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The impact of primary care on cancer screening program performance: strategies to increase uptake and effectiveness

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The impact of primary care on cancer screening program performance: strategies to increase uptake and effectiveness

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Editorial: The impact of primary care on cancer screening program performance: strategies to increase uptake and effectiveness

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Editorial on the Research Topic
The impact of primary care on cancer screening program performance: strategies to increase uptake and effectiveness

Cancer screening is recommended in many countries, and is often implemented in the form of free, organized, Public Health interventions, especially in the case of breast, cervical, and colorectal cancer (CRC). Indeed, CRC screening with either fecal immunochemical testing (FIT) or colonoscopy—targeting women and men equally—results in similarly significant reductions in both CRC-related incidence and mortality (1, 2). However, the uptake of screening varies greatly across countries and even smaller regions. CRC screening is an extreme example: participation remains suboptimal in several countries, in average-risk and in familial-risk populations (3–5). In recent years, a study from Crete reported an increased incidence of CRC among young adults (<50 years), in a population with historically low incidence (6). It is fundamental to investigate uptake as the effectiveness of screening depends, among other factors, on a high participation by the target population (7). In addition, changes in the epidemiology of several preventable cancers highlight the importance of early intervention in primary care. For example, while the incidence of breast cancer is slowly rising in two European regions (Östergötland, Sweden, and Crete, Greece), mortality has increased in Crete compared with Sweden (8). Several studies suggest that Primary Care Physicians, or General Practitioners (GPs), have a substantial influence on the screening adherence of their assisted subjects' (9–12), as counseling by GPs has been associated to higher participation (11). Yet, thus far, interventions targeting GPs have rarely been tested in order to improve the uptake and appropriateness of cancer screening (13–16). The present Research Topic aimed to collect and highlight quality evidence on the impact of GPs on the performance of screening programmes using, for instance, risk-stratification or other organizational changes.

The work by Petrik et al. provides insights on a multi-component strategy employed by primary care clinics (PCCs) to increase participation to FIT, in the rural areas of Oregon, United States. In this study, the clinics adhering to the intervention adopted a strategy including posting of FIT kits, and training and support to medical assistants, who then navigated the patients resulting positive, through the phone. Higher FIT return and CRC screening rates were more likely in clinics which were able to mail an introductory letter, had experience in CRC screening, and attended the health plan-clinic meetings. Similarly, Kruse-Diehr et al. pilot-tested a method to increase participation to CRC screening in Appalachian Kentucky, finding that the great majority of individuals returned a FIT when it was provided in combination with an exploratory "talking card." These approaches, although dependant on the organization of each PCC, are promising for countries such as the United States and Australia (17, 18), where remoteness is a much greater issue than in Europe (19, 20).

Similarly, research on cervical cancer screening also verified the impact of a strategy to improve uptake, although in the setting of opportunistic screening in Catalonia. Peremiquel-Trillas et al. distributed HPV self-sampling kits through pharmacies (upon SMS invitation), finding a participation rate of 80%. Self-sampling was already shown to improve participation (21), and Catalonia is set to implement it within its population-based programme. Gezimu et al., instead, conducted a narrative review of the perception of cervical screening by female healthcare professionals. Most of the examined studies reported poor knowledge, unfavorable attitudes, and low uptake, but also suboptimal service accessibility, and lack of training. If confirmed, these findings call for improved screening access and training of providers.

Concerning risk-based screening programmes, research is still ongoing on their effectiveness and feasibility (22). Some algorithms are long-established, as is the case for breast cancer (23), for which personalized screening schedules are being tested in RCTs (22), aiming to reduce not only the incidence of advanced cancers, but also the overall tests and procedures (24). Guan et al., in a qualitative study set in Georgia, conducted interviews among PCC professionals, to assess their attitudes toward genetic risk-based breast screening, and observed that the only obstacles to intensifying screening tests in high-risk women were the limited knowledge and unclear referral protocols, while performing fewer tests in low-risk women was less acceptable.

Moving away from conventionally recommended screening, two papers explored the opportunity to screen for melanoma, a rarer but rapidly growing malignancy (25). The intervention tested by Becker et al. was an educational campaign, including online and on-site training, developed to promote an effective skin examination, and disseminated throughout PCCs in Oregon. Over two thousand primary care providers participated to at least one training component, corresponding to about one quarter of those contacted, and the campaign is still ongoing. Further, the study by Pillai et al. proposes a deep-learning algorithm, which reached accuracy, in identifying the malignant nature and the diagnostic category, both above 90%, suggesting that similar tools could become a precious aid within primary care.

More in general, Jeong et al. investigated whether changes in demography correspond to changes in the participation to screening programmes, in Korea. Indeed, decreases in the size of the population were associated with lower participation to cancer screening, for a reduction of about 10%. In a country where out-of-pocket accounts for a substantial part of the health expenditure (26), the elderly groups remaining in depopulated regions are likely unappealing to PCCs (27). Their findings underscore the importance of promptly adapting primary care to specific demographic patterns, and to implement care pathways which integrate services from primary to tertiary hospitals (26).

Finally, Jerjes et al. warn against the underestimation of cancer risk in younger patients. A rise in CRC incidence in young adults was recently reported in the literature (6), and, while differential diagnosis justifiably takes cancer in little account for young patients, GPs should not entirely disregard it. A constant update on the epidemiological trends and appropriate diagnostic procedures is recommended, as well as the introduction of standardized digital decision-support tools, which may aid professionals in the timely identification of malignancies (28).

Despite the evidence linking advice by GPs to cancer screening uptake, studies involving primary care providers and targeted at improving the effectiveness of cancer screening programmes are still scarce. Future efforts should be directed at performing pragmatic experimental research, investigating both effectiveness and financial sustainability. The evidence that this Research Topic conveys could facilitate the design of the future work.

Author contributions

CA: Conceptualization, Writing – original draft. EQ: Conceptualization, Supervision, Writing – review & editing. CL: Conceptualization, Writing – review & editing, Supervision.

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Feasibility and efficacy of a novel audiovisual tool to increase colorectal cancer screening among rural Appalachian Kentucky adults

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Introduction: Residents of Appalachian regions in Kentucky experience increased colorectal cancer (CRC) incidence and mortality. While population-based screening methods, such as fecal immunochemical tests (FITs), can reduce many screening barriers, written instructions to complete FIT can be challenging for some individuals. We developed a novel audiovisual tool ("talking card") to educate and motivate accurate FIT completion and assessed its feasibility, acceptability, and efficacy.

Materials and methods: We collected data on the talking card via: (1) cross-sectional surveys exploring perceptions of images, messaging, and perceived utility; (2) follow-up focus groups centered on feasibility and acceptability; and (3) efficacy testing in community-based FIT distribution events, where we assessed FIT completion rate, number of positive vs. negative screens, demographic characteristics of participants, and primary drivers of FIT completion.

Results: Across the three study phases, 692 individuals participated. Survey respondents positively identified with the card's sounds and images, found it highly acceptable, and reported high-to-very high self-efficacy and response efficacy for completing FIT, with nearly half noting greater likelihood to complete screening after using the tool. Focus group participants confirmed the acceptability of the individuals featured on the card. Nearly 75% of participants provided a FIT accurately completed it, with most indicating the talking card, either alone or combined with another strategy, helped with completion.

Discussion: To reduce CRC screening disparities among Appalachian Kentuckians, population-based screening using contextually relevant implementation strategies must be used alongside clinic-based education. The talking card represents a novel and promising strategy to promote screening uptake in both clinical and community settings.

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colorectal cancer, cancer screening, health communication, Appalachia, rural

1 Introduction

Along with increased colorectal cancer (CRC) incidence (1) and mortality (2) (Figure 1), CRC screening prevalence is lower in rural Appalachian regions of Kentucky than in non-Appalachian regions (3), a disparity partly related to fewer and more geographically dispersed regional specialists available to perform colonoscopy (Figure 2). Individuals living in Appalachian counties tend to earn less money, are more likely to be unemployed, have lower educational attainment, and report poorer health than their non-Appalachian counterparts (4). Additionally, less than a quarter of Appalachian residents hold a bachelor's degree or higher, a proportion that drops to around 15% for residents living in the most rural parts of Appalachia (4), making health literacy a primary concern for addressing the health needs of Appalachian residents (5). Particularly in rural Kentucky, individuals often live in extremely close-knit communities, and research has shown that Appalachian residents tend to prefer health communication materials reflective of local culture to mass-produced mainstream campaigns (6). Furthermore, addressing patient factors specific to this population–including knowledge of CRC, misperceptions of CRC and screening, fear, and stigma–is critical for increasing CRC screening uptake (7, 8). Methods, materials, images, and communication styles used in screening programs should all reflect local interests, values, and context while simultaneously accounting for varying literacy levels in the intended audience (9).

Particularly in rural environments where outpatient services may be limited or geographically dispersed (10), offering a range of evidence-based screening options is critical to increasing overall community screening rates. The use of fecal immunochemical test (FIT) kits as a screening modality has been shown to improve CRC screening by reducing or removing common misperceptions and barriers associated with other screening modalities (e.g., colonoscopy) (11, 12). FIT kits also can be completed in the privacy of one's home, thereby reducing potential test stigma. Nevertheless, individuals can be confused by the processes required to complete FIT accurately, and instructions included with kits are not always appropriate for low-literacy populations (13). In response to these needs, the Kentucky Cancer Consortium (KCC) (Kentucky's Comprehensive Cancer Control Coalition) partnered with the American Cancer Society to develop and promote a custom-recordable audio communication tool ("talking card") intended to help increase CRC screening via FIT. The card provides audio-guided instructions about the importance of CRC screening, the ease of using FIT, and the process for completing a FIT kit. Local CRC survivors from rural Kentucky, one male and one female, are featured on the front of the cards alongside a brief, simple written message about the importance of CRC screening. The inside of the card includes pictorial descriptions of the specific steps needed to complete FIT, as well as audio instructions of those same steps recorded by the individuals on the front of the cards. The talking card size was designed to match the dimensions of the Polymedco OC-Light® FIT mailer, thus allowing them to be used as a potential implementation strategy to increase screening uptake in mailed FIT interventions (Figure 1). The printing cost of the talking card was $3.15 per card, making it an economically feasible strategy to add to a mailed FIT campaign, an evidence-based approach previously proven to be both feasible and cost-effective in eastern Kentucky clinical settings (14) (Figure 3).

For nearly 20 years, one of the focus areas for KCC has been implementing strategies to increase CRC screening by promoting coordination and collaboration among member organizations, which include health care systems. In particular, given the novelty (e.g., simple audiovisual technology that does not require internet connectivity) and contextual focus (e.g., uses images and voices of local individuals with simple audio instructions) of the talking card, KCC wanted to assess both its feasibility and utility before scaling out this

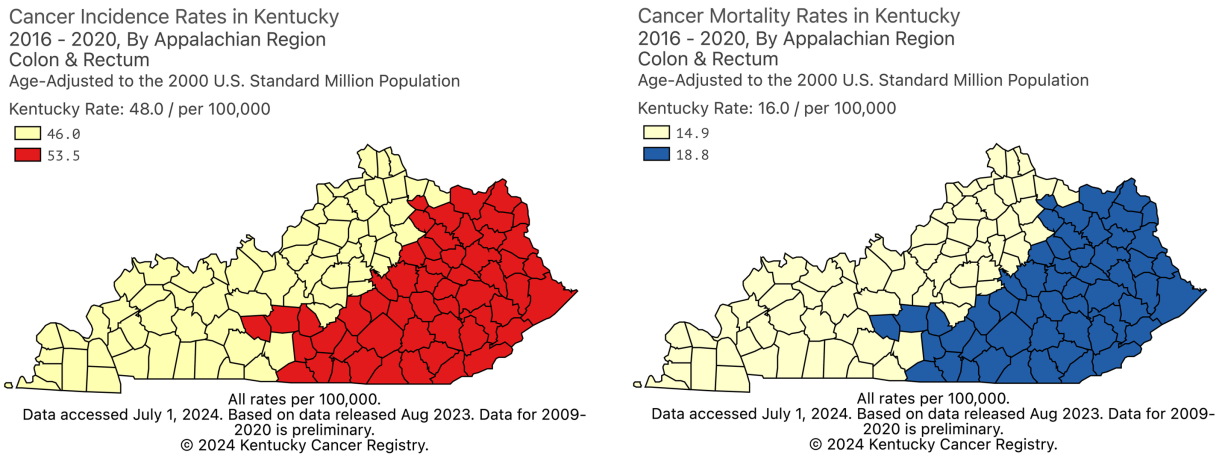

FIGURE 1
CRC incidence and mortality rates in Kentucky, by Appalachian region.

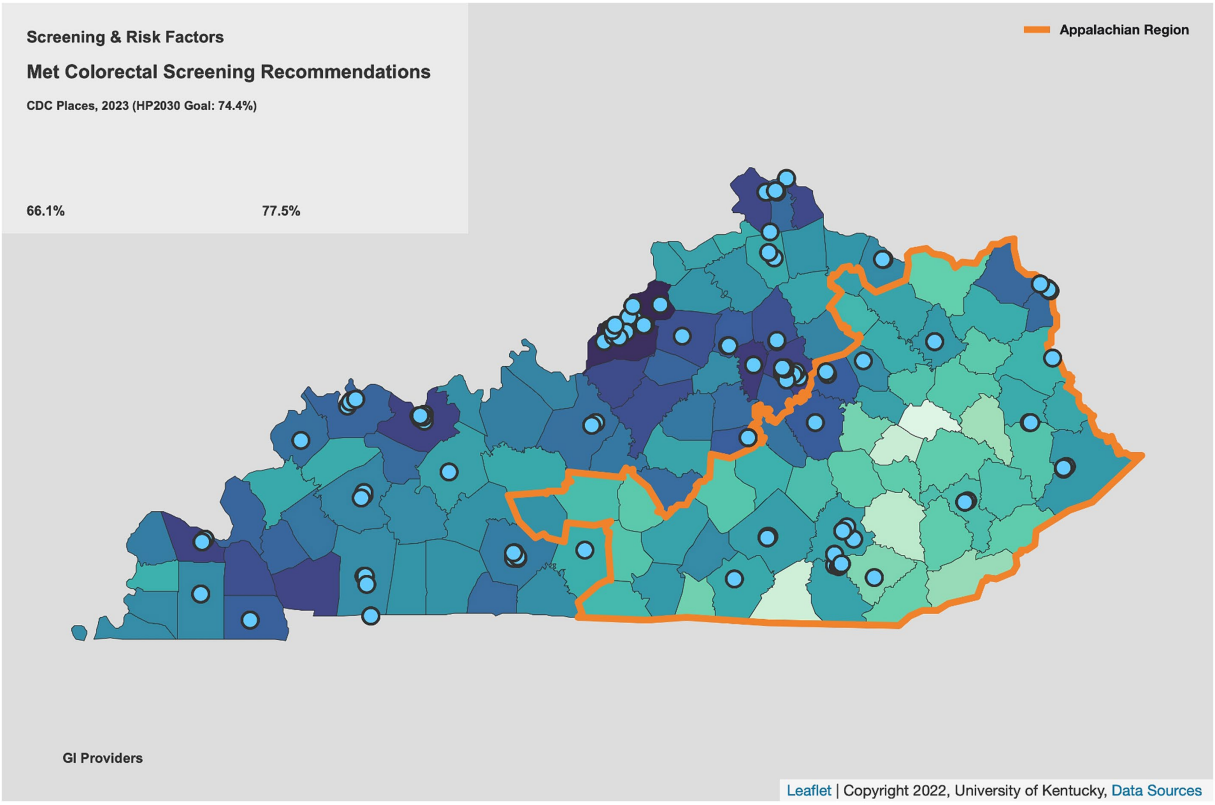

FIGURE 2
CRC screening rates and distance to GI services in Appalachian Kentucky.

FIGURE 3
Male-targeted audiovisual tool front cover.

strategy to health care systems. Specifically, KCC sought to (a) identify whether the intended population perceived the talking card to be feasible and appropriate and (b) test its efficacy at increasing CRC screening rates. To do this, KCC convened organizational, clinical, and academic partners in a multi-phased effort to explore the feasibility, acceptability and efficacy of the talking cards to increase CRC screening among rural Kentucky residents as part of a mailed FIT campaign.

2 Materials and methods

Research on the talking cards have been ongoing since 2018 and have focused both on feasibility and efficacy via three major efforts: (1) cross-sectional surveys exploring perceptions of the cards' images, messaging, and perceived utility (i.e., feasibility); (2) follow-up focus groups to explore specific characteristics related to the cards' feasibility and acceptability; and (3) efficacy testing of the talking card in conjunction with community-based FIT distribution events. These efforts were coordinated by KCC in partnership with the University of Kentucky (research assistance), Kentucky Cancer Program (screening/awareness events), the Markey Cancer Center (FIT kits), the Kentucky CancerLink (patient navigation services) and the American Cancer Society (audio supplement cards). All methods, materials, and designs were approved by the University of Kentucky Institutional Review Board or were designated as Not Human Research (NHR) due to being conducted as quality improvement activities within the scope of an organization's (KCC, Kentucky Cancer Program, Kentucky CancerLink) existing standard operating procedures.

2.1 Design, setting and participants

Feasibility and acceptability data for the talking card were collected via a mixed-methods (i.e., QUAN ➔ qual) design consisting of both (1) survey mailings to local screening-eligible patients of three partner family medicine clinics in eastern Kentucky, and (2) two follow-up focus groups with screening-eligible individuals in Appalachian eastern Kentucky. Eligibility criteria for potential participants included being: (1) aged 45–75, (2) a resident of eastern Kentucky, and (3) at average risk for CRC as determined by US Preventive Services Task Force (USPSTF) guidelines (i.e., eligible to use FIT as a CRC screening modality). Surveys were mailed to up to 200 patients randomly selected from each clinic's list of eligible patients (as determined by their electronic health record system) using a 4-wave survey mailing process (15) (described under "Data Collection" below). Since the focus of the survey was feasibility and because results were intended to be descriptive in nature, there was no power calculation to guide the sample size. Focus group participants were purposively selected with the assistance of community organization partners in eastern Kentucky.

To determine efficacy of the talking cards, outreach partners invited screening-eligible potential participants to local community-clinical linkage events. The events were health-focused, sometimes included a large inflatable colon that participants could "walk through" and were usually part of a larger outreach and awareness event. Events occurred at local hospitals or clinics as well as through community-wide events. Those at risk for colon cancer who participated in the event and showed an interest in the FIT kit had an opportunity to participate. The outreach partners filled out a contact/eligibility form and submitted it to a partner for patient navigation services. The patient navigation partner evaluated the individual's information and determined eligibility (50–75 years old, screening nonadherent, at average risk). Critically, patient navigators also engaged primary care physicians and insurance companies, when possible, to connect this project with participants' health care services. To promote consistency across medical records, patient navigators sent either a fax or letter to each participant's primary care provider with the completed FIT test and attempted to contact their insurance company to provide FIT results.

2.2 Data collection

2.2.1 Surveys

Survey mailings featured a 4-wave mailing process (15) in which a packet was sent out to each eligible participant, consisting of six items: (1) a cover letter, signed by a provider at the respective clinic, explaining the study; (2) a brief, simple, pictorial explanation of FIT as a CRC screening modality; (3) a gender-specific version of the talking card; (4) a 3-page survey assessing the talking card; (5) a self-addressed stamped envelope (SASE); and (6) a $2 bill as an incentive. Wave 2 included all items except the $2 incentive, Wave 3 included all items except for the $2 bill and the talking card itself (due to printing cost considerations), and Wave 4 consisted of a postcard reminder. The combined instrument contained both scales created by a health communication expert (SV), as well as previously validated scales. Items assessed self-efficacy (16) and response efficacy regarding FIT, identification with the talking card's sounds and images, behavioral intentions to get screened for CRC, and perceived acceptability (17) of the talking card.

2.2.2 Focus groups

Follow-up focus groups were facilitated by a qualitative research expert (AK-D) and a community organization partner with extensive experience in community-based cancer education (EH) to contextualize survey findings. Focus group participants were consented, provided photocopies of gender-congruent talking cards and asked to listen as the focus group facilitator opened a talking card and demonstrated its use. The facilitator used a semi-structured interview protocol focused on knowledge of CRC screening and FIT, as well as perceptions of ways in which the talking cards' messages and images might educate and motivate CRC screening via FIT. Each focus group lasted approximately 1 h. Upon completion, participants completed a survey comprised of three parts: (1) a brief 12-item measure of intervention acceptability, appropriateness, and feasibility (17); (2) a 4-item instrument assessing screening history, recommendation, and perceived barriers; and (3) a demographic component.

2.2.3 Efficacy testing

Finally, statewide community-clinical linkage events were used purposively to collect data on efficacy of the talking cards across three implementation waves. At these events, KCP, Markey Cancer Center and/or Kentucky CancerLink discussed colorectal cancer screening with participants, determined eligibility and had participants fill out

eligibility/contact forms which were reviewed by Kentucky CancerLink staff. Those who met eligibility requirements received a mailed FIT kit, talking card, and self-addressed stamped postcard (Figure 4) with an opportunity to provide feedback. Kentucky CancerLink patient navigators contacted participants up to three times and sent a mailed letter to non-responders to assist participants with FIT completion. Upon receipt of FIT, Kentucky CancerLink processed the sample in their CLIA-certified lab; contacted the participant with results; and asked permission to share the results with the patient's primary care provider, including assisting patients in securing a primary care physician if they did not have one already; and navigating patients with a positive FIT to get a follow-up screening colonoscopy.

2.3 Data analysis

Survey data were imputed into an Excel spreadsheet which was uploaded into IBM SPSS Statistics (18) for analysis. Findings from the surveys helped inform focus group questions, which were intended to provide additional context. The two focus groups were audio-taped, transcribed verbatim by a professional transcription service, and spot checked for accuracy by the principal investigator. Transcripts were coded thematically by two members of the research team (AK-D, EH) as per Braun and Clarke (19). Codes related both to broad question topics and were also developed inductively based on conversations that emerged from open conversation within the focus groups and were compiled using a template-based codebook with code operationalizations and exemplars. After individual coding, the investigators met to refine codes and their operationalizations before developing broad themes to describe the focus groups' primary findings. Although we were unable to apply "member checking" to our themes due to the challenging nature of recruiting our sample, we referenced published literature on CRC screening barriers as well as American Cancer Society community projects to ensure our findings were aligned with prior recent work. Ultimately, no changes were deemed necessary.

Efficacy testing examined the impact of the talking card implementation (i.e., FIT completion rate, number of positive vs. negative screens) as primary outcomes, data on primary drivers of FIT completion from the self-addressed stamped postcard (i.e., any combination of talking card, patient navigation, or family/friend encouragement) as secondary outcomes, and demographic characteristics of participants (i.e., insurance status, race/ethnicity, gender). These data were compiled in an Excel spreadsheet and compared descriptively across 3 waves of implementation.

3 Results

3.1 Study sample

A total of 692 individuals participated across all three study phases. For the survey mailings, of 353 eligible participants, 67 surveys (19% response rate) were completed and returned. Participants were mainly female (60%), white (98.5%), insured via Medicare (58%), and had a median age of 68 years old (see Table 1). A plurality had a bachelor's degree or higher (40%) and reported an annual household income of less than $25,000 (25%). A total of 24 individuals participated in the two focus groups. They were also predominantly female (75%), white (91.7%), and between 61 and 70 years old (50%). Most had an educational attainment of associate degree or below (66.6%), a household annual income of between $35,000 and $74,000 (54.2%) and were insured either by an employer plan (54.2%) or Medicare (45.8%). A large majority (87.5%) reported having at least one person they considered their primary medical provider.

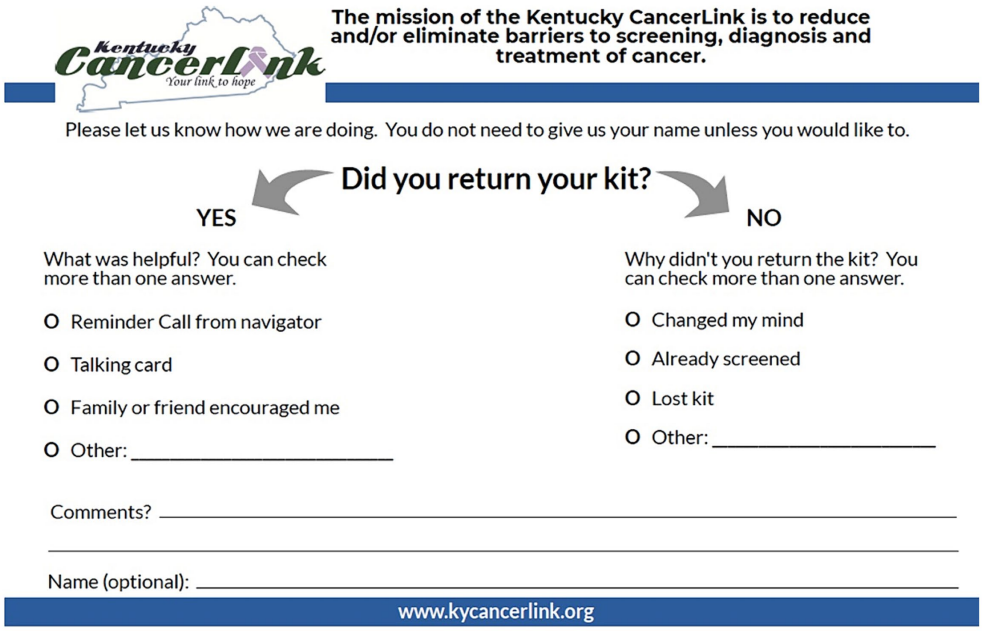

FIGURE 4
Feedback postcard for community-based FIT distribution campaign.

TABLE 1 Survey and focus group participant demographics.

	Surveys		Focus Groups	
	n	%	*n*	%
Age				
45–50	2	3.0	1	4.2
51–55	6	9.0	6	25.0
56–60	10	14.9	1	4.2
61–65	13	19.4	6	25.0
66–70	11	16.4	6	25.0
71–75	23	34.3	3	12.5
76+	1	1.5	1	4.2
No response	1	1.5	0	0
Gender				
Female	40	59.7	18	75.0
Male	24	35.8	6	25.0
No response	3	4.5	0	0
Race/ethnicity[a]				
White	66	98.5	22	91.7
American Indian or Alaska Native	2	3.0	0	0
Hispanic or Latnix	1	1.5	0	0
Black or African American	0	0	1	4.2
No answer	0	0	1	4.2
Highest level of education				
Some high school (did not complete)	6	9.0	2	8.3
High school or GED	14	20.9	6	25.0
Some college (did not complete)	16	23.9	3	12.5
Associate degree	0	0	5	20.8
Bachelor's degree or higher	27	40.3	8	33.4
No response	3	4.5	0	0
Total household annual income				
Less than $25,000	17	25.4	2	8.3
$25,000 to $34,999	6	9.0	1	4.2
$35,000 to $49,999	9	13.4	7	29.2
$50,000 to $74,999	11	16.4	6	25.0
$75,000 to $99,999	11	16.4	2	8.3
$100,000 or more	9	13.4	5	20.9
No response	4	6.0	1	4.2
Type of medical insurance[a]				
Medicare	39	58.2	11	45.8
Employer plan (self or spouse's)	24	35.8	13	54.2
Medicaid	7	10.4	1	4.2
Plan I purchased myself	6	9.0	0	0
Plan through VA	4	6.0	0	0
I do not have medical insurance	2	3.0	1	4.2
Do not know/Not sure	0	0	1	4.2
Has one or more people considered primary medical care provider				
Yes	56	83.6	21	87.5
No	9	13.4	2	8.3
No response	2	3.0	1	4.2
Any type of colorectal cancer screening recommended by medical care provider, ever				
Yes	51	76.1	21	87.5
No	11	16.4	3	12.5
Do not know/Not sure	5	7.5	0	0
Stool-based test recommended by medical care provider,past year				
Yes	15	22.4	–	–
No	49	73.1	–	–
Do not know/Not sure	3	4.5	–	–
Type of colorectal cancer screening tests taken, past year[a]				
None	34	50.7	–	–
Colonoscopy or sigmoidoscopy	17	25.4	–	–
Stool blood test like (FIT or Cologuard)	17	25.4	–	–
Other type of colon exam	1	1.5	–	–
No response	2	3.0	–	–
Type of colorectal cancer screening tests taken, ever[a]				
Colonoscopy	–	–	22	91.7
Stool blood test (FOBT/FIT or Cologuard)	–	–	6	25.0
Sigmoidoscopy	–	–	3	12.5
CT colonography	–	–	1	4.2
None	–	–	2	8.3
What reasons for not getting screened for CRC have you heard other people say?[a]				
Concerned the test is messy	–	–	10	41.7
Worried the test is difficult	–	–	9	37.5
No family history of colorectal cancer	–	–	14	58.3
Belief screening is only for symptoms	–	–	10	41.7
Difficulty finding transportation	–	–	5	20.8
Colonoscopy preparation is unpleasant	–	–	19	79.2
Concerned the test is painful	–	–	11	45.8
Embarrassed to discuss with doctor	–	–	12	50.0
Do not believe they are at risk	–	–	15	62.5
Concerned about costs or insurance	–	–	11	45.8
Difficult to take time off	–	–	20	83.3
None	–	–	1	4.2
What reasons have kept you from getting screened for CRC?[a]				
Concerned the test is messy	–	–	0	0
Worried the test is difficult	–	–	1	4.2
No family history of colorectal cancer	–	–	0	0
Belief screening is only for symptoms	–	–	0	0
Difficulty finding transportation	–	–	2	8.3
Colonoscopy preparation is unpleasant	–	–	5	20.8

(Continued)

TABLE 1 (Continued)

	Surveys		Focus Groups	
	n	%	*n*	%
Concerned the test is painful	–	–	1	4.2
Embarrassed to discuss with doctor	–	–	0	0
Do not believe they are at risk	–	–	1	4.2
Concerned about costs or insurance	–	-	1	4.2
Difficult to take time off	–	–	1	4.2
None	–	–	13	54.2
Other	–	–	2	8.3
How often do you need help reading written material from the doctor or pharmacy?				
Never	48	71.6	14	58.3
Rarely	11	16.4	5	20.8
Sometimes	3	4.5	3	12.5
Often	3	4.5	0	0
Always	2	3.0	2	8.3

Surveys: $n = 66$; Focus Groups: $n = 24$. [a]Percentages do not equal 100% because participants selected all applicable response options.

In efficacy testing, across 3 years of implementation, a total of 601 eligible participants from 73 out of 120 Kentucky counties were identified, 425 of whom (71%) completed a FIT kit. Participants were predominantly female, White, and had some sort of insurance. Only 30 individuals (11%) reported not having any type of insurance.

3.2 Feasibility

Survey respondents positively identified with the audiovisual tool's sounds and images and found it highly acceptable. They also reported high-to-very high self-efficacy ($M = 3.65$, SE = 0.62 on a 4-point scale ranging from *completely disagree* to *completely agree*) and response efficacy ($M = 3.43$, SD = 0.69) for completing FIT after using the audiovisual tool. Nearly half stated they felt better about FIT (46%) and would be more likely to complete screening (48%) after using the tool. While a majority (71.6%) noted never needing help reading written material from the doctor or pharmacy, 12% reported either sometimes, often, or always requiring assistance.

Focus group participants ($n = 24$) stated that CRC screening, in general, is often considered "taboo" in their communities, with one participant stating, "We do not talk about that. You can talk to your kids about [going to the bathroom], but adults…it's some sort of embarrassing shameful thing." Other concerns related primarily to colonoscopy, specifically the preparation process and perceptions of discomfort related to the procedure itself. When presented with the talking card, focus group members perceived it to be an improvement over current screening educational materials. One individual commented positively on the audio component, stating that "there [are] probably a lot [of patients] who cannot read or write." Additionally, the card's technology was preferred over other approaches such as videos or QR codes due to concerns about spotty internet in rural Kentucky, as well as potential issues with technological literacy. Participants also considered the individuals whose pictures and voices were featured on the cards to be appropriate, noting their Appalachian accents, clear diction, and CRC survivorship; in particular, having a CRC survivor as the face and voice of the card was considered by most to be preferable to a doctor or nurse as the card's representative. Other participants focused on the uniqueness of the card in general, remarking that they would show it to their family and friends. Furthermore, the simplicity of the card was often cited positively: "[It] just walks you right through it. I mean, step by step. Just bam, bam, bam… And you can listen to it as many times as you want in case you get lost." Participants universally endorsed the talking card as a strategy to incentivize FIT completion but noted that a primer letter from a physician should be sent first, or people might mistake the mailing as junk mail.

In the summative focus group survey, participants rated the talking card as highly acceptable [average of 4.76 (SD = 0.43) on a 5-point scale, ranging from *strongly disagree* to *strongly agree*], appropriate ($M = 4.79$, SD = 0.36), and feasible ($M = 4.85$, SD = 0.31) to motivate their screening intentions, scores that were reflected in focus group discussion, where every participant noted a high-to-very high level of confidence that they would be able to complete a FIT kit after viewing the talking card. Notably, compared to survey mailings, focus group participants had a higher percentage (20.8%) of participants who reported either sometimes, often, or always requiring assistance reading written materials from the doctor or pharmacy. Table 1 displays participant demographics for both survey mailings and focus groups.

3.3 Efficacy

Efficacy testing for the talking card yielded promising findings, with 67% ($n = 425$) of eligible participants accurately completing their FIT kit. Of those completers, 305 (79%) had a negative screen, while 82 (21%) had a positive screen and were navigated to receive follow-up colonoscopy, 42 (51%) of whom completed the procedure, though all patients and their providers were given results of the screen regardless. From those colonoscopies, 24 patients (57% of positive screens) had polyps removed, and one patient was diagnosed with CRC (Table 2). Notably, several patients in the 2nd and 3rd years of the study expressed hesitance to receive a colonoscopy due to rising concerns over COVID-19.

A total of 140 participants (33%) who completed a FIT kit returned their postcard with feedback on drivers of screening completion. Most reported that the talking card helped them successfully complete their FIT kit, either alone or in combination with something else, including patient navigation, friend/family support, or other types of support ($n = 91$; 65%). The talking card in combination with follow-up patient navigation was cited by 29% ($n = 41$), and the talking card alone by 14% ($n = 20$), as the primary motivator(s) for FIT completion (Table 3).

4 Discussion

The purpose of this study was to explore the feasibility, acceptability and efficacy, of a novel audiovisual tool ("talking card") among mostly rural Kentucky residents. Stool-based testing, which includes the fecal occult blood test and FIT, is one of two USPSTF recommended (20) screening modalities for CRC screening, along with direct visualization (typically colonoscopy). Screening eligible individuals often cite barriers such as disgust (21), overall cost of the procedure (22), day of

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TABLE 2 Wellness event participation demographics.

	Year 1		Year 2		Year 3		Total	
	n	%	*n*	%	*n*	%	*N*	%
Eligible participants								
Completed FIT	161	87	140	65	124	62	425	67
Did not complete FIT	63	28	75	35	76	38	214	33
FIT screening results								
Negative	98	61	113	81	94	76	305	79
Positive	25	20	27	19	30	24	82	21
Follow-up colonoscopy	11	44	17	63	14	47	42	51
Polyps removed	7	64	12	71	5	36	24	57
Gender[a]								
Female	140	75	98	70	84	68	–	–
Male	46	25	42	30	40	32	–	–
Race/ethnicity[a,b]								
Black/African American	16	9	11	8	14	11	–	–
White	165	89	115	82	99	80	–	–
Hispanic/Latinx	4	2	8	6	9	7	–	–
Other	1	1	6	4	2	2	–	–
Participant insurance type[a,c]								
Private	71	38	–	–	62	50	–	–
Medicare	49	26	–	–	26	21	–	–
Medicaid	17	9	–	–	13	10	–	–
VA or government	4	2	–	–	–	–	–	–
Insured	–	–	116	83	–	–	–	–
Uninsured	9	5	19	14	11	9	30	11
No answer	36	19	5	4	12	10		
Counties reached[d]	39	33	49	41	35	29	73	61

$N = 601$. [a]Gender, race/ethnicity, and insurance data were each collected from all eligible participants in year 1 and from only FIT completers in years 2–3. [b]Percentages do not equal 100 because participants selected all that apply. [c]Year 2 data were only collected as insured/uninsured. [d]Percentage denominator is 120, the total number of Kentucky counties.

procedure requirements for transportation and requesting time off work (23), and fear and embarrassment (24) as common barriers to colonoscopy. The promotion of noninvasive stool-based modalities is particularly important in disparate populations that might be disproportionately impacted by these barriers.

Research has indicated that CRC interventions are most effective when they include multicomponent strategies that address multilevel barriers to screening uptake (25–27). The talking card represents a unique and contextually relevant implementation strategy to increase screenings among residents of Appalachian Kentucky, a region with unique barriers to CRC screening that may contribute to excess CRC mortality (28). Our early, but promising, feasibility and efficacy findings suggest that the talking card would add a strategic layer to improve CRC screening uptake in eastern Kentucky, a region with markedly higher CRC incidence and mortality (1, 2) and lower rates of screening (3). Even for people who may not have adequate health literacy to comprehend medical instructions (5), the talking card can provide clear and relatable audio and pictorial instructions to assist in FIT completion.

Primary care represents an ideal setting to promote CRC screening. The use of *inreach* strategies (29) in the primary care setting, such as patient and provider reminders or use of shared decision making aids, has been shown to be effective at increasing patient screening adherence (30, 31). Inreach focuses on providing cancer screenings to those who already utilize health care services (29) and often includes face-to-face discussions with clinicians to determine CRC screening need based on health history (30, 32). Because of this dedicated one-on-one time with patients, primary care physicians are uniquely positioned to assess patients presenting with CRC-related symptoms and recommend screening colonoscopy (33). In Appalachian Kentucky, these physicians often live in their communities, have developed years of rapport with their patients, and can easily fill this important role. Inreach alone, however, may not be sufficient in every clinical setting, making the use of population-based *outreach* (i.e., mailed FIT) also necessary for diagnosing CRC, particularly among asymptomatic patients or those do not regularly utilize health care services (33).

Ultimately, research suggests using a combination of strategies to augment both inreach and outreach is likely most effective at increasing population-based screening rates (29, 34). Outreach strategies in mailed FIT campaigns include phone calls, follow-up mailers, awareness campaigns, and mass media to reach individuals within the community who are less likely to use medical services consistently (35, 36). In eastern Kentucky, rural clinic personnel have

TABLE 3 Strategies that helped patients complete FIT.

	Year 1		Year 2		Year 3		Total	
	n	%	*n*	%	*n*	%	*N*	%
Post card returned[a]	51	32	58	41	31	25	140	33
Talking card alone	8	16	9	16	3	10	20	14
Talking card + patient navigation	19	37	17	29	5	16	41	29
Talking card alone *or* in combination with any other option[b]	34	67	36	62	21	68	91	65

Percentages do not equal 100 because participants could select more than one response. [a]Denominator refers to patients who completed FIT. [b]Other options included patient navigation, friend/family support and a generic "other" response.

cited time and workload concerns as barriers to promoting CRC screening (28), highlighting the need for outreach strategies in addition to any existing clinic-based inreach. Furthermore, combining multiple outreach strategies has been shown to increase FIT return rates more than using an isolated strategy (27, 37–39), a finding echoed in the present study where nearly two-thirds of participants in the efficacy component noted that the talking card combined with another strategy was most helpful for them in completing their FIT. Although it is not known which specific strategies (or number of strategies) would be most effective at increasing screening uptake in eastern Kentucky, our nascent findings suggest the talking card might be useful as an outreach (e.g., added to a mailed FIT campaign) strategy. Future research should focus on exploring the talking card's efficacy as an inreach strategy, such as being used by clinicians as a shared decision making tool to promote screening.

4.1 Limitations

Although we sought to evaluate the feasibility, acceptability, and efficacy of the talking card comprehensively and across multiple years among Kentucky residents, our findings should nonetheless be interpreted with a few limitations in mind. First, our efficacy testing was conducted in community settings. Screening promotion at community events tends to yield higher uptake than in clinical settings because these events often minimize barriers associated with health care settings (40), including cost. Additionally, individuals who attend health fairs tend to be more health-conscious generally, given that they willingly choose to attend these events, perhaps partly explaining why our FIT screening positivity rate was slightly higher than in other (mostly primary care-based) studies (41, 42). Future studies should consider testing the effectiveness of the talking card in population-based mailed FIT campaigns. Second, whereas screening adherence is critical to reduce late-stage CRC incidence and mortality, modification of risk behaviors is also necessary to prevent CRC; our study did not assess prevalence of risk behaviors, including diet or activity, in our participants, though attendees of the community events were provided educational pamphlets that described health promoting behaviors for preventing CRC. Third, our focus group findings utilized purposive sampling, and it is possible our participants' views were not representative of those of other individuals living in Appalachian Kentucky, though our study sample largely mirrored the demographic characteristics of Kentuckians as a whole; similarly, survey respondents might differ from nonrespondents in significant ways, including regarding health (and general) literacy. Fourth, the lack of a control group only allows us to make preliminary inferences on the efficacy of the talking card, and future studies should examine its effectiveness in a randomized controlled trial. Fifth, though our talking card represents an inexpensive strategy, costing just over $3 per card to produce, we were unable to collect return-on-investment data for the card; future studies should include a rigorous cost effectiveness analysis, particularly when it is used in primary care settings. Finally, an overwhelming majority of our participants reported having health insurance and at least one person they considered a primary care provider. It is possible, and likely, that both uninsured individuals and those who do not typically access health care services have different perceptions and needs related to CRC screening than the individuals who participated in this study. This possibility nevertheless underscores the importance of conducting population-based CRC screening outreach in Appalachian Kentucky.

5 Conclusion

Appalachian Kentucky residents have lower CRC screening rates (3) and subsequently higher CRC mortality (2) than non-Appalachian Kentuckians, necessitating attention to developing and testing strategies that might mitigate barriers and increase screening in this unique population. The talking card represents a novel strategy featuring the voices and images of local Appalachian CRC survivors to motivate and educate about CRC screening. Our findings suggest that Kentucky residents found the talking cards to be feasible, acceptable, and appropriate to promote screening, and our early findings suggest they are effective at increasing FIT return when distributed at community health events. Future research will focus on their utility at increasing screening uptake in clinical settings and in mailed FIT campaigns, particularly in rural, Appalachian regions of Kentucky.

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 University of Kentucky Institutional Review Board approved of all phases of this study in accordance with local legislation and institutional requirements. Focus group

participants provided written informed consent to participate in this study, and survey recipients provided implied consent via response. Efficacy testing data were determined to be Not Human Research by the University of Kentucky Institutional Review Board because all data were obtained by an outside organization as part of their standard operating procedure, and investigators had no access to personal health information or identifiers when viewing or analyzing data. Written informed consent was obtained from individuals for the publication of any potentially identifiable images or data included in this article.

Author contributions

AK-D: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Supervision, Writing – original draft, Writing – review & editing. DC: Writing – original draft, Writing – review & editing. EH: Conceptualization, Formal analysis, Methodology, Writing – original draft, Writing – review & editing. JE: Methodology, Writing – original draft, Writing – review & editing. SV: Methodology, Writing – original draft, Writing – review & editing. MK: Conceptualization, Data curation, Writing – original draft, Writing – review & editing. KB: Conceptualization, Data curation, Writing – original draft, Writing – review & editing. MR: Conceptualization, Data curation, Investigation, Writing – original draft, Writing – review & editing. ER: Conceptualization, Writing – original draft, Writing – review & editing. JK: Conceptualization, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, 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.

Publisher's note

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Enhanced skin cancer diagnosis through grid search algorithm-optimized deep learning models for skin lesion analysis

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Skin cancer is a widespread and perilous disease that necessitates prompt and precise detection for successful treatment. This research introduces a thorough method for identifying skin lesions by utilizing sophisticated deep learning (DL) techniques. The study utilizes three convolutional neural networks (CNNs)—CNN1, CNN2, and CNN3—each assigned to a distinct categorization job. Task 1 involves binary classification to determine whether skin lesions are present or absent. Task 2 involves distinguishing between benign and malignant lesions. Task 3 involves multiclass classification of skin lesion images to identify the precise type of skin lesion from a set of seven categories. The most optimal hyperparameters for the proposed CNN models were determined using the Grid Search Optimization technique. This approach determines optimal values for architectural and fine-tuning hyperparameters, which is essential for learning. Rigorous evaluations of loss, accuracy, and confusion matrix thoroughly assessed the performance of the CNN models. Three datasets from the International Skin Imaging Collaboration (ISIC) Archive were utilized for the classification tasks. The primary objective of this study is to create a robust CNN system that can accurately diagnose skin lesions. Three separate CNN models were developed using the labeled ISIC Archive datasets. These models were designed to accurately detect skin lesions, assess the malignancy of the lesions, and classify the different types of lesions. The results indicate that the proposed CNN models possess robust capabilities in identifying and categorizing skin lesions, aiding healthcare professionals in making prompt and precise diagnostic judgments. This strategy presents an optimistic avenue for enhancing the diagnosis of skin cancer, which could potentially decrease avoidable fatalities and extend the lifespan of people diagnosed with skin cancer. This research enhances the discipline of biomedical image processing for skin lesion identification by utilizing the capabilities of DL algorithms.

KEYWORDS

deep learning (DL), Convolutional Neural Network (CNN), grid search algorithm, binary classification, multiclass classification, skin cancer, skin lesions

1 Introduction

The body's largest organ, the skin (1), is the soft, flexible outer tissue separating a human body's internal systems and organs from its environment. It has a complex structure which is further divided into three layers: the epidermis, the dermis, and the hypodermis. It serves three major tasks: Protection, Sensation, and Regulation. It protects the body from heat, light, injury, and infection. It also assists in regulating the temperature of the human body (2) and serves as a sensory organ, providing a sense of touch to humans. As it covers the entire human body, it has a total surface area of 20 square feet, making it an essential human organ. Various internal and external factors, such as aging, sun exposure, infections, and injuries, lead to skin lesions (3). They are characterized as any anomaly in the skin's color, texture, or appearance, including lesions, lumps, or bumps. Based on the underlying causes, skin lesions can be categorized as infectious, neoplastic, or inflammatory. Skin lesions can be categorized based on their appearance and where they occur. A skin lesion can be categorized as benign or malignant (4) based on whether the lesion develops into cancer and spreads to other body parts. A lesion is considered benign when the cells do not invade other tissues and remain contained within the lesion. Malignant lesions contain cancerous cells that spread to other tissues and cause significant harm to the infected regions. Thus, it is essential to categorize skin lesions timely and accurate to detect whether a lesion is a form of skin cancer.

Skin cancer (5), the most common category of cancer (6), refers to abnormal cell duplication caused by DNA mutation. This condition results when the DNA of skin cells gets damaged due to UV rays (7) from the sun or artificial sources for prolonged periods. This leads to the damaged skin cells growing abnormally to form tumors. Skin cancer can be categorized into Basal Cell Carcinoma (BCC), Squamous Cell Carcinoma (SCC), and Melanoma (8). BCC and SCC are the two most frequent skin cancer types. BCC affects the basal cells of the lower part of the epidermis, causing lesions to be formed on the skin's surface. SCC is due to the abnormally increased development of squamous cells in the epidermis due to prolonged exposure to sunlight. The least common type of skin cancer, which is melanoma, is the most risky and invasive form of skin cancer with the highest probability of fatality. Also known as 'black tumor,' it accounts only for 1% of all cancers but is the cause of most significant of the demises caused by skin cancer. The WHO, in its 'World Cancer Report: Cancer Research for Cancer Development, (9) stated that every year, over 13 lakh cases of melanoma and around 25 lakh cases of non-melanoma are reported worldwide annually e, accounting for every third cancer diagnosis. Traditionally, examining the skin visually and doing a biopsy are conventional ways of finding skin lesions. The appearance of the skin lesion is commonly examined by a dermatologist, who may also study the lesion's anatomy using a dermatoscope, a portable magnifying instrument (10). A tissue sample is detached in biopsy and then sent to a laboratory for investigation to help identify the skin lesion's presence. Although these approaches are viable, they are laborious and arbitrary, resulting in many false positives and negatives. In medical image analysis (11), machine learning (ML) procedures (12), specifically DL architectures (13), have made significant advancements recently. DL is a kind of ML that uses massive datasets to train neural networks (NN) to recognize patterns and predict future outcomes. DLNNs, called Convolutional Neural Networks (CNNs), are exceptionally proficient at image identification and classification tasks. This research aims to develop a system of fully automated CNNs for multi-classifying skin lesions using datasets developed by ISIC (14). For this research, the classification of the images was divided into three Tasks. Three different CNNs were implemented for the three different classification Tasks. For Task 1, binary classification of images was carried out to ascertain whether Skin Lesions were detected. For Task 2, binary classification of images was carried out to ascertain whether the lesion detected was benign or malignant. For Task 3, multi-classification of images was carried out to confirm one of the seven types of skin lesions: Actinic Keratosis & Intraepithelial Carcinoma/Bowen's Disease (AKIEC), Basal Cell Carcinoma (BCC), Benign Keratosis-like Lesions (BKL), Dermatofibroma (DF), Melanoma (MEL), Melanocytic Nevi (NV), & Vascular Lesions (VASC). A separate dataset was created for each task taken from the ISIC Archive. The dataset is divided into two sets: train and test. After training, the performance of the proposed CNN models was evaluated. Performance evaluation was achieved using methods such as Loss Analysis, Accuracy Analysis, and Confusion Matrix. The Confusion Matrix (15) is a square table representation of the true labels and predicted labels of the images by a CNN model. It is used to derive various performance characteristics, including Accuracy, Precision, Recall/Sensitivity, F1 Score, and Specificity.

The significant contributions of this research are presented as follows:

- A CNN model-based approach is used to diagnose skin lesions. Three CNN models are presented for three classification tasks: detecting a skin lesion, determining if the lesion is benign or malignant, and categorizing the skin lesion by kind.
- To train and evaluate the proposed CNN models, images from the ISIC Archive were used to create three datasets with class-annotated images based on the three separate classification tasks. Data Augmentation was used to increase the variety of the datasets. The datasets were divided into two sets for training and testing the models.
- The CNN models' performance was assessed using Analysis Plots for Loss and Accuracy during training and testing and the Confusion Matrix. The Confusion Matrix is utilized to calculate performance metrics such as Accuracy, Precision, Recall/Sensitivity, and F1 Score, which provide a complete picture of the proposed CNN model for the intended classification job.

The remaining sections of the research paper are as follows: Section II explores previous research studies conducted in this domain. The methodology employed to carry out the proposed research is described in Section III. The results of the proposed study have been emphasized in Section IV. The concluding thoughts on the proposed research effort and its potential scope are provided in Section V.

2 Literature work

Dorj et al. (16) implemented an SVM to classify skin diseases. The authors utilized an AlexNet transfer learning (TL) model to extract features. The dataset employed for the study consisted of 3,753 images procured from the internet. The research achieved a classification accuracy of 92.3% for AKIEC, 91.8% for BCC, 95.1% for SCC, and 94% for MEL. Maron et al. (17) proposed using a customized CNN model with 112 dermatologists to classify skin diseases. The images were obtained from the HAM10000 dataset, supplemented with more images from the ISIC archive. The input dataset consisted of 11,444 dermatoscopic images of various skin-related diseases, including multiple types of skin lesions. Amin et al. (18) performed skin lesion segmentation by utilizing the Otsu algorithm. Pre-processing of images was performed to resize the images. The authors merged different datasets to generate a novel dataset of 7,849 images. A fusion of AlexNet and VGG16 features was implemented to classify images of MEL and BCC. The research attained an accuracy of 99%, sensitivity of 99.52%, and specificity of 98.41%. Hekