.82 (0.59, 1.15)	0.254
Quartile 3	0.60 (0.42, 0.85)	**0.004**	0.56 (0.39, 0.79)	**0.001**	0.62 (0.43, 0.91)	**0.015**
Quartile 4	0.48 (0.34, 0.69)	**<0.001**	0.45 (0.31, 0.64)	**<0.001**	0.61 (0.42, 0.90)	**0.012**
P for trend		**<0.001**		**<0.001**		**0.005**

Model 1: Crude. Model 2: Adjusted for Age, Gender, Race, Insurance. Model 3: Adjusted for Model2 + SOFA + Charlson comorbidity index + APS III + Hemoglobin, Anion gap, INR, Total Bilirubin, and Sepsis. PNI, Quartile 1 (9.00–24.00), Quartile 2 (24.00–28.02), Quartile 3 (28.02–33.00), Quartile 4 (33.00–55.01). PNI, prognostic nutritional index; SOFA, Sequential organ failure assessment; APS III, Acute Physiology Score III; INR, International normalized ratio. The variables with bold *p*-values are statistically significant.

3.4 Subgroup analysis

After adjusting for covariates, interaction tests were conducted in predefined subgroups (Figure 4). Significant interaction effects were observed for gender ($p = 0.025$ at 30 days, $p = 0.035$ at 60 days, $p = 0.018$ at 90 days) and sepsis ($p = 0.041$ at 30 days) (Figure 4).

3.5 Robustness analyses

Sensitivity analyses showed that the association between higher PNI and lower 30-day all-cause mortality remained consistent in both the non-imputed dataset (HR = 0.96, 95% CI: 0.93–0.98; $p < 0.001$) and the full ICU cohort including patients with stays <24 h (HR = 0.96, 95% CI: 0.94–0.98; $p < 0.001$). In addition, PNI remained significantly associated with 360-day mortality (HR = 0.98, 95% CI: 0.96–0.99; $p = 0.037$) (Supplementary Table S5).

4 Discussion

This study explored the association between PNI and clinical outcomes in critically ill ICU patients with IO. Results demonstrated that patients with lower PNI had significantly higher 30-day, 60-day, and 90-day all-cause mortality rates compared to those with higher PNI. After adjusting for potential confounders, higher PNI remained consistently associated with lower mortality across these timeframes, supporting PNI as an independent risk factor. Therefore, PNI may serve as a valuable tool for assessing nutritional status and predicting mortality risk in critically ill patients with IO.

Previous studies on mortality in IO patients have often focused on inflammatory markers, such as RDW (7), C-reactive protein (8), and NLR (9). While these markers provide valuable insights into the systemic inflammatory response, they have notable limitations. Primarily, they do not reflect the patient's overall nutritional status or long-term immune competence. In contrast, PNI has been investigated in various disease contexts—ranging from gastrointestinal malignancies to cardiovascular conditions—and has consistently demonstrated prognostic utility (11, 12). Building on these findings, our study extends the application of PNI to a critically ill ICU cohort with IO, a group particularly vulnerable to nutritional and metabolic derangements. By taking advantage of PNI's simplicity, rapid risk stratification can be performed on the first day of ICU admission. This novel focus addresses a critical gap in existing research and highlights the importance of incorporating nutritional assessments into the management of IO patients admitted to the ICU.

The pathophysiological characteristics of IO—such as prolonged fasting, increased intraluminal pressure (13), bacterial translocation, and systemic inflammatory responses—directly impact albumin levels and

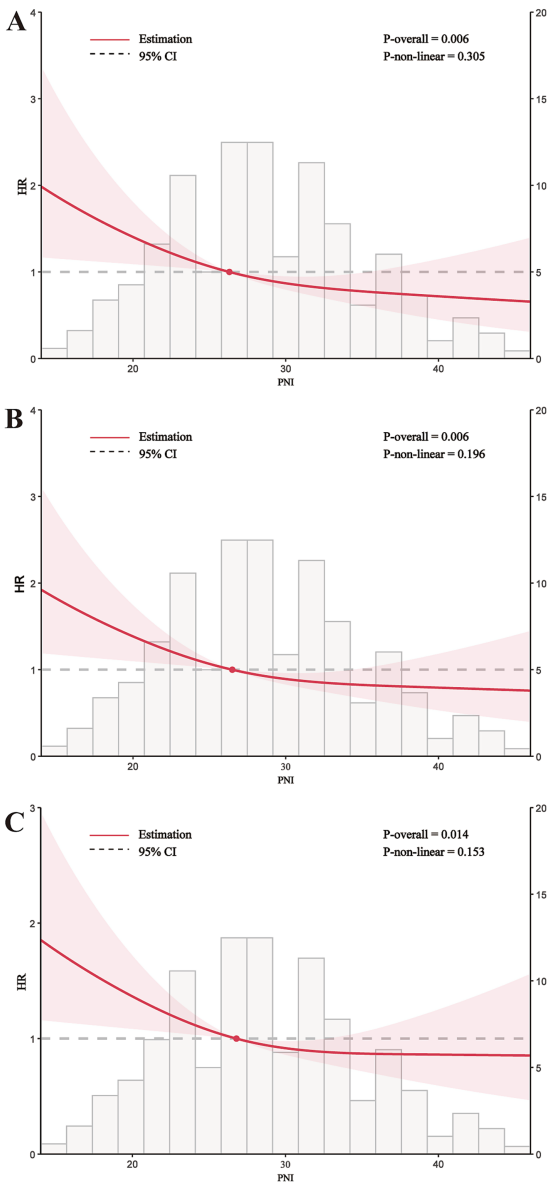

FIGURE 3
Restricted cubic spline curves for PNI hazard ratio. The central lines represent the adjusted hazard ratios, while the shaded ribbons indicate the 95% confidence interval (CI). **(A)** 30-day, **(B)** 60-day, and **(C)** 90-day all-cause mortality. HR, hazard ratio; CI, confidence interval; PNI, Prognostic Nutritional Index.

lymphocyte counts, which are critical components of the PNI. Given that both hypoalbuminemia and lymphopenia are independently linked to adverse clinical outcomes (14, 15), the prognostic utility of PNI likely stems from the integrated contributions of its two components. Albumin, a negative acute-phase reactant, decreases not only due to reduced nutritional intake caused by fasting but also because of heightened inflammatory processes inherent to obstruction (16, 17). The increased capillary permeability, cytokine release, and hepatic reprioritization of protein synthesis during systemic inflammation lead to a decline in circulating albumin levels (18). Hypoalbuminemia subsequently disrupts oncotic pressure, contributing to fluid shifts, tissue edema, and impaired perfusion, which ultimately compromise organ function and healing (19). Lymphocyte counts, another key element of the PNI, are suppressed both by malnutrition and the systemic inflammatory environment (20). Prolonged fasting and poor caloric intake diminish lymphopoiesis, while ongoing inflammation induces lymphocyte apoptosis and shifts immune cell populations toward a myeloid-dominant response (21). The lymphocyte depletion weakens cellular immunity, rendering patients more susceptible to infections and sepsis (22). In the context of intestinal obstruction, this loss of immune competence is particularly concerning because bacterial translocation from the compromised gut barrier further amplifies systemic inflammation and the risk of secondary infections (23). Together, these processes form a feedback loop: intestinal obstruction drives systemic inflammation, which further depletes albumin and lymphocytes (24). The resulting hypoalbuminemia and lymphopenia weaken healing capacity, reduce immune defense, and exacerbate organ dysfunction, ultimately leading to disease progression and a significantly increased risk of mortality in patients with intestinal obstruction (25).

In the subgroup analysis, the protective effect of PNI on mortality was more pronounced in females and patients without sepsis. A possible mechanism is that females often have higher levels of certain immune cells, such as dendritic cells and T-helper cells, which play a key role in immune responses to infections and tissue damage (26). These differences in immune function may allow females to more effectively combat illness, promoting better recovery when nutritional status is optimized (27). Additionally, there are metabolic differences between males and females that may influence how they utilize nutrients and recover from illness. For example, females may have more efficient mitochondrial function, which is crucial for energy production and immune function, further aiding their recovery when nutritional status is optimized. Nevertheless, we acknowledge the possibility of residual confounding, including unmeasured hormonal or inflammatory factors, and these findings should be further explored in future studies with biomarker-based stratification. In contrast, immune dysregulation and heightened systemic inflammation in septic patients likely diminish the predictive utility of PNI. In patients without sepsis, the absence of excessive inflammation allows PNI to better reflect baseline nutritional and immune reserves, making it a more reliable predictor of mortality. Similarly, PNI did not reach statistical significance in patients younger than 65 years and those with malignant tumors. A possible explanation is that younger patients may have better nutritional reserves, which could diminish the observable impact of PNI on mortality, as they often receive more aggressive interventions and have better recovery potential. In patients with malignant tumors, cancer-related systemic inflammation and cachexia often dominate the clinical picture, overshadowing the role of PNI, while tumor-specific factors, such as tumor burden and treatment response, may play a more significant role in determining mortality risk.

Our findings have important clinical implications for the management of critically ill IO patients. Integrating PNI into the standard risk assessment protocol at ICU admission allows clinicians to quickly identify patients with a poor nutritional and immune profile who are at elevated risk of adverse outcomes. Early recognition of these high-risk patients provides a critical window for timely interventions, including individualized nutritional supplementation (such as albumin infusion), more aggressive management of fluid and electrolyte imbalances, and targeted monitoring of organ function. In addition, leveraging PNI as a prognostic tool can help guide decisions about resource allocation—such as prioritizing the use of advanced imaging modalities or more frequent laboratory testing—to ensure that the most vulnerable patients receive the appropriate level of care. Nevertheless, in low-resource ICU settings, delayed or unavailable albumin and lymphocyte measurements may limit the real-time applicability of PNI, which should be considered in future implementation. Beyond

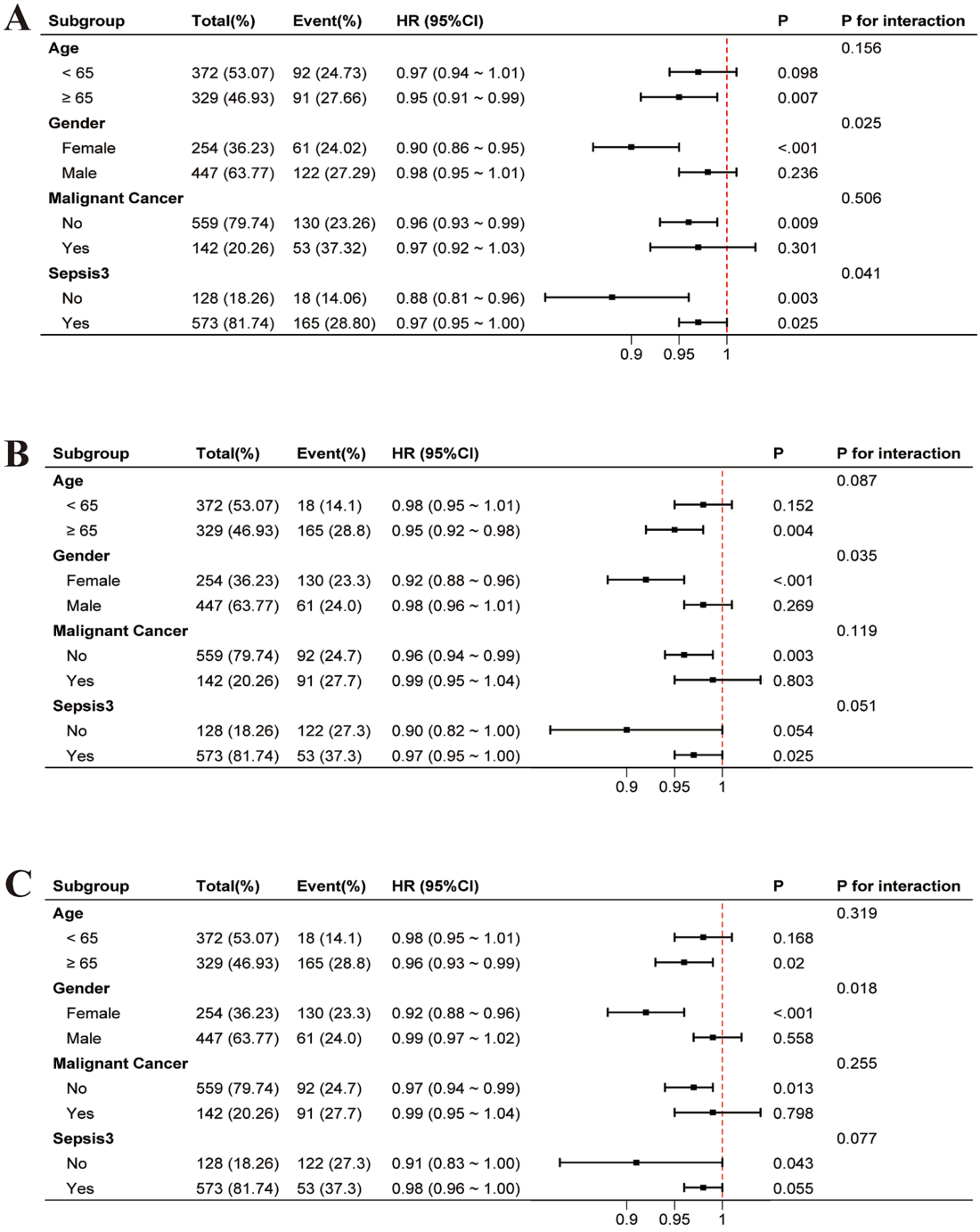

FIGURE 4
Adjusted forest plots of HR for all-cause mortality by subgroup, accounting for covariates: **(A)** 30-day, **(B)** 60-day, and **(C)** 90-day. HR, hazard ratio; CI, confidence interval.

short-term outcomes, the routine use of PNI can inform the development of more personalized, evidence-based treatment pathways that optimize long-term survival and recovery for IO patients in the ICU setting. By shifting the focus to an integrated assessment of both inflammatory and nutritional parameters, our study addresses a crucial gap in the current standard of care and paves the way for more comprehensive risk stratification and intervention strategies in this high-risk population.

This study has several limitations. First, the retrospective design of this study may introduce selection bias. Although we adjusted for multiple confounding variables, residual confounding cannot be entirely excluded due to the limited inclusion of certain clinical factors or interventions, such as surgical treatments. However, the primary aim of this study was to rapidly assess nutritional status and perform early risk stratification based on PNI at ICU admission, and our analysis remains clinically informative within this context. Moreover, as an observational study, this research demonstrates association rather than causation. Further prospective cohort studies and interventional trials are needed to elucidate the causal relationship between PNI and mortality. Second, we excluded patients without albumin or lymphocyte measurements, which may have introduced

selection bias and, to some extent, limited the generalizability of the findings. Third, this study assessed only the PNI value at ICU admission for the purpose of early risk stratification in critically ill IO patients. However, given that nutritional and immune status may fluctuate significantly throughout the ICU stay, the absence of serial PNI measurements limited our ability to evaluate its temporal trends and prognostic value. In addition, due to substantial missingness of CRP data and the absence of IL-6 measurements in our dataset, we were unable to validate the proposed inflammation-related mechanisms underlying hypoalbuminemia and lymphopenia. Additionally, relying solely on PNI as a primary nutritional marker may not capture more dynamic or comprehensive aspects of nutritional status, such as body composition or micronutrient levels. Although this study evaluated survival at multiple time points, long-term functional status could not be assessed due to data limitations, which should be explored in future research. Lastly, the generalizability of our findings is restricted, as the patient cohort from the MIMIC-IV database may not be representative of more diverse populations across different healthcare systems or regions. Future studies should focus on large-scale, multicenter, prospective cohorts across diverse racial and ethnic populations to further validate our findings and refine risk stratification methods.

5 Conclusion

In this study, we demonstrated that a higher PNI is independently associated with lower mortality in critically ill ICU patients with IO, even after adjusting for potential confounders. These findings suggest that PNI provides a valuable measure of both nutritional and immune status, offering an integrated alternative to traditional inflammatory markers and highlighting the importance of nutritional assessments in this high-risk population. By facilitating early risk stratification and guiding targeted interventions, PNI has the potential to improve patient outcomes and optimize resource allocation in the ICU setting. However, while our results underscore the promise of PNI as a prognostic tool, further prospective studies are needed to confirm its utility and clarify its role in clinical decision-making for critically ill IO patients.

Data availability statement

Publicly available datasets were analyzed in this study. This data can be found at: All data and materials are accessible at https://mimic.mit.edu/.

Ethics statement

The studies involving humans were approved by The MIMIC-IV database adheres to the principles of the Helsinki Declaration and has been approved by the Institutional Review Board (IRB) of Beth Israel Deaconess Medical Center (2001P-001699/14). The IRB evaluated the data collection process and the creation of the research resource, authorized the data-sharing initiative, and exempted the need for informed consent. 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

YG: Data curation, Formal analysis, Methodology, Writing – original draft. ZW: Writing – review & editing. CZ: Conceptualization, Supervision, Writing – review & editing.

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Development and validation of a questionnaire for the knowledge assessment and management of PLADO diet in kidney and healthy population in Cyprus

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Chronic kidney disease (CKD) requires dietary strategies that balance protein restriction, nutritional adequacy, and sustainability. As plant-dominant dietary models gain prominence in renal nutrition, understanding public perceptions of protein sources and their health impacts is increasingly critical. However, no validated assessment tool exists to evaluate such perceptions within the Cypriot population. This study presents the development and validation of a novel questionnaire designed to assess perceptions of sustainability, nutritional value, and health impacts of plant- and animal-based proteins, with a focus on kidney health. The instrument was developed through literature review, expert input ($n = 10$), cognitive pretesting, and pilot testing ($n = 120$). Validation included content validity indexing (I-CVI), Modified Kappa statistics, internal consistency via Cronbach's alpha, and exploratory factor analysis (EFA). Expert agreement was high, with an S-CVI/Ave of 0.89 and 93% of items achieving I-CVI $\geq$ 0.83. Internal consistency across subscales ranged from $\alpha = 0.71$ to 0.82. EFA supported construct validity, explaining 36% of the variance. The final 42-item questionnaire covers eight domains, including sustainability beliefs, dietary behavior, and protein knowledge. A unique feature is its embedded educational content—glossary terms, visuals, and explanatory prompts—designed to evaluate baseline knowledge and learning outcomes. Pilot results revealed knowledge gaps and uncertainty about the sustainability of plant-based proteins among CKD respondents. This validated tool fills a significant gap in renal nutrition education and research and offers a reliable, culturally relevant means to assess dietary perceptions. It supports patient education, public health interventions, and clinical practice in promoting sustainable, kidney-friendly diets. Broader application and cross-cultural adaptation are recommended to enhance global utility.

KEYWORDS

chronic kidney disease, protein perception, questionnaire validation, plant-based diet, sustainability, renal nutrition, dietary education, Cyprus

1 Introduction

Understanding consumer perceptions of sustainability, nutrition, and the health impact of dietary protein sources is increasingly relevant in the context of evolving dietary guidelines and public health strategies. In particular, individuals with chronic kidney disease (CKD) require careful dietary management, especially regarding protein intake,

to maintain kidney function and overall wellbeing. CKD affects over 10% of the global population and is frequently underdiagnosed (1). Its prevalence increases significantly with age—affecting 42% of those over 75, 21% of individuals aged 65–74, and 6% among those aged 18–54. CKD is commonly comorbid with cardiovascular disease and diabetes, further increasing morbidity and mortality risk (2).

While animal-based proteins have traditionally been the primary dietary source, recent trends emphasize the potential health and environmental benefits of plant-based proteins. Although existing research explores the physiological effects of various protein sources in CKD management, limited attention has been given to how consumers perceive these dietary alternatives—particularly in specific populations such as Cypriots with or at risk of CKD. Given that dietary behaviors are shaped by knowledge, attitudes, and beliefs (3), it is crucial to develop valid tools to assess consumer perceptions regarding sustainability and the health impacts of plant- and animal-based proteins.

The global rise in chronic kidney disease (CKD), linked with metabolic disorders, calls for early intervention strategies grounded in nutritional prevention. Plant-based, low-protein dietary patterns are increasingly recognized for their potential to delay CKD progression and reduce cardiovascular risk (4). However, adherence remains low, often due to cultural beliefs, knowledge gaps, and concerns over nutritional adequacy. The Plant-Dominant Low-Protein Diet (PLADO) framework offers a structured approach emphasizing plant protein, portion control, and sustainability—yet its adoption requires targeted educational tools. Sustainable dietary interventions not only support individual health but also align with global environmental goals (5, 6). Thus, a validated questionnaire is needed to measure perceptions across both health and ecological dimensions, particularly in culturally diverse settings.

In Cyprus, a Mediterranean country with diverse dietary practices, food choices are influenced by cultural norms, environmental awareness, and evolving dietary trends (7). A recent review highlights the potential for plant-dominant low-protein diets (PLADO) as a culturally relevant and clinically effective approach for CKD management in Cyprus, integrating both traditional cuisine and nutritional science (5). As public interest in sustainable eating grows, it becomes essential to understand how Cypriots perceive the interplay between diet, health, and environmental responsibility (8). This is particularly relevant for individuals with CKD, whose dietary habits can significantly influence disease progression and quality of life. Despite increased awareness of protein sustainability and its health implications, no validated tool currently exists to assess such perceptions among Cypriot populations.

To address this gap, we developed a structured questionnaire designed to evaluate beliefs, attitudes, and knowledge related to sustainable dietary practices and the health implications of protein choices, with a focus on CKD. The questionnaire integrates educational content—such as brief definitions and illustrated food comparisons—to evaluate baseline understanding and the potential effect of targeted nutrition education. This dual approach facilitates the assessment of both pre-existing knowledge and post-intervention perception shifts.

Although Cyprus shares many characteristics with Mediterranean dietary patterns—such as olive oil use, fresh vegetables, and moderate wine consumption—it also exhibits distinct regional features. Notably, traditional Cypriot cuisine includes a high intake of pork products, halloumi cheese, and grilled meats (8, 9), setting it apart from the plant-rich diets of other Mediterranean populations like Greece or Italy. Additionally, plant-dominant dietary models are less culturally ingrained in Cyprus, where meat consumption remains a central part of communal meals and festivals (10). These cultural differences underscore the importance of developing a regionally adapted questionnaire to accurately capture perceptions of protein sources and their health and sustainability implications within the Cypriot context.

In addition to health considerations, the sustainability of dietary choices is increasingly important—especially for individuals with CKD, who require specific protein intake adjustments. Plant-based proteins, when compared to animal sources, are associated with lower greenhouse gas emissions, reduced land and water use, and lower ecological burden. Mediterranean populations, including Cypriots, are well-positioned to adopt plant-dominant low-protein diets (PLADO) due to traditional food patterns that emphasize legumes, grains, and seasonal produce. Integrating sustainability into CKD nutrition offers a dual benefit: mitigating disease progression and supporting environmentally responsible eating practices.

The primary objective of this study is to develop and validate a questionnaire that captures consumer perceptions and knowledge related to sustainable dietary practices, with specific focus on early-stage CKD prevention and management. This questionnaire was developed for use in both the general Cypriot population and individuals diagnosed with early to moderate stages of CKD (stages 1–3), based on self-reported or clinician-confirmed eGFR data. Individuals on dialysis or those with kidney transplants were excluded from the study. The instrument is intended to support both the prevention of CKD progression through education and the early-stage dietary management of the disease via sustainable and renal-appropriate protein choices. The tool is designed to explore three main domains:

First, it examines consumer understanding of sustainability in relation to protein sources. With mounting concerns about environmental impact and food system sustainability, it is important to evaluate how well consumers recognize these factors in their food choices.

Second, it assesses awareness of the nutritional differences between plant-based and animal-based proteins in the context of CKD management. Excess protein intake, particularly from certain animal sources, can accelerate CKD progression. Evaluating consumer knowledge in this area informs education strategies.

Third, the questionnaire explores how dietary protein choices are perceived to affect kidney function and health. For individuals at risk of or living with CKD, it is vital to assess their understanding of the potential health consequences of different protein sources.

A unique feature of the tool is the integration of evidence-based educational content, including visual guides and simplified definitions to enhance comprehension. This approach enables evaluation of baseline knowledge and post-intervention learning,

identifying gaps and misconceptions regarding protein intake, sustainability, and CKD.

Validation ensures the questionnaire reliably captures both baseline knowledge and changes following educational exposure. The full validation framework, including content relevance, clarity, and construct structure, is described in detail in the Methods section.

To address the research gap and support culturally relevant dietary interventions, the scope of the study was defined as follows. This study aimed to develop and validate a culturally appropriate questionnaire assessing consumer perceptions of sustainability, nutritional knowledge, and health impacts of dietary protein sources—specifically targeting individuals at risk of or living with chronic kidney disease (CKD) in Cyprus. The instrument is intended for use in public health education, clinical nutrition counseling, and future research focused on plant-dominant low-protein diets (PLADO) and kidney health.

2 Methods and materials

2.1 Questionnaire development

The questionnaire was developed to assess three primary constructs: sustainability perceptions, dietary habits, and awareness of health impacts related to protein intake, particularly among individuals at risk of or living with chronic kidney disease (CKD). Constructs were identified through an extensive literature review on plant-based and animal-based protein consumption and their effects on kidney health. Development procedures followed recommended best practices for health-related scale creation, including guidelines proposed by Boateng et al. (11), Ranganathan et al. (12), and the COSMIN checklist for content validity.

2.1.1 Questionnaire domains and objectives

The questionnaire was structured around four domains:

Sustainability Perceptions—assessed awareness of environmental impacts of protein sources, including greenhouse gas emissions, water usage, and ethical considerations.

Example item: "A plant-based or vegetarian diet yields less meat, less greenhouse gas emissions, more love for the planet's animals, less waste of water and land... Can vegetable proteins be considered a viable alternative?"

Dietary Habits—included 14 items modeled on the MedScore framework and dietary classification systems (e.g., vegan, DASH, PLADO). Food frequency items measured plant- vs. animal-protein intake.

Example item: "How frequently do you consume legumes?"

Health Impacts—evaluated knowledge of how protein choices affect weight management, kidney function, and clinical biomarkers.

Example item: "Which type of protein do you think can negatively affect kidney function when consumed in large quantities over time?"

Knowledge Assessment—examined understanding of protein roles in the body and nutrient composition.

Example item: "Do you know how many grams of protein one slice of white bread contains?"

This domain structure ensured comprehensive assessment of perceptions, habits, and knowledge surrounding sustainable, kidney-friendly protein choices. Supplementary Table 1 provides representative items from each domain of the questionnaire, illustrating the thematic focus and assessment scope used to evaluate sustainability beliefs, dietary habits, protein knowledge, and health perceptions relevant to CKD.

2.1.2 Item generation process

Item generation was informed by a systematic review of the literature conducted through PubMed and the University of Nicosia Library databases. Search terms included: (Animal protein OR vegetarian protein OR plant-based) AND (Health populations OR Kidney patients) AND (Questionnaire OR Tool) AND (Health impact). From 84 articles screened, 11 utilized questionnaires, and only two involved the development of knowledge-based assessment tools (13, 14).

Items were designed iteratively in collaboration with domain experts in nutrition, nephrology, and public health. Educational materials, including visual aids, glossary definitions, and culturally adapted language examples, were incorporated to enhance participant comprehension.

2.1.3 Initial questionnaire design and cognitive pretesting

The initial draft comprised five sections:

- Demographics and health history (including kidney status and biomarker history)
- Food frequency for vegetarian and animal protein consumption
- Protein functions and nutrient knowledge
- Mediterranean Diet adherence scoring (MedScore; Yes/No format)
- Perceptions of sustainability

A cognitive pretesting phase was conducted with ten undergraduate nutrition students to evaluate face validity and comprehension. Feedback led to simplifications in terminology, enhanced visual supports, and inclusion of culturally relevant food examples (e.g., lentils with rice).

2.2 Questionnaire validation process

2.2.1 Content and face validity

Content validity was evaluated by a panel of nine domain experts (nutrition, nephrology, dietetics), who independently rated each item's relevance, clarity, and simplicity using a 5-point Likert scale. Item-level Content Validity Index (I-CVI) scores were calculated, with I-CVI $\geq$0.78 considered acceptable. Scale-level CVI (S-CVI/Ave) was also computed to assess overall coverage. Modified Kappa statistics were applied to adjust for chance agreement, interpreted as $\geq$0.74 (excellent), 0.60–0.74 (good), 0.40–0.59 (fair), and $<$0.40 (poor).

Face validity was further assessed during cognitive pretesting, leading to refinements in item clarity, visual formatting, and educational materials.

2.2.2 Construct validity (exploratory and confirmatory factor analysis)

Construct validity was explored using Exploratory Factor Analysis (EFA) based on Classical Test Theory. Factors were extracted using eigenvalues >1, scree plot evaluation, and theoretical interpretability. A minimum factor loading of 0.40 was used for item retention. Confirmatory Factor Analysis (CFA) was performed subsequently to validate the factor structure, with model fit evaluated via indices such as RMSEA, TLI, and BIC.

2.2.3 Internal consistency and reliability testing

Internal consistency reliability was assessed using Cronbach's alpha, with $\alpha \geq 0.70$ considered acceptable. Additional item-level analyses included:

- Missing value analysis (15).
- Critical value analysis (16).
- Item-total correlation assessment (17).
- Homogeneity testing (18).

Although internal consistency was assessed, test–retest reliability was not performed in this phase and is recommended for future validation.

2.2.4 Criterion validity assessment

Criterion validity was assessed through correlations between the MedDietScore-derived dietary adherence results and scores obtained from the validated Mediterranean Diet Adherence Screener (19).

2.3 Pilot testing procedures

2.3.1 Cognitive pilot study ($n = 10$)

A cognitive validation process was conducted with 10 participants to assess item clarity, relevance, and interpretability. The expert panel included one biostatistician, eight academic professionals and clinical dietitians with specialization in kidney nutrition, and one patient with chronic kidney disease. Experts were invited via formal email communication and participated by independently reviewing the questionnaire through an online Google Form. They rated each item for clarity, importance, and simplicity using a structured scale. Feedback from this panel informed refinements to item phrasing, educational glossaries, and scoring instructions. This procedure aligns with established best practices in instrument development and content validation (20).

2.3.2 Field psychometric pilot study ($n = 120$)

A subsequent field pilot study was conducted with 120 adult participants recruited through nephrology clinics and public advertisements. Inclusion criteria were: age ≥18 years, Greek-speaking, and internet access. The questionnaire used in this phase consisted of 42 items organized across 8 thematic domains, including sustainability beliefs, dietary habits, CKD knowledge, and protein-related behaviors. Exclusion criteria included dialysis dependence, kidney transplantation, or cognitive impairment. Participants completed the 42-item questionnaire administered via Google Forms. Data collected included demographics, dietary habits, health history, and protein knowledge. CKD diagnosis was determined based on self-reported medical history and confirmed through documented eGFR values, as captured in the questionnaire (Data Sheet 1, Question 14). Participants who reported dialysis dependence or kidney transplantation were excluded from the analysis.

2.4 Data analysis

Statistical analyses were performed using Python-based libraries: `pandas`, `scipy.stats`, and `statsmodels` for reliability analyses, and `sklearn` for confirmatory factor analyses. Visualizations were created using `matplotlib` and `seaborn`. Scoring procedures included the summation of correct responses for knowledge domains, binary coding for Mediterranean Diet adherence, and frequency-based categorization for sustainability and protein intake patterns scoring procedures were standardized:

- Mediterranean Diet Score (14 dichotomous Yes/No items).
- Knowledge scores (sum of correct responses).
- Sustainability and protein perceptions (categorical variables).

All procedures involving human participants were approved by the Cyprus National Bioethics Committee (Protocol number EEBK ΕΠ 2024.01.53).

3 Results

3.1 Content validity

The content validity of the questionnaire was evaluated by a panel of nine domain experts specializing in nutrition, nephrology, and dietetics. Each item was assessed for relevance, clarity, and simplicity using a 5-point Likert scale. Item-Level Content Validity Index (I-CVI) scores were calculated, with 93% of items achieving an I-CVI ≥0.83 and 68% attaining a perfect score of 1.00. The Scale-Level CVI (S-CVI/Ave) was 0.89, indicating excellent overall agreement on content relevance. Modified Kappa statistics, adjusting for chance agreement, demonstrated that most items fell within the "excellent" ($\kappa \geq 0.74$) or "good" ($\kappa = 0.60$–0.74) categories. These findings substantiate the strong content validity of the questionnaire. Full I-CVI and Modified Kappa statistics are presented in Supplementary Table 2.

3.2 Face validity

Face validity was assessed through cognitive pretesting with a small pilot group of 10 undergraduate nutrition students.

Participants provided feedback on item clarity, terminology, and conceptual understanding, particularly related to protein knowledge. Based on the feedback, modifications were made to simplify definitions, incorporate additional educational visuals, and enhance the accessibility of technical concepts. These revisions improved the comprehensibility and usability of the instrument.

3.3 Internal consistency and reliability

Internal consistency reliability of the questionnaire was evaluated using Cronbach's alpha across key subscales. The MedDietScore subscale (14 binary items) demonstrated good reliability ($\alpha = 0.82$). The Sustainability Beliefs subscale showed acceptable reliability ($\alpha = 0.76$), and the CKD Protein Knowledge subscale also achieved acceptable consistency ($\alpha = 0.71$). The Food Frequency subscale exhibited borderline acceptable internal consistency ($\alpha = 0.69$), suggesting potential areas for future refinement. Full internal consistency statistics are provided in Supplementary Table 2.

3.4 Construct validity

Construct validity was assessed through exploratory factor analysis (EFA). Factors were extracted using eigenvalues >1 and scree plot examination. Factor loadings exceeded 0.40 for most items, supporting the presence of coherent latent constructs. The dominant factor explained 36% of the total variance, supporting the structural validity of the questionnaire. Confirmatory factor analysis (CFA) further supported model adequacy, although improvements could enhance fit indices in future refinements. Details of factor analysis results are presented in Supplementary Table 3.

3.5 Pilot study demographics

A field pilot study was conducted with 120 adult participants to evaluate demographic representation and psychometric performance. The sample had a balanced gender distribution (52.5% male, 47.5% female), with a mean age in the late twenties, and the majority possessing tertiary education qualifications (92.5%). Employment status was diverse, comprising 60% employed individuals and 30% students. Full demographic characteristics are provided in Supplementary Table 4.

3.6 Pilot sample CKD stratification and scores

The pilot study included 120 participants, of whom 35.8% ($n = 43$) self-reported having chronic kidney disease (CKD). Based on available data, CKD stages were distributed as follows: Stage 1 (eGFR $\geq$ 90)–12%, Stage 2 (eGFR 60–89)–14%, and Stage 3a−3b (eGFR 30–59)–9.8%. Individuals with an eGFR below 30, those undergoing dialysis, or who had received a kidney transplant were excluded from the sample.

Participants with CKD scored slightly lower on the protein knowledge scale (Mean = 1.67, SD = 1.39) compared to those without CKD (Mean = 2.11, SD = 1.24). The overall mean Mediterranean Diet Score (MedDiet Score) was 7.75 $\pm$ 2.38, reflecting moderate adherence to Mediterranean dietary principles. Perceptions around sustainability—especially plant-based protein adequacy—were more variable among CKD participants, with many expressing uncertainty regarding nutritional sufficiency. These comparative results are summarized in Supplementary Table 4.

4 Discussion

This study presents the development and psychometric validation of a novel questionnaire designed to assess perceptions of sustainability, nutritional knowledge, and health impacts of plant- and animal-based protein sources, with a particular emphasis on kidney health. The questionnaire demonstrated strong content validity, acceptable to good internal consistency across subscales, and promising construct coherence. These findings support its utility as a reliable and culturally tailored instrument for assessing dietary perceptions within the Cypriot population.

The content validation process showed high expert consensus, with a scale-level content validity index (S-CVI/Ave) of 0.89 and most items reaching excellent or good agreement in Modified Kappa statistics. Face validity testing through cognitive pretesting further improved the clarity and comprehensibility of the instrument, particularly by refining educational components and technical terminology. Feedback from this pretesting phase and subsequent modifications are summarized in Supplementary Table 5.

Internal consistency reliability, assessed via Cronbach's alpha, was acceptable across most subscales ($\alpha = 0.71$–0.82), consistent with established thresholds for health-related questionnaires. Specifically, the MedDietScore and Sustainability Beliefs subscales exhibited strong reliability, while the Protein Source Frequency subscale demonstrated borderline acceptability, suggesting potential areas for future refinement. As shown in Supplementary Table 6, internal consistency varied across subscales. The *MedDietScore* subscale achieved the highest reliability ($\alpha = 0.82$), followed by *Sustainability Beliefs* ($\alpha = 0.76$). Lower alpha values in the *24-h Recall Consistency* ($\alpha = 0.65$) and *Protein Source Frequency* ($\alpha = 0.69$) subscales suggest potential item heterogeneity and indicate areas for future refinement.

Construct validity was supported by exploratory factor analysis (EFA), which revealed a dominant clarity-related factor explaining 36% of the total variance. Factor loadings for most items exceeded 0.40, indicating a coherent underlying structure. Detailed EFA results, including factor loadings and variance explained, are provided in Supplementary Table 7. Confirmatory factor analysis (CFA) further explored model fit, with indices such as RMSEA and BIC supporting structural adequacy, although the Tucker-Lewis Index (TLI) suggested opportunities for model improvement.

Moreover, inter-item reliability among expert ratings of relevance, clarity, and simplicity was high, with standardized

Cronbach's alpha values exceeding 0.90, reinforcing the robustness of the content validation phase (Supplementary Table 8).

In addition to the psychometric properties, the discussion now emphasizes pilot results more directly. Participants with CKD scored lower on protein knowledge and expressed greater uncertainty around the sustainability of plant-based diets—particularly the sufficiency of plant proteins for kidney health. These findings suggest knowledge gaps that may undermine adherence to recommended low-protein dietary regimens such as PLADO.

While the PLADO framework has gained attention for its potential to delay CKD progression and reduce cardiovascular burden, recent literature also raises concerns regarding its nutritional adequacy—particularly for *protein and* micronutrient sufficiency in advanced CKD stages (21, 22). These findings highlight the need for evidence-based educational interventions to guide patients toward safe implementation. Our questionnaire aims to fill this gap by evaluating both the perceived risks and informational gaps that may hinder safe adherence.

Perceptions of sustainability varied substantially, with many CKD participants unsure about the environmental or nutritional adequacy of plant-based options. This reinforces earlier findings from Mediterranean and Cypriot contexts, where plant-based transitions face cultural and informational barriers. Our tool is the first to explicitly integrate both health and environmental dimensions of protein intake in the context of kidney disease.

Comparison with existing instruments shows that while tools such as the MedDietScore assess overall dietary quality, they lack integration of sustainability or kidney-specific considerations. Our instrument bridges this gap and enables targeted interventions through clinical and community settings.

Furthermore, the suggested tool incorporates visual elements—such as portion-size diagrams and annotated glossaries—to improve comprehension and dietary self-efficacy. This design feature aligns with recent findings demonstrating that visual aids enhance adherence to healthy dietary patterns, particularly in CKD populations (23–25). These elements strengthen the questionnaire's utility not only as a perception assessment tool but also as a behaviorally-informed educational intervention that may be applied in both clinical and community settings.

The questionnaire is structured for adaptability and future global use. Cross-cultural validation, digital deployment, and translation will be key next steps. The tool is positioned to support both individual-level dietary counseling and broader public health strategies—especially relevant in regions with rising CKD prevalence and shifts toward sustainable diets (26–32).

Several strengths characterize this study. The multi-phase validation approach—spanning expert evaluation, cognitive pretesting, field pilot testing, and psychometric assessment—strengthens the scientific rigor and credibility of the findings. Additionally, the incorporation of educational content to measure baseline knowledge and post-assessment learning represents an innovative and practical advancement (5, 27–35).

Nonetheless, several limitations should be acknowledged. First, the pilot sample predominantly consisted of younger adults with higher education levels, potentially limiting generalizability to other population groups (36–45). Second, test–retest reliability was not assessed in this phase and should be incorporated into future longitudinal validation efforts (46–57). Third, while preliminary construct and criterion validity findings were promising (Supplementary Table 9), further validation against clinical outcomes, such as biomarkers of kidney function, is necessary to confirm predictive validity (10, 13, 58–68).

Future research should focus on confirming the questionnaire's temporal stability through test–retest reliability studies, evaluating its predictive validity in CKD progression, and conducting cross-cultural adaptation studies to enhance broader applicability. Furthermore, applying the tool in different CKD stages and in general population cohorts could provide deeper insights into dietary behavior modification strategies and public health interventions (69–85).

Finally, this validated questionnaire offers a culturally relevant, psychometrically sound tool to support clinical practice, public health initiatives, and research efforts aimed at promoting sustainable and kidney-friendly dietary behaviors (5, 11, 86–90).

5 Conclusion

This study presents a rigorously developed and validated questionnaire that uniquely integrates sustainability, nutritional knowledge, and kidney-specific dietary principles. The instrument demonstrates strong psychometric properties and cultural relevance, particularly for Cypriot and Mediterranean populations. Its potential for cross-cultural adaptation, digital deployment, and clinical use positions it as a valuable tool for promoting informed, sustainable dietary choices among individuals at risk for or living with CKD.

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 Cyprus National Bioethics Committee (Protocol number EEBK ΕΠ 2024.01.53). 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

AM: Formal analysis, Conceptualization, Methodology, Validation, Data curation, Writing – original draft, Writing – review & editing, Resources, Investigation. CZ: Validation, Writing – review & editing. IS: Validation, Writing – review & editing. KT: Writing – review & editing, Validation. EA: Writing – review & editing, Funding acquisition, Resources, Supervision, Writing – original draft, Formal analysis, Investigation, Project administration, Software, Data curation, Methodology, Conceptualization, Visualization, Validation.

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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.

Generative AI statement

The author(s) declare that no Gen AI was used in the creation of this manuscript.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fnut.2025.1619237/full#supplementary-material

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Comparative assessment of sarcopenia screening tools for patients with bone tumors: insights for enhanced clinical application

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Background: Sarcopenia screening in bone tumor patients is challenging due to limited awareness, complex procedures, and high costs-especially since most research targets older adults, overlooking younger patients in this group. This study aims to compare the screening efficacy of five different tools for sarcopenia, and to identify the most appropriate screening tool for patients with bone tumors.

Methods: The five sarcopenia screening tools assessed were SARC-F, SARC-Calf, SARC-F + EBM, and the Chinese versions of the Mini-Sarcopenia Risk Assessment scales (MSRA-5 and MSRA-7). The 2019 Asia Working Group for Sarcopenia (AWGS) criteria served as the reference standard for sarcopenia screening.

Results: Among 300 bone tumor patients, 26% were found to have sarcopenia based on AWGS 2019 criteria. The screening tools varied in performance, with SARC-Calf showing the highest sensitivity and MSRA-7 the lowest specificity. Positive and negative predictive values were moderate across tools, with combined screening methods generally improving sensitivity. The highest overall accuracy (AUC) was observed when using a combination of SARC-F, SARC-Calf, and EBM, which provided both high sensitivity and acceptable specificity.

Conclusion: The SARC-Calf and SARC-F + EBM tools demonstrated high accuracy in screening sarcopenia among bone tumor patients. The combined use of SARC-F, SARC-Calf, and SARC-F + EBM yielded superior screening performance, making them suitable for preliminary sarcopenia screening in this patient population.

KEYWORDS

sarcopenia, screening tool, sensitivity and specificity, bone tumor, Chinese patients

1 Introduction

Bone tumors originate from bone tissue or other components within the bone, encompassing primary bone tumors as well as metastases from other malignancies, most commonly from the lungs and breasts. Bone metastases affect over 1.5 million cancer patients globally and spread through the blood or lymphatic system (1). Primary bone tumors, although rare, account for approximately 2–3% of all cancers and are frequently located at the ends of long bones, such as the distal femur, proximal tibia, and proximal humerus (2). In China, an estimated 24,200 bone tumor cases were reported in 2015, representing about 0.62% of all cancers (3). Factors such as chemotherapy, immunodeficiency, tumor-induced catabolism, fear of movement, pain, and poor sleep contribute to an increased risk of muscle loss in bone tumor patients (4, 5).

Sarcopenia is a progressive, systemic condition characterized by the loss of skeletal muscle mass, strength, and physical performance (6). The prevalence of sarcopenia varies according to diagnostic criteria and environmental factors, ranging from 5.5 to 25.7% (7). Among cancer patients, sarcopenia prevalence can be as high as 43% (8), significantly impacting clinical outcomes, such as increased chemotherapy toxicity, higher rates of complications, prolonged hospital stays, reduced quality of life, and elevated mortality risk (6, 9).

The diagnosis of sarcopenia is challenging due to variability in measurement techniques and diagnostic thresholds. Commonly used methods include computed tomography (CT), magnetic resonance imaging (MRI), dual-energy X-ray absorptiometry (DXA), ultrasound, and bioelectrical impedance analysis (BIA) (6). While CT and MRI are considered the gold standards for assessing muscle mass, their high costs, limited accessibility, and need for specialized personnel restrict their routine use (10). DXA provides inconsistent results across different instrument brands, and ultrasound lacks standardized cutoff values (11, 12). BIA, although affordable, is affected by factors such as body composition and fluid retention.

Given these limitations, screening tools like the SARC-F (strength, assistance with walking, rise from a chair, climb stairs and falls), SARC-CalF (SARC-F combined with calf circumference), EBM (elderly and body mass index information), Mini sarcopenia risk assessment-5 (MSRA-5), and Mini sarcopenia risk assessment-7 (MSRA-7) have gained attention as alternatives for early detection of sarcopenia (7). The 2018 European Working Group on Sarcopenia in Older People (EWGSOP) and the 2019 Asian Working Group for Sarcopenia (AWGS) recommend using screening tools to identify individuals at risk of sarcopenia to facilitate timely intervention (6, 13). However, these tools have primarily been validated in older adults and patients with other chronic conditions (1). Research on sarcopenia screening in cancer patients, especially those with bone tumors, remains limited, necessitating further investigation into the efficacy and applicability of these tools in this study population. Therefore, this study aims to compare the screening efficacy of five different tools for sarcopenia, and to identify the most appropriate screening tool for patients with bone tumors.

2 Materials and methods

This cross-sectional study was conducted at a provincial cancer hospital between August 2023 and November 2023. It is part of a broader investigation into the development and application of a risk prediction model for sarcopenia in patients with bone tumors. The study obtained the ethical approval from the studied hospital's ethics committee (SLKYLX2023-171). All participants provided written informed consent and voluntarily took part in the study.

2.1 Study participants

All study participants were recruited using convenience sampling. The inclusion criteria were: (1) a diagnosis of primary or metastatic bone tumors; (2) a disease duration of at least 3 months; and (3) age 18 years or older. The exclusion criteria included: (1) presence of lower limb edema; (2) mental disorders; (3) severe hearing, vision, or speech impairments; (4) inability to stand; (5) presence of metallic implants; (6) limb amputations; (7) limbs wrapped in bandages or casts; and (8) use of medications that could affect body composition measurements.

2.2 AWGS 2019 sarcopenia diagnosis

According to the 2019 AWGS criteria (7), sarcopenia is diagnosed based on three key components: (1) Muscle Strength: Defined as reduced grip strength, with thresholds of < 28 kg for men and < 18 kg for women; (2) Muscle Mass: Assessed using bioelectrical impedance analysis (BIA), with an icular skeletal muscle mass index of < 7.0 kg/m^2 for men and < 5.7 kg/m^2 for women; (3) Physical Performance: Evaluated by gait speed, where a speed of < 1 m/s over a 6-m walk indicates impaired performance.

2.3 Data collection tools

2.3.1 General information sheet

This information sheet was developed based on a comprehensive literature review to collect demographic and clinical information. This included details such as age, gender, education level, marital status, icular skeletal muscle mass index, body mass index, calf circumference, grip strength, and gait speed.

2.3.2 SARC-F questionnaire

The SARC-F, developed by Malmstrom and Morley (14), assesses five domains: strength, assistance in walking, rising from a chair, climbing stairs, and fall history. Each item is scored from 0 to 2, with the total score ranging from 0 to 10. A score of ≥ 4 suggests a high risk of sarcopenia. The scale was translated into Chinese: its reliability (Cronbach's alpha = 0.849), and the criterion-related validity ($r = 0.878$) (15).

2.3.3 SARC-Calf questionnaire

The SARC-Calf integrates the SARC-F with calf circumference measurements developed by Barbosa-Silva et al. (16). For males

with a calf circumference ≤ 34 cm or females with ≤ 33 cm, 10 points are added to the SARC-F score. The total possible score ranges from 0 to 20, with a score of ≥ 11 indicating a high risk of sarcopenia.

2.3.4 SARC-F + EBM questionnaire

The SARC-F + EBM, developed by Kurita et al. (17), combines the SARC-F with an expanded body mass index (EBM) assessment, incorporating calf circumference measurements. A total score of ≥ 11 points denote a high risk of sarcopenia.

2.3.5 MSRA-5 and MSRA-7 questionnaires

The Mini Sarcopenia Risk Assessment (MSRA) was developed by Rossi et al. (18), and later translated into Chinese by Yang et al. (19). The MSRA-5 consists of five items: age, history of hospital stays, physical activity level, daily meals, and weight loss, with a total score of ≤ 45 indicating sarcopenia risk. The MSRA-7 expands on this by including dairy and protein consumption, and a score of ≤ 30 suggests a sarcopenia risk.

2.4 Data collection

One nurse researcher (the first author) collected the data. Within 24 h of admission, eligible patients were informed about the study, and written consent was obtained. They were then asked to complete the five questionnaires, with assistance provided if needed. Calf circumference was measured three times while patients were seated with their dominant leg exposed, and the average of the three measurements was recorded. Before treatment, assessments of grip strength, walking speed, and icular skeletal muscle mass index were conducted. Grip strength was measured using an electronic grip strength meter (Xiangshan EH-101) with the dominant hand, or with the unaffected hand for patients with arm tumors, and the highest value from three attempts was recorded. Walking speed was measured twice over a 6-m distance, and the average speed was calculated. The icular skeletal muscle mass was assessed using an InBody 770 body composition analyzer.

2.5 Statistical analysis

Data were analyzed using SPSS version 25.0. Continuous variables were presented as means with standard deviations, while categorical variables were reported as frequencies and percentages. Receiver operating characteristic (ROC) curves were generated based on the 2019 sarcopenia diagnostic criteria, and the area under the ROC curve (AUC) along with 95% confidence intervals (CI) were calculated. For each screening tool, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), kappa value, and their respective 95% CIs were compared. The DeLong test was employed to evaluate differences between the AUCs of the screening tools. Youden's index was calculated to identify optimal cutoff points. A $p < 0.05$ was considered statistically significant.

3 Results

3.1 Characteristics of study participants

This study included 300 bone tumor patients, aged 19–81 years, with a median age of 58 years (mean = 55.18, SD, 14.28 years). Based on the AWGS 2019 sarcopenia diagnostic criteria, the prevalence of sarcopenia among bone tumor patients was 26%. The difference of characteristics of patients with sarcopenia and without sarcopenia was presented in Table 1.

3.2 Accuracy analysis of five sarcopenia screening tools

Using the AWGS 2019 diagnostic criteria as a reference, we assessed the sensitivity, specificity, positive predictive value, negative predictive value, and AUC for five sarcopenia screening tools. The results are summarized in Table 2.

3.3 Optimal cutoff values for the five sarcopenia screening tools

Among the five screening tools, the SARC-F + EBM questionnaire showed the highest AUC (0.88) with an optimal cutoff point of 10.5. The ROC curve is shown in Figure 1. At this cutoff, the sensitivity and specificity were 61.5 and 93.7%, respectively (Supplementary Table 1).

3.4 AUC Comparison between the five screening tools

The AUC comparison revealed that the SARC-F + EBM questionnaire had a significantly higher AUC of 0.88 than the SARC-F, MSRA-7, and MSRA-5 questionnaires. Similarly, the SARC-Calf questionnaire had a higher AUC of 0.85 than the SARC-F, MSRA-7, and MSRA-5 questionnaires. There were no significant differences in AUC between the other tools (Table 3).

3.5 Comparison of sarcopenia screening results of the five tools with AWGS 2019 sarcopenia diagnostic criteria

Based on the screening results of the five tools, patients were classified into sarcopenia and non-sarcopenia groups. A comparison with the AWGS 2019 diagnostic criteria showed that the Kappa values for the SARC-F, SARC-Calf, SARC-F + EBM, MSRA-7, and MSRA-5 questionnaires were 0.307, 0.556, 0.468, 0.321, and 0.288, respectively (all $P < 0.001$), indicating moderate agreement (Table 4).

TABLE 1 General characteristics of Chinese bone tumor patients (N = 300).

Variable		Non-sarcopenic(n = 222)	Sarcopenic (n = 78)	U/t/χ^2	p-value
Gender	Men	112	42	0.266	0.606
	Women	110	36		
Age (years)		56.47 ± 12.27	63.86 ± 10.60	3.53	0.001
GSa (kg)	Men	30.38 ± 6.51	23.37 ± 6.06	6.06	<0.001
	Women	19.94 ± 4.04	15.06 ± 5.15	5.19	<0.001
GSb (m/s)		1.08 ± 0.09	0.94 ± 0.14	8.71	<0.001
ASMI (kg/m^2)	Men	8.00 ± 0.64	6.65 ± 0.48	15.45	<0.001
	Women	6.54 ± 0.58	5.41 ± 0.30	15.13	<0.001
CC (cm)	Men	33.45 ± 2.94	30.19 ± 2.67	6.54	<0.001
	Women	32.91 ± 2.52	28.90 ± 3.16	6.92	<0.001
BMI (kg/m^2)		23.54 ± 3.13	19.80 ± 2.21	11.46	<0.001
Educational level	Primary school and below	96	49	9.25	0.026
	High school	63	13		
	College	37	8		
	University and above	24	8		
Marital status	Single	17	9	3.22	0.35
	Married	197	67		
	Divorce	5	0		
	Widower	3	2		

ASMI, icular Skeletal Muscle Mass Index; BMI, Body Mass Index; CC, Calf circumference; GSa, Grip strength; GSb, Gait speed.

TABLE 2 Accuracy analysis of five screening tools for sarcopenia based on AWGS 2019 (N = 300).

Screening tools	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	AUC (95%CI)
SARC-F	32.05	93.69	64.10	79.69	0.79 (0.73–0.85)
SARC-Calf	80.77	81.08	60.00	92.31	0.85 (0.81–0.90)
SARC-F + EBM	44.87	95.50	77.78	83.14	0.88 (0.84–0.92)
MSRA-7	74.36	65.32	42.03	87.88	0.77 (0.71–0.83)
MSRA-5	74.36	62.16	40.28	87.34	0.78 (0.72–0.84)

SARC-F, strength, assistance with walking: rise from a chair, climb stairs and falls; SARC-Calf, SARC-F combined with calf circumference; EBM, elderly and body mass index information; MSRA-5, mini sarcopenia risk assessment-5; MSRA-7, mini sarcopenia risk assessment-7.

3.6 Combined use of SARC-F and MSRA screening tools

When the SARC-F and SARC-Calf tools were used together, the AUC under the ROC curve was 0.86. Combining SARC-F with SARC-F + EBM resulted in an AUC of 0.88. Using all three tools (SARC-F, SARC-Calf, and SARC-F + EBM) together further increased the AUC to 0.89. In contrast, when MSRA-7 and MSRA-5 were combined, the AUC was 0.78. The corresponding ROC curves are shown in Figure 2, and results are summarized in Table 5.

4 Discussion

This study, using the AWGS 2019 sarcopenia screening criteria (20), found that the prevalence of sarcopenia in bone tumor patients was 26%, higher than previous similar studies with a prevalence of 22% (21–23). This may be due to bone tumors compressing spinal cord nerves, leading to paralysis and reduced physical activity (24). Additionally, bone tumor patients are less likely to experience early-stage digestive dysfunction compared to patients with gastrointestinal cancers, where insufficient nutritional intake increases the risk of sarcopenia (4, 25). Although the findings differ across studies, they highlight that sarcopenia in bone tumor patients is a significant concern (21, 22).

Most research on sarcopenia focuses on older adults, but bone tumor patients include younger individuals. The lack of awareness about sarcopenia, coupled with its complex screening process and the high costs of assessment, makes it challenging to screen these patients effectively (13). Therefore, healthcare professionals should emphasize early screening and prevention of sarcopenia in bone tumor patients to delay its onset and mitigate complications. Given the unique risks in bone tumor patients, Distinguishing sarcopenia from cachexia is essential, as they are distinct but can coexist,

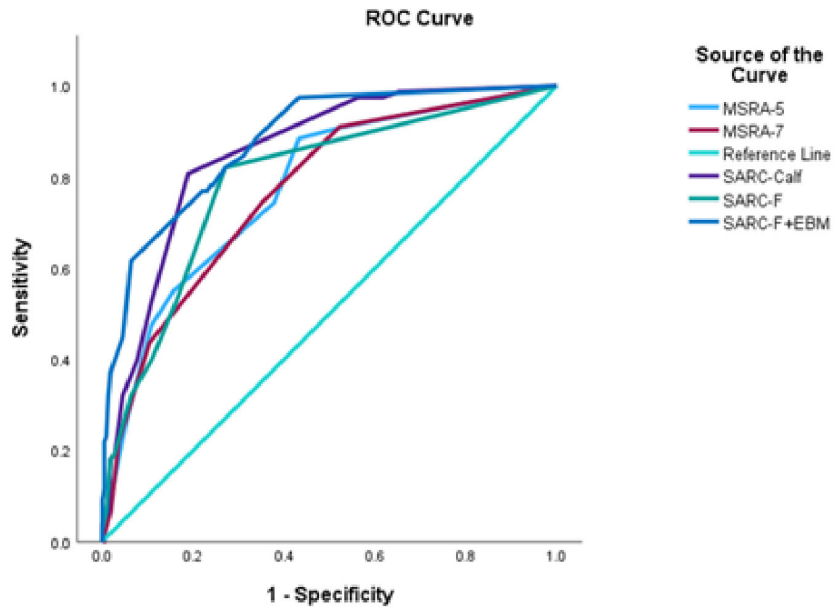

FIGURE 1
Comparisons of five screening tools for sarcopenia based on AWGS 2019. SARC-F, strength, assistance with walking, rise from a chair, climb stairs and falls; SARC-Calf, SARC-F combined with calf circumference; EBM, elderly and body mass index information; MSRA-5, mini sarcopenia risk assessment-5; MSRA-7, mini sarcopenia risk assessment-7.

TABLE 3 The results of pairwise comparison of the area under the ROC curve of 5 screening tools (N = 300).

Screening tools	Z-value	p-value
SARC-F—SARC-Calf	−3.84	0.001
SARC-F—SARC-F + EBM	−3.13	0.002
SARC-F—MSRA-7	1.41	0.159
SARC-F—MSRA-5	0.43	0.651
SARC-Calf—SARC-F + EBM	−1.60	0.228
SARC-Calf—MSRA-7	3.49	< 0.001
SARC-Calf—MSRA-5	2.52	0.012
SARC-F + EBM—MSRA-7	4.51	< 0.001
SARC-F + EBM—MSRA-5	3.39	0.001
MSRA-7—MSRA-5	−2.10	0.035

ARC-F, strength, assistance with walking; rise from a chair, climb stairs and falls. SARC-Calf, SARC-F combined with calf circumference; EBM; elderly and body mass index information; MSRA-5, mini sarcopenia risk assessment-5; MSRA-7, mini sarcopenia risk assessment-7.

TABLE 4 Comparison of screening results of 5 sarcopenia screening tools with AWGS 2019 diagnostic criteria for sarcopenia (N = 300).

Screening tools		AWGS 2019 diagnostic criteria for sarcopenia (n)		Total (n)	Kappa value	p-value
		Yes	No			
SARC-F	(+)	25	14	39	0.31	< 0.001
	(−)	53	208	261		
	Total	78	222	300		
SARC-Calf	(+)	63	42	105	0.56	< 0.001
	(−)	15	180	195		
	Total	78	222	300		
SARC-F + EBM	(+)	35	10	45	0.47	< 0.001
	(−)	43	212	255		
	Total	78	222	300		
MSRA-7	(+)	58	77	138	0.32	< 0.001
	(−)	20	145	165		
	Total	78	222	300		
MSRA-5	(+)	58	84	144	0.29	< 0.001
	(−)	20	138	158		
	Total	78	222	300		

SARC-F, strength, assistance with walking, rise from a chair, climb stairs and falls; SARC-Calf, SARC-F combined with calf circumference; EBM, elderly and body mass index information; MSRA-5, mini sarcopenia risk assessment-5; MSRA-7, mini sarcopenia risk assessment-7.

particularly in cancer settings (26, 27). Future research should address this overlap to refine screening and intervention strategies for all age groups affected by bone tumors.

In this study, the SARC-F questionnaire had high specificity but low sensitivity, consistent with previous research, indicating its limited ability to detect sarcopenia, leading to a high misdiagnosis rate. This is because SARC-F mainly reflects muscle strength and physical performance but does not assess muscle mass, a key diagnostic criterion for sarcopenia (28). The ROC analysis revealed an optimal cutoff value of 0.5, which aligns with Ma et al.'s findings (29), but differs from other studies (30, 31) due to regional and population differences. Adjusting the cutoff improved the sensitivity and balanced specificity, enhancing the screening performance of SARC-F for bone tumor patients. This suggests that clinicians need to determine optimal cutoff values

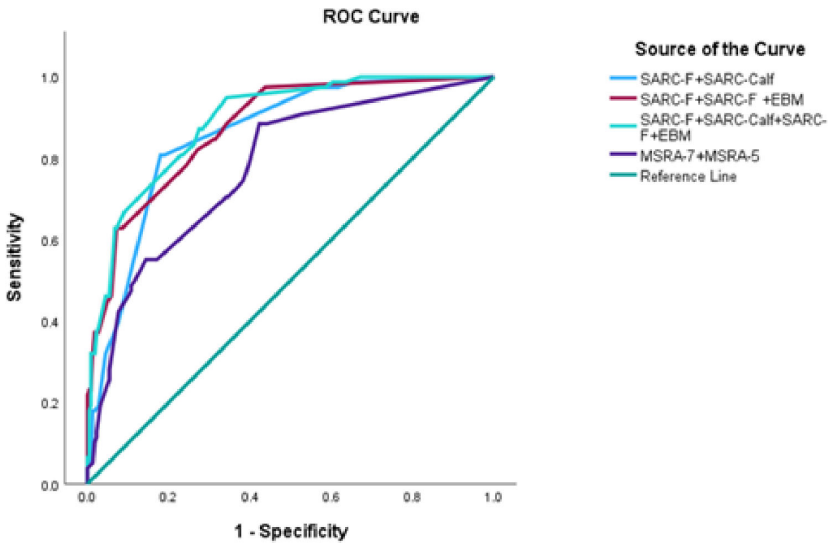

FIGURE 2
Comparisons of combined use of screening tools for sarcopenia based on AWGS 2019. SARC-F, strength, assistance with walking, rise from a chair, climb stairs and falls; SARC-Calf, SARC-F combined with calf circumference; EBM, elderly and body mass index information; MSRA-5, mini sarcopenia risk assessment-5; MSRA-7, mini sarcopenia risk assessment-7.

TABLE 5 Comparison results of combined use of SARC-F related scales and MSRA related scales (*N* = 300).

Screening tools	Youden index	Sensitivity (%)	Specificity (%)	AUC
SARC-F + SARC-Calf	0.63	80.8	82.0	0.86 (0.81–0.90)
SARC-F + SARC-F + EBM	0.56	62.8	92.8	0.88 (0.83–0.92)
SARC-F + SARC-Calf + SARC-F + EBM	0.61	94.9	94.1	0.89 (0.85–0.93)
MSRA-7 + MSRA-5	0.45	88.5	89.2	0.78 (0.72–0.84)

SARC-F, strength, assistance with walking, rise from a chair, climb stairs and falls; SARC-Calf, SARC-F combined with calf circumference; EBM, elderly and body mass index information; MSRA-5, mini sarcopenia risk assessment-5; MSRA-7, mini sarcopenia risk assessment-7.

tailored to specific populations to maximize the effectiveness of screening tools.

The SARC-Calf questionnaire, which incorporates calf circumference, showed higher sensitivity and specificity compared to SARC-F, offering better diagnostic value (Kappa value of 0.556). However, it still demonstrated low PPV and high NPV, consistent with previous research (32). Calf circumference is a reliable marker of skeletal muscle mass (33) and has been validated in diagnosing sarcopenia among older adults (7), patients with chronic liver diseases (34), and stroke survivors (35). However, the optimal cutoff value varies by study and population. For example, studies in Turkey and Taiwan found cutoffs of 33 cm for men and 32–33 cm for women (7, 36), while Japanese researchers recommend 34 cm for men and 33 cm for women (37). These variations may stem from differences in ethnicity, culture, and lifestyle (38). The AWGS2019-recommended cutoffs used in this study were appropriate for this population.

The SARC-F + EBM questionnaire, which adds age and BMI to the SARC-F tool, had higher sensitivity, specificity, and overall diagnostic performance than SARC-F alone, consistent with previous research (17). This is particularly meaningful for elderly patients with bone tumors, who are at greater risk of muscle loss due to reduced mobility and long-term bed rest. Moreover, studies have shown that low BMI ($\leq$ 21 kg/m^2) is associated with undernutrition, which increases the risk of sarcopenia (39, 40). Bone tumor patients often experience malnutrition due to chemotherapy-related gastrointestinal side effects and cachexia, further increasing sarcopenia risk. With an AUC of 0.88, the SARC-F + EBM tool demonstrated strong screening performance.

The MSRA-7 questionnaire showed high sensitivity but lower specificity and a lower PPV. Among the five screening tools, it had the smallest AUC (0.77). One possible explanation is that patients undergoing chemotherapy may have been hospitalized frequently during the past year, affecting their scores, even though their condition may have improved post-chemotherapy. Furthermore, the inclusion of daily dairy consumption as a factor may not align with typical Chinese dietary habits, impacting the tool's performance. After removing dairy and protein consumption items, the MSRA-5 questionnaire performed better in terms of sensitivity and specificity, though its agreement with diagnostic outcomes was still suboptimal. Future research should aim to revise the MSRA tool for better applicability in bone tumor patients in China.

When SARC-F-related scales and MSRA-related scales were used in combination, the diagnostic performance improved. Specifically, the combined use of SARC-F, SARC-Calf, and SARC-F + EBM yielded the best diagnostic results, offering a comprehensive evaluation of muscle strength, physical

performance, muscle mass, age, and nutrition. This combination provides a more practical and efficient method for early screening of sarcopenia in bone tumor patients.

Bone tumors and sarcopenia are interrelated. The disease itself, alongside treatments and psychological stressors, increases the prevalence of sarcopenia in bone tumor patients. Nurses play a crucial role in early detection, assessment, and intervention, making it essential to incorporate validated and practical sarcopenia screening tools into routine nursing assessments. By identifying patients at risk of sarcopenia early, nurses can implement tailored interventions that focus on maintaining or improving muscle strength, nutritional status, and overall physical function. This proactive approach can enhance postoperative recovery, reduce the severity of chemotherapy side effects, shorten hospital stays, and lower healthcare costs among bone tumor patients.

Additionally, the study highlights the importance of individualized patient education. Nurses can educate bone tumor patients and their families about the risks of sarcopenia, the importance of maintaining muscle mass through proper nutrition and physical activity, and how to recognize early signs of sarcopenia. These efforts can empower patients to take an active role in their care, potentially improving outcomes and quality of life in bone tumor patients. The study underscores the need for further research to validate and refine sarcopenia screening tools specifically for bone tumor patients, considering the unique characteristics of this population.

4.1 Study limitations

This study compared the effectiveness of five sarcopenia screening tools in bone tumor patients, identifying the best tools for early detection and providing a basis for prevention and further research. Although these tools were primarily developed for elderly populations, the inclusion of younger patients ($\geq$ 18 years old) highlighted that sarcopenia can also affect non-elderly individuals. This emphasizes the need for healthcare professionals to pay greater attention to sarcopenia in bone tumor patients. However, the study has several limitations. First, the sample was small and drawn from a single hospital. Future studies should expand the sample size and include multicenter surveys of different types and stages of bone tumors to enhance the predictive power of these tools. Second, the study did not conduct longitudinal follow-up or evaluate the predictive value of the tools for adverse outcomes. Third, while BIA was used for muscle measurement, more accurate methods, such as CT, MRI, or dual-energy X-ray, could provide more precise assessments. Furthermore, the study focused on a specific cancer type and a particular ethnic group, which may limit the applicability of the findings to other cancer types or ethnicities. Finally, this study is the use of single-center, convenience-based sampling and the cross-sectional nature of the study, which may limit the generalizability of the findings.

4.2 Study implications

This study identified the SARC-F + EBM questionnaire and the combined use of SARC-F, SARC-Calf, and SARC-F + EBM as the top-performing tools for sarcopenia screening in bone tumor patients. The SARC-F + EBM demonstrated exceptional diagnostic performance, with high sensitivity, specificity, and an AUC of 0.88, making it highly effective for early detection. The combined approach further improved accuracy by comprehensively assessing muscle strength, physical performance, muscle mass, age, and nutritional status. For practical implementation, healthcare professionals should prioritize early screening using these validated tools in clinical settings, particularly for bone tumor patients at risk due to reduced mobility or malnutrition. Nurses should be trained to incorporate these tools into routine assessments to facilitate timely intervention. Additionally, individualized patient education on maintaining muscle mass through nutrition and physical activity is essential to improve outcomes. Further research is recommended to refine these tools for bone tumor patients and adapt them to diverse populations.

5 Conclusion

The study concludes that among these five screening tools for sarcopenia in bone tumor patients, the SARC-F + EBM and SARC-Calf methods exhibit higher accuracy than the SARC-F, MSRA-7, and MSRA-5 tools, for identifying sarcopenia in patients with bone tumors. These two tools are recommended as the most effective for clinical healthcare professionals in screening for sarcopenia. Furthermore, the combined use of SARC-F, SARC-Calf, and SARC-F + EBM yields even greater screening efficacy.

Data availability statement

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

Ethics statement

This study involving human subjects was approved by the Ethics Committee of Yunnan Cancer Hospital (SLKYLX2023-171). The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent for participation in this study was provided by the participants' legal guardians/next of kin.

Author contributions

JY: Conceptualization, Data curation, Formal Analysis, Methodology, Software, Writing – original draft. QG: Conceptualization, Investigation, Software, Supervision, Validation, Visualization, Writing – original draft. YC: Data curation, Formal Analysis, Methodology, Project administration, Software, Writing – original draft. LZ: Resources, Supervision, Validation, Visualization, Writing – original draft. JC: Conceptualization, Investigation, Supervision, Validation, Visualization, Writing – review & editing. YZ: Conceptualization, Writing – original draft, 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.

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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.2025.1584706/full#supplementary-material

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The mediating role of Body Roundness Index in the association between Life's Crucial 9 and infertility: a cross-sectional study using NHANES 2013–2018

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Background: Recent findings indicate a possible connection among heart health, obesity, and infertility. Yet, the processes through which obesity affects the link between heart health and infertility are still not well-understood. The newly created Life's Crucial 9 (LC9) serves as a measure for evaluating heart health, and the Body Roundness Index (BRI) offers a more accurate and innovative approach to measuring central obesity. The objective of this research is to explore the link between LC9 and infertility and determine if BRI serves as an intermediary in this connection.

Methods: The data for this cross-sectional analysis was sourced from the 2013 to 2018 National Health and Nutrition Examination Survey (NHANES). Following the application of exclusion criteria, 2,319 women aged between 18 and 45 years were incorporated. To investigate the link between LC9, BRI, and infertility, methods like weighted multivariable logistic regression models, restricted cubic spline (RCS) analysis, and subgroup analyses were utilized. Furthermore, an analysis of mediation was performed to determine if BRI played a mediating role in the link between LC9 and infertility.

Results: Within the demographic of the study, infertility occurred in 13% of cases. Post-adjustment for every covariate, a rise of 10 units in LC9 correlated with a 29% decrease in infertility rates (OR = 0.71, 95% CI: 0.61–0.84, $P < 0.001$). In contrast, a one-unit rise in BRI correlated with a 14% increase in infertility rates (OR = 1.14, 95% CI: 1.07–1.23, $P < 0.001$). Analysis using the RCS method revealed a direct negative relationship between LC9 and infertility, and a positive correlation between BRI and infertility. Mediation analysis showed that BRI mediated 16.26% of LC9's overall impact on infertility ($P < 0.001$), suggesting a substantial influence of central obesity in this correlation.

Conclusion: There is a significant negative correlation between LC9 and infertility, with BRI playing a partial mediating role. These findings highlight the importance of cardiovascular health and obesity management in reproductive health and suggest that reducing central obesity may lower the risk of infertility.

Further research is needed on potential intervention strategies targeting metabolic and cardiovascular health to prevent infertility.

KEYWORDS

Life's Crucial 9, Body Roundness Index, infertility, NHANES, mediation analysis

Introduction

Infertility is a significant public health concern, affecting an estimated 10%–15% of couples worldwide (1, 2). The condition is characterized by the inability to conceive after 12 months of regular, unprotected intercourse, imposing substantial psychological, social, and economic burdens on affected individuals and society (3). The prevalence of infertility has been rising, potentially due to a combination of environmental, lifestyle, and metabolic factors (4). Despite advancements in assisted reproductive technologies, infertility remains a challenging condition with limited treatment success rates (5, 6). Identifying modifiable risk factors that contribute to infertility is crucial for developing preventive strategies, ultimately reducing its burden and improving reproductive health outcomes.

Previous studies have suggested a complex interplay between infertility and cardiovascular health (7, 8). Emerging evidence indicates that individuals with infertility, particularly women, may have an increased risk of developing cardiovascular diseases later in life (9). This connection underscores the importance of evaluating lifestyle and cardiometabolic factors in the context of infertility. Life's Crucial 9 (LC9), a composite measure of cardiovascular and metabolic health developed by the American Heart Association, encompasses key lifestyle and biological factors such as diet, physical activity, blood glucose, and body mass index (10). Given the shared metabolic pathways between cardiovascular disease and reproductive dysfunction, exploring the relationship between LC9 and infertility could provide novel insights into potential prevention strategies. However, the extent to which LC9 is associated with infertility remains underexplored, necessitating further investigation.

Obesity has long been recognized as a key contributor to both cardiovascular conditions and reproductive dysfunction, primarily through its effects on endocrine balance, chronic inflammation, and metabolic disturbances (11, 12). Conventional measures like body mass index (BMI), though widely used, fall short in capturing fat distribution patterns and do not fully reflect the associated metabolic risks (13). The Body Roundness Index (BRI), a novel obesity metric, incorporates both waist circumference and height to better capture central adiposity and its associated health risks (14, 15). Given that obesity plays a critical role in both cardiovascular health and infertility, examining whether BRI mediates the relationship between LC9 and infertility could provide mechanistic insights into obesity's contribution to reproductive dysfunction. The National Health and Nutrition Examination Survey (NHANES) 2013–2018 cycles offer a unique opportunity to investigate this relationship in a large, nationally representative sample. NHANES provides comprehensive health and lifestyle data, allowing for robust statistical analyses to elucidate the mediating role of BRI in the LC9-infertility association. Understanding these interrelationships may inform targeted interventions to improve reproductive and cardiometabolic health outcomes.

Materials and methods

Study participants

We conducted a cross-sectional study utilizing data collected from the 2013 to 2018 cycles of the National Health and Nutrition Examination Survey (NHANES). This nationwide program, administered by the National Center for Health Statistics (NCHS), is designed to evaluate the health and dietary patterns of the United States population using a stratified, multistage sampling approach to achieve demographic representativeness. Ethical oversight was provided by the NCHS Institutional Review Board, and informed consent was obtained from all participants prior to data collection. Since this study was a secondary data analysis based on a public database and did not involve personal privacy information, no additional ethical review approval was required in accordance with the STROBE guidelines for cross-sectional studies.

We initially screened 29,400 participants from the 2013 to 2018 NHANES dataset. Individuals who did not meet the age range (18–45 years) or were male were subsequently excluded (n = 25,077). Of the remaining 4,323 women, participants with incomplete LC9 information (n = 1,973) and individuals with infertility or missing BRI data (n = 31) were further excluded. Finally, a total of 2,319 eligible participants were included in the analysis of this study (see Supplementary Figure 1 for details).

Definition of Life's Crucial 9

Life's Crucial 9 serves as an integrative metric designed to evaluate overall cardiometabolic wellbeing, encompassing nine core elements. These include four lifestyle-related behaviors—dietary habits, physical exercise, tobacco exposure, and sleep patterns—and five physiological indicators: body weight, arterial pressure, glucose regulation, lipid levels, and psychological status. Each dimension is quantified based on standardized procedures outlined in the NHANES framework, with scoring criteria aligned with contemporary cardiovascular health recommendations.

For each participant, the LC9 total score is obtained by averaging the scores of these nine components, and the

score range of each indicator is 0–100. Among them, dietary quality is assessed based on the Healthy Eating Index-2015 (HEI-2015), and the detailed scoring method is listed in Supplementary Table 2. Information on physical activity, tobacco use, and sleep quality is collected via standardized self-report questionnaires. In contrast, indicators such as BMI, blood pressure, glucose levels, and serum lipids are measured directly by qualified healthcare professionals using clinical and laboratory-based procedures.

Mental health status was assessed using the Patient Health Questionnaire-9 (PHQ-9), which reflects the severity of depressive symptoms through different score intervals. The specific scoring criteria and quantification methods for each LC9 component are detailed in Supplementary Table 1.

Definition of BRI and infertility

The BRI is a new anthropometric index that aims to more accurately reflect the distribution of body fat, especially central obesity, compared with the traditional BMI. BRI combines waist circumference and height as two key parameters to more effectively assess the degree of abdominal obesity and the health risks it brings, such as cardiovascular disease and metabolic disorders. The calculation of BRI is based on a standardized formula that can provide a quantitative estimate of individual fat distribution.

Regarding the identification of infertility, this study determined the infertility status of participants based on two key questions in the NHANES Reproductive Health Questionnaire. The two questions are:

> RHQ074: "Have you tried to get pregnant for more than 1 year but failed?"

> RHQ076: "Have you ever visited a doctor or other medical institution because of difficulty in getting pregnant?"

If the participant answered "yes" to any of the above questions, they were classified as "having a history of infertility" and included in the infertility group; if they answered "no" to both questions, they were considered to have no infertility experience and were classified as the non-infertility group.

Covariates

This study accounted for a range of covariates, encompassing sociodemographic variables—such as age, ethnicity, marital condition, educational attainment, and the poverty-to-income ratio (PIR)—as well as key clinical indicators, including the presence of hypertension, diabetes mellitus, and elevated blood lipid levels. Age was divided into three groups: 18–25, 26–34, and 35–45 years. Participants were categorized by race into groups such as Mexican American, Black (non-Hispanic), White (non-Hispanic), and a collective group of other ethnicities. Marital classification distinguished individuals as either "married" or "unmarried," based on whether they were in a legal or cohabiting partnership. The PIR index was used to assess socioeconomic status, where PIR < 1.3 indicated poverty.

The definition of clinical covariates followed the NHANES criteria. Diabetes was determined based on self-reported history of diabetes, glycated hemoglobin (HbA1c) level $\geq$ 6.5%, or fasting blood glucose $\geq$ 126 mg/dL. Hypertension was defined as a self-reported history of hypertension, taking antihypertensive medication, systolic blood pressure (SBP) $\geq$ 140 mmHg, or diastolic blood pressure (DBP) $\geq$ 90 mmHg. The diagnostic criteria for hyperlipidemia included triglycerides (TG) $\geq$ 150 mg/dL, total cholesterol (TC) $\geq$ 200 mg/dL, low-density lipoprotein (LDL) $\geq$ 130 mg/dL, or high-density lipoprotein (HDL) $<$ 40 mg/dL (male) or $<$ 50 mg/dL (female); in addition, individuals taking lipid-lowering drugs were also considered to have hyperlipidemia. The specific definitions and classifications of all covariates are detailed in Supplementary Table 3.

Statistical analysis

All statistical computations were performed with R (v4.3.1), applying the designated NHANES weighting scheme to derive population-representative outcomes. The weighting variable "WTMEC2YR" was used, and for the 2013–2018 NHANES cycles, a new weight was calculated as 1/3 $\times$ WTMEC2YR to account for the combined survey periods. Continuous variables were presented as mean $\pm$ standard deviation (SD), with weighted *t*-tests used to compare differences between groups. Categorical variables were expressed as weighted percentages (*N*, %), and group differences were assessed using weighted chi-square tests. To explore the links among LC9, BRI, and infertility, we utilized multivariate logistic regression with a three-tier modeling approach:

1. Model 1: Baseline analysis without covariate adjustment.
2. Model 2: Controlled for age, marital status, educational background, income level (PIR), and ethnicity.
3. Model 3: Further adjusted for clinical comorbidities including hypertension, diabetes, and dyslipidemia.

To capture potential non-linear associations, a restricted cubic spline (RCS) approach was employed. Stratified analyses were also carried out to detect heterogeneity across subpopulations defined by demographic and clinical parameters. Furthermore, mediation analysis was conducted to assess the extent to which the effect of LC9 on infertility was mediated by BRI. We used a non-parametric bootstrap resampling procedure with 5,000 iterations to estimate the indirect, direct, and total effects (16). The indirect effect was defined as the product of the regression coefficient from LC9 to BRI (Path A) and from BRI to infertility (Path B), while the direct effect (Path C') represented the association between LC9 and infertility after adjusting for BRI. The total effect (Path C) was calculated as the sum of direct and indirect effects. The proportion of mediation was computed as: (indirect effect/total effect) $\times$ 100. All mediation models were implemented using the R package "mediation," and statistical significance was determined based on bootstrap-derived confidence intervals and two-tailed *P*-values < 0.05.

Results

Baseline characteristics

This study ultimately enrolled 2,319 individuals who met the inclusion criteria, representing approximately 26.15 million United States adults. The overall prevalence of infertility is 13%, equivalent to approximately 3.27 million people affected. Compared with individuals without infertility, infertile patients had significant differences in multiple aspects, including age, marital status, the prevalence of hypertension, diabetes, hyperlipidemia, LC9 scores, and BRI levels (all $P < 0.05$).

Specifically, the average age of participants in the infertile group was older, the prevalence of cardiovascular and metabolic diseases (such as hypertension, diabetes, and hyperlipidemia) was higher, and the LC9 score was significantly lower, indicating that their overall health behaviors and physiological status were poor. In addition, the BRI level was significantly increased in the infertile group, and the proportion of individuals with high BRI (the highest tertile group) was also higher, reflecting the higher concentration of central obesity in the infertile population. These results suggest that cardiovascular and metabolic health status may play an vital role in the occurrence of infertility. Detailed data on relevant baseline characteristics are shown in Table 1.

Association between LC9, BRI, and infertility

As illustrated in Table 2, a trio of logistic regression models was applied to examine the link between LC9, BRI, and infertility. Across all models, LC9 consistently showed a statistically significant inverse association with infertility risk ($P < 0.001$). Specifically, in Model 3—which controlled for variables including age, educational background, marital status, poverty-income ratio (PIR), ethnicity, hypertension, diabetes, and hyperlipidemia—each 10-point increment in LC9 corresponded to a 29% decrease in infertility prevalence [odds ratio (OR): 0.71, 95% confidence interval (CI): 0.61–0.84].

When stratified by tertiles, individuals falling into the highest LC9 group (T3) demonstrated a 61% lower infertility rate compared to those in the lowest category (T1) [OR: 0.39, 95% CI: 0.22–0.69, $P = 0.002$].

Similarly, BRI was positively associated with infertility in all models ($P < 0.001$). In Model 3, each unit increase in BRI was associated with a 14% higher infertility prevalence [OR: 1.14, 95% CI: 1.07–1.23]. When analyzed by tertiles, participants in the highest BRI tertile (T3) had a 2.64-fold higher prevalence of infertility compared to those in the lowest tertile (T1) [OR: 2.64, 95% CI: 1.49–4.69, $P = 0.002$], demonstrating a significant trend.

Findings from the RCS analysis (Figure 1) demonstrated a clear dose-response association involving LC9, BRI, and infertility. A negative linear trend was detected between LC9 scores and infertility rates, whereas BRI showed a positive correlation with infertility prevalence. Stratified analyses based on variables such as age, ethnicity, marital status, educational attainment, PIR, and cardiometabolic status (Figure 2) validated these trends across the majority of subgroups. Notably, a significant interaction effect emerged between LC9 and age ($P < 0.05$), indicating that the influence of cardiometabolic health on infertility outcomes may differ depending on age group. No meaningful interactions were identified for other factors, including educational level and PIR.

Mediation effect

The mediation model is illustrated in Figure 3, with LC9 as the independent variable, infertility as the dependent variable, and BRI as the mediator. As shown in Supplementary Table 4, a significant association was observed between LC9 and BRI after adjusting for all covariates ($\beta = -1.00$, 95% CI: −1.10, −0.93, $P < 0.001$), indicating that lower LC9 scores were associated with higher BRI levels.

The mediation analysis further confirmed the indirect effect of BRI in the association between LC9 and infertility. As shown in the Figure 3, the total effect of LC9 on infertility was significant (-8.24×10^{-2}, $P < 0.001$). Following the adjustment for all covariates, the direct effect of LC9 on infertility remained statistically significant ($\beta = -6.90 \times 10^{-2}$, $P < 0.001$), while the indirect effect mediated by BRI was also significant ($\beta = -1.34 \times 10^{-2}$, $P < 0.001$). The proportion of the total effect mediated by BRI was estimated to be 16.26% ($P < 0.001$), indicating that BRI partially mediates the relationship between LC9 and infertility. These findings suggest that obesity, as captured by BRI, plays a crucial role in the pathway linking cardiovascular health with infertility risk.

Discussion

This analysis included data from 2,319 women enrolled in the 2013–2018 NHANES cycles. The results indicated an inverse relationship between LC9 scores and infertility risk, whereas BRI showed a direct positive correlation with infertility. Further mediation analysis revealed that BRI served as a partial mediator in the LC9–infertility pathway, explaining approximately 16.26% of the total effect. These findings highlight the critical role of cardiovascular and metabolic health in reproductive function and suggest that obesity, particularly central adiposity, may be a key pathway linking poor cardiovascular health to infertility.

To our knowledge, this is the first study to examine the relationship between LC9 and infertility with BRI as a mediator. Previous studies have linked cardiovascular health and metabolic dysfunction with reproductive health outcomes, with obesity being recognized as a significant contributor to anovulation, hormonal imbalances, and systemic inflammation (17–20). Our findings are consistent with prior research demonstrating that poor cardiovascular health, as measured by Life's Simple 7 (LS7) or other cardiovascular health indices, is associated with reduced fertility (21, 22). Similarly, BRI has been shown to be a strong predictor of metabolic syndrome and obesity-related infertility (23, 24), aligning with our results that indicate higher BRI is significantly associated with increased infertility prevalence. However, previous studies have largely focused on BMI-based assessments of obesity (25), which do not accurately reflect body fat distribution and metabolic risk. By incorporating BRI, our study provides a more precise evaluation of central obesity's impact on infertility.

TABLE 1 Weighted baseline characteristics stratified by infertility status.

Characteristic	Overall, *N* = 26,147,035 (100%)	Non-infertility, *N* = 22,872,649 (87%)	Infertility, *N* = 3,274,386 (13%)	*P*-value
No. of participants in the sample	2,319	2,043	276	–
Age (%)				< **0.001**
18–25	6,219,351 (24%)	5,845,220 (26%)	374,131 (11%)	–
26–34	8,707,347 (33%)	7,714,940 (34%)	992,407 (30%)	–
35–45	11,220,338 (43%)	9,312,490 (41%)	1,907,848 (58%)	–
Race (%)				0.428
Non-Hispanic White	14,819,649 (57%)	12,817,421 (56%)	2,002,228 (61%)	–
Other	4,752,502 (18%)	4,275,874 (19%)	476,628 (15%)	–
Non-Hispanic Black	3,402,249 (13%)	2,998,983 (13%)	403,266 (12%)	–
Mexican American	3,172,635 (12%)	2,780,371 (12%)	392,263 (12%)	–
Married/live with partner (%)				< **0.001**
No	10,578,918 (40%)	9,835,008 (43%)	743,910 (23%)	–
Yes	15,568,117 (60%)	13,037,641 (57%)	2,530,475 (77%)	–
Education level (%)				0.731
Below high school	2,783,558 (11%)	2,415,019 (11%)	368,539 (11%)	–
High School or above	23,363,477 (89%)	20,457,630 (89%)	2,905,847 (89%)	–
PIR (%)				0.088
Poor	6,998,474 (29%)	6,228,667 (29%)	769,807 (24%)	–
Not Poor	17,524,388 (71%)	15,105,830 (71%)	2,418,558 (76%)	–
Hypertension (%)				**0.001**
No	22,343,080 (85%)	19,772,606 (86%)	2,570,473 (79%)	–
Yes	3,803,955 (15%)	3,100,043 (14%)	703,912 (21%)	–
Diabetes (%)				**0.005**
No	24,877,400 (95%)	21,890,152 (96%)	2,987,249 (91%)	–
Yes	1,269,635 (4.9%)	982,498 (4.3%)	287,137 (8.8%)	–
Hyperlipidemia (%)				**0.020**
No	12,294,565 (47%)	11,043,683 (48%)	1,250,881 (38%)	–
Yes	13,852,470 (53%)	11,828,966 (52%)	2,023,504 (62%)	–
Mean LC9 score [mean (SD)]	76.03 (13.52)	76.78 (13.27)	70.78 (14.13)	< **0.001**
LC9, tertile (%)				< **0.001**
T1	8,636,800 (33%)	7,121,334 (31%)	1,515,466 (46%)	–
T2	8,604,254 (33%)	7,517,443 (33%)	1,086,810 (33%)	–
T3	8,905,982 (34%)	8,233,872 (36%)	672,110 (21%)	–
Mean psychological health score [mean (SD)]	86.71 (25.81)	87.42 (25.01)	81.71 (30.43)	**0.034**
Mean HEI-2015 diet score [mean (SD)]	38.21 (31.73)	38.69 (31.96)	34.88 (29.87)	0.177
Mean physical activity score [mean (SD)]	77.59 (38.77)	78.14 (38.34)	73.74 (41.50)	0.170
Mean tobacco exposure score [mean (SD)]	75.50 (39.10)	76.37 (38.54)	69.39 (42.35)	**0.028**
Mean sleep health score [mean (SD)]	84.62 (23.25)	85.06 (22.96)	81.48 (25.00)	0.086
Mean body mass index score [mean (SD)]	60.02 (36.97)	61.67 (36.42)	48.46 (38.72)	**0.001**
Mean blood lipid score [mean (SD)]	80.21 (26.32)	80.87 (25.89)	75.59 (28.77)	**0.041**
Mean blood glucose score [mean (SD)]	93.86 (16.60)	94.51 (15.82)	89.31 (20.76)	< **0.001**
Mean blood pressure score [mean (SD)]	87.52 (22.05)	88.24 (21.58)	82.44 (24.52)	**0.005**

(Continued)

TABLE 1 (Continued)

Characteristic	Overall, *N* = 26,147,035 (100%)	Non-infertility, *N* = 22,872,649 (87%)	Infertility, *N* = 3,274,386 (13%)	*P*-value
BRI [mean (SD)]	5.40 (2.70)	5.25 (2.60)	6.47 (3.14)	< **0.001**
BRI, tertile (%)				< **0.001**
T1	8,719,893 (33%)	8,069,353 (35%)	650,540 (20%)	–
T2	8,714,472 (33%)	7,699,087 (34%)	1,015,385 (31%)	–
T3	8,712,670 (33%)	7,104,209 (31%)	1,608,460 (49%)	–

Continuous variables are expressed as mean (standard deviation), with *P*-values derived from weighted Student's *t*-tests. Categorical variables are reported as weighted counts and percentages (*N*, %), and their group differences were assessed using the weighted chi-square test. LC9, Life's Crucial 9; BRI, Body Roundness Index; PIR, poverty-income ratio. Bold values indicate $p < 0.05$.

TABLE 2 Association between LC9, BRI, and infertility.

Characteristics	Model 1 [OR (95% CI)]	*P*-value	Model 2 [OR (95% CI)]	*P*-value	Model 3 [OR (95% CI)]	*P*-value
LC9 - infertility						
Continuous (per 10 scores)	0.73 (0.64,0.84)	< 0.001	0.71 (0.62, 0.80)	< 0.001	0.71 (0.61, 0.84)	< 0.001
Tertile						
T1	1 (ref.)	–	1 (ref.)	–	1 (ref.)	–
T2	0.68 (0.47, 0.98)	0.040	0.64 (0.44, 0.93)	0.020	0.68 (0.45, 1.02)	0.060
T3	0.38 (0.23, 0.63)	< 0.001	0.36 (0.22, 0.59)	< 0.001	0.39 (0.22, 0.69)	0.002
P for trend	< 0.001		<0.001		0.002	
BRI - infertility						
Continuous	1.15 (1.08, 1.23)	< 0.001	1.16 (1.08, 1.23)	< 0.001	1.14 (1.07, 1.23)	< 0.001
Tertile						
T1	1 (ref.)	–	1 (ref.)	–	1 (ref.)	–
T2	1.64 (1.06, 2.51)	0.030	1.60 (0.97, 2.63)	0.060	1.55 (0.93, 2.59)	0.090
T3	2.81 (1.72, 4.60)	< 0.001	2.85 (1.66, 4.92)	< 0.001	2.64 (1.49, 4.69)	0.002
P for trend	< 0.001		< 0.001		0.001	

Model 1: unadjusted, with no confounding variables included. Model 2: adjusted for demographic and socioeconomic factors—age, educational attainment, marital status, PIR, and ethnicity. Model 3: further incorporated clinical covariates, including hypertension, diabetes, and dyslipidemia, in addition to Model 2 variables. LC9, Life's Crucial 9; BRI, Body Roundness Index; PIR, poverty-income ratio; OR, odds ratio; CI, confidence interval.

Potential mechanisms linking LC9, BRI, and infertility

The components of LC9 influence reproductive health through several biological mechanisms. Dietary quality, physical activity, and metabolic control are crucial factors in maintaining optimal hormonal balance and ovulatory function (26). Poor dietary habits, particularly excessive intake of ultra-processed foods and refined carbohydrates, contribute to systemic inflammation and insulin resistance, which are closely linked to polycystic ovary syndrome (PCOS), anovulation, and impaired endometrial receptivity (27, 28). Conversely, adherence to a heart-healthy diet rich in fiber, antioxidants, and essential micronutrients can improve metabolic function and reproductive outcomes (29, 30).

Physical activity, another critical component of LC9, influences infertility through multiple pathways. Regular moderate-to-vigorous exercise improves insulin sensitivity, reduces systemic inflammation, and regulates reproductive hormone levels, particularly androgens and estrogen, thereby promoting ovulatory function (31, 32). Additionally, increased physical activity reduces abdominal fat accumulation, which is a major contributor to hormonal imbalances and infertility risk (33).

Obesity, particularly central adiposity as measured by BRI, plays a crucial role in reproductive dysfunction. The accumulation of visceral adipose tissue (VAT) is associated with low-grade chronic inflammation, increased oxidative stress, and elevated levels of inflammatory cytokines (e.g., IL-6, TNF-α, CRP), all of which negatively impact ovarian reserve and endometrial receptivity (34–36). VAT is also strongly linked to insulin resistance and hyperinsulinemia, which can disrupt hypothalamic-pituitary-ovarian (HPO) axis function, leading to anovulation and subfertility (37). Our mediation analysis suggests that central obesity, as reflected by BRI, is a significant intermediary in the association between LC9 and infertility, highlighting the importance of obesity management in reproductive health interventions.

Subgroup findings and implications

Subgroup analyses revealed a significant interaction between LC9 and age, indicating that the protective effects of LC9 on

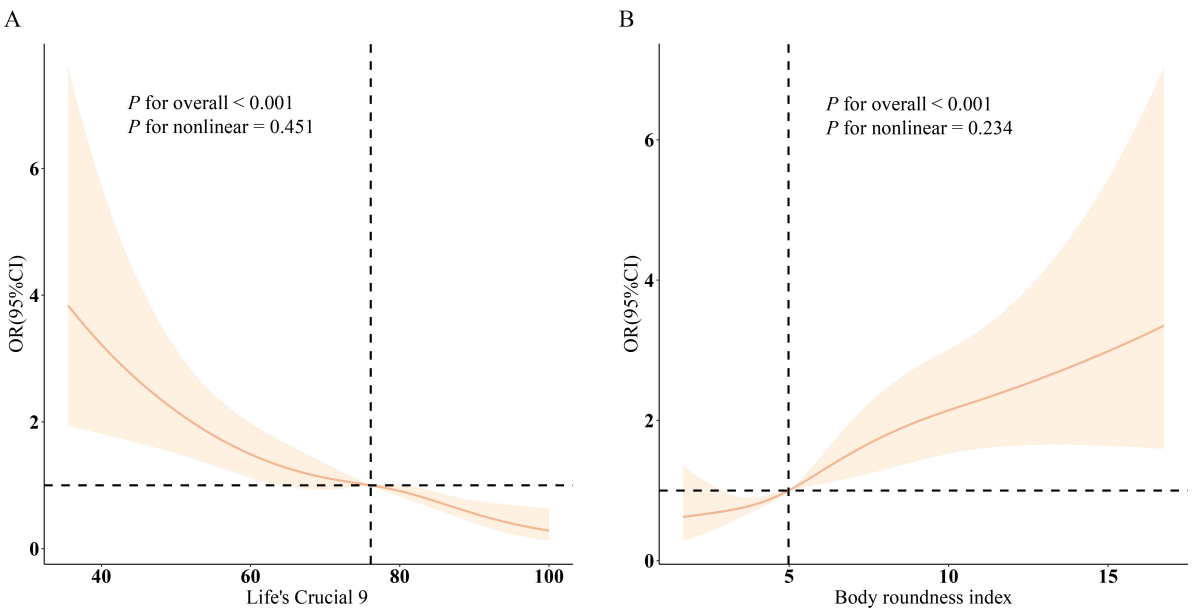

FIGURE 1
Dose–response curves depicting the associations between Life's Crucial 9 (LC9), Body Roundness Index (BRI), and infertility risk. **(A)** shows the relationship between LC9 and infertility, while **(B)** illustrates the association for BRI. Odds ratios (solid lines) with corresponding 95% confidence intervals (shaded regions) were estimated after adjusting for age, marital status, educational level, poverty-to-income ratio (PIR), race, and cardiometabolic comorbidities including hypertension, diabetes, and hyperlipidemia.

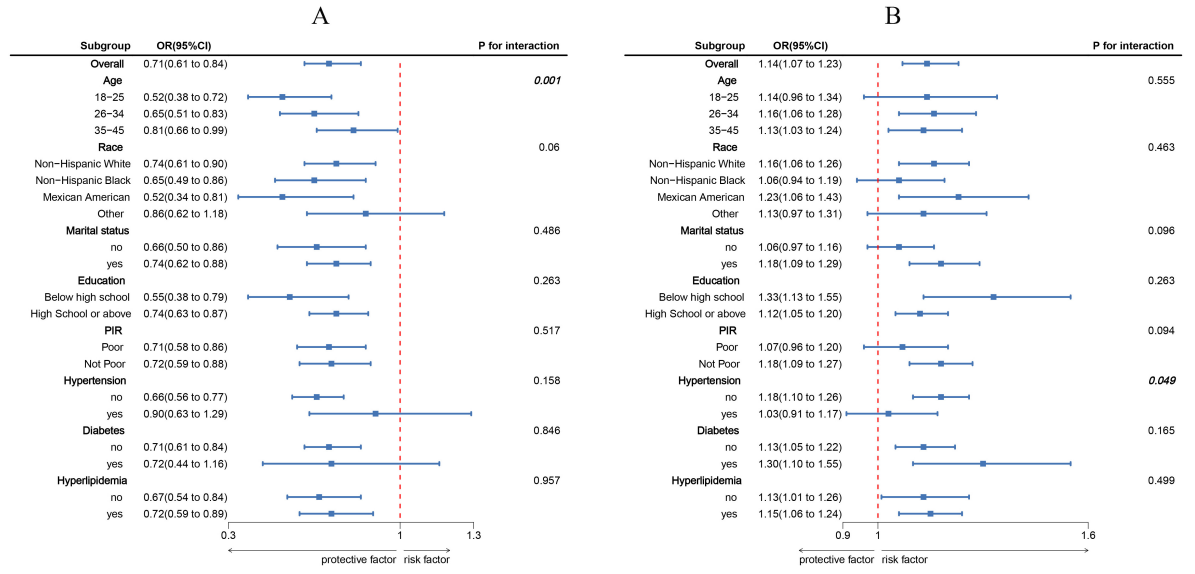

FIGURE 2
Subgroup analyses exploring the associations of Life's Crucial 9 (LC9) and Body Roundness Index (BRI) with infertility across various populations. **(A)** illustrates the effect of LC9 (per 10-point increment), while **(B)** presents the impact of BRI (per standard deviation increase). All estimates were derived from models adjusted for age, marital status, educational attainment, poverty-to-income ratio (PIR), race/ethnicity, and comorbid conditions including hypertension, diabetes, and dyslipidemia.

infertility were more evident in women aged 26–45 years, while the association was weaker and statistically non-significant in the youngest age group (18–25 years), potentially due to limited cases of infertility. Aging is a well-established risk factor for diminished ovarian reserve and reduced fertility, and poor cardiovascular health may further exacerbate this decline (38, 39). Future longitudinal studies are warranted to investigate whether improving LC9 components in early adulthood could delay reproductive aging and enhance fertility outcomes.

This study has several strengths. First, it is the first large-scale, population-based study to examine the association between LC9, BRI, and infertility using nationally representative NHANES data, enhancing the generalizability of our findings. Second, the

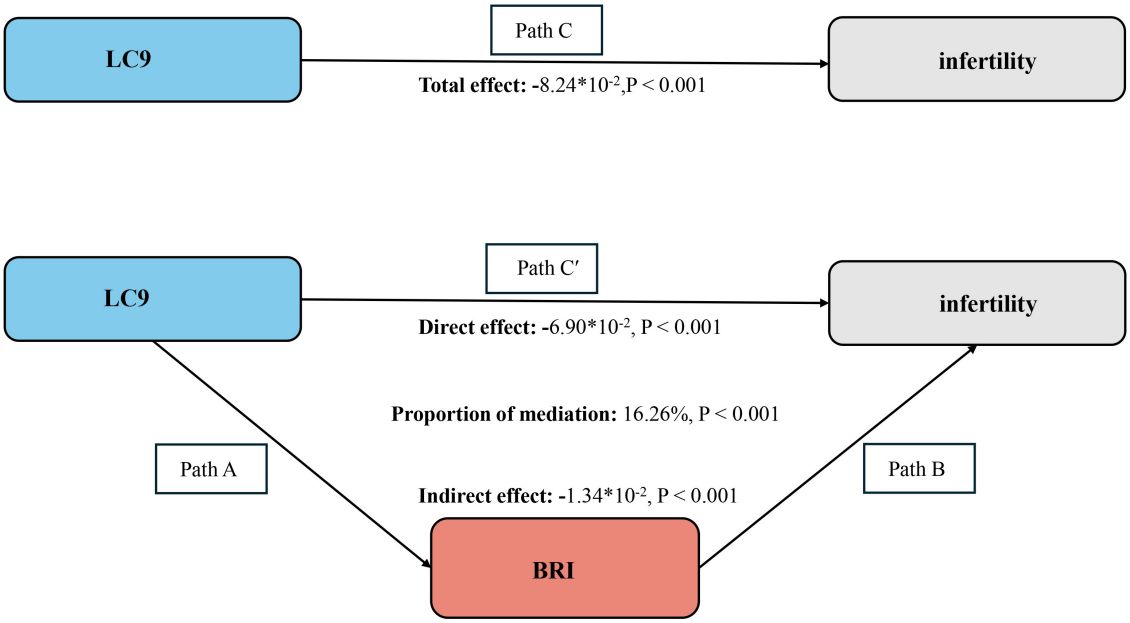

FIGURE 3
Bootstrap-based mediation framework showing BRI's indirect effect between LC9 and infertility. Path C represents the overall effect, while path C′ corresponds to the direct effect. The indirect effect is derived by multiplying paths A and B (A × B). The proportion mediated is calculated as: indirect effect ÷ (indirect effect + direct effect) × 100%. LC9, Life's Crucial 9; BRI, Body Roundness Index. All models were adjusted for age, marital status, education level, poverty-income ratio (PIR), race, hypertension, diabetes, and dyslipidemia.

use of BRI instead of traditional BMI measures provides a more accurate assessment of body fat distribution, addressing limitations of prior obesity-related infertility studies. Third, our study employs multiple statistical approaches, including multivariable logistic regression, RCS analysis, and mediation analysis, allowing for a comprehensive evaluation of the direct and indirect effects of LC9 on infertility.

However, several limitations should be acknowledged. First, the cross-sectional design of NHANES prevents us from establishing causality between LC9, BRI, and infertility. Future prospective cohort studies are needed to confirm whether improving cardiovascular health and reducing central adiposity can directly enhance fertility outcomes. Second, infertility in this study was assessed through self-reported responses to two NHANES questionnaire items, which may introduce recall bias and potential misclassification. Specifically, because the survey did not differentiate between primary and secondary infertility, participants who experienced either condition were grouped together. This lack of distinction may lead to heterogeneity within the infertility group and could influence the observed associations. Future studies should incorporate more detailed clinical assessments or validated diagnostic criteria to distinguish between different infertility subtypes, thereby improving the accuracy and interpretability of findings. Third, while we adjusted for major confounders, unmeasured variables, such as genetic predisposition, environmental exposures, and psychosocial stress, may also contribute to infertility risk and were not accounted for in this analysis. Fourth, the study population was limited to women aged 18–45 years, and our findings may not be generalizable to adolescent or postmenopausal populations.

Conclusion

This study provides evidence that better cardiovascular health, as measured by LC9, is associated with a lower risk of infertility, while higher central adiposity, captured by BRI, is linked to an increased risk of infertility. Furthermore, BRI was found to partially mediate the association between LC9 and infertility, suggesting that obesity, particularly excess abdominal fat, plays a significant role in the relationship between cardiovascular health and reproductive function. These findings highlight the need for a broader, integrative approach to infertility prevention, focusing not only on reproductive health but also on metabolic and cardiovascular wellbeing.

Given the cross-sectional design of this study, future longitudinal research is necessary to confirm these associations and explore whether interventions targeting cardiovascular health and obesity management can improve fertility outcomes. Additionally, further studies should investigate other potential mediators and confounders, such as inflammatory markers, hormonal profiles, and mental health factors, to gain a more comprehensive understanding of the mechanisms underlying the LC9-infertility relationship. Addressing these factors may contribute to more effective public health strategies and clinical interventions aimed at improving both cardiovascular and reproductive health.

Data availability statement

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

Ethics statement

The NHANES study protocol received approval from the Ethics Review Board of the National Center for Health Statistics. The participants provided their written informed consent to participate in this study. As this analysis utilized publicly accessible and anonymized datasets, no further ethical review was necessary.

Author contributions

YW: Conceptualization, Methodology, Data curation, Writing – original draft, Visualization. LG: Investigation, Software, Conceptualization, Writing – original draft, Data curation. QZ: Formal analysis, Writing – original draft, Conceptualization, Data curation. LB: Methodology, Writing – original draft, Investigation. JX: Supervision, Writing – review & editing, Project administration, Validation, Resources. LZ: Resources, Project administration, Validation, Supervision, 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.

Generative AI statement

The authors declare that no Generative AI was used in the creation of this manuscript.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fnut.2025.1605601/full#supplementary-material

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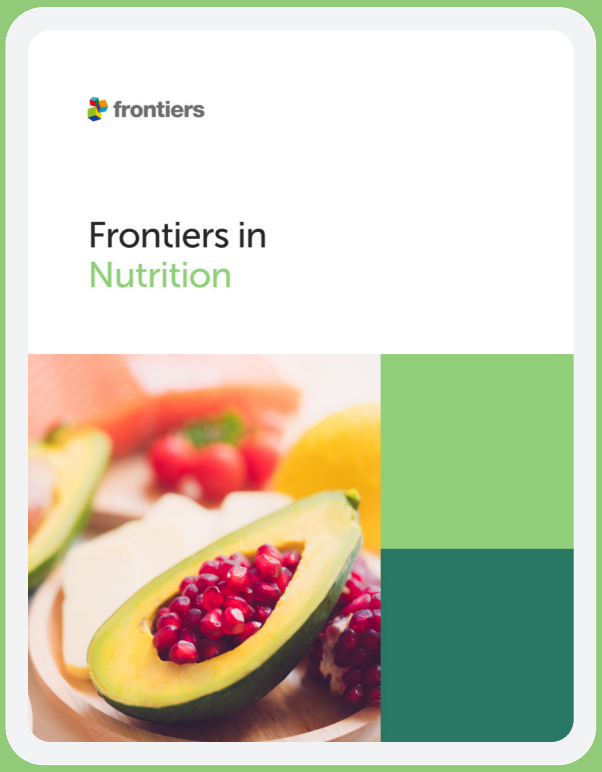

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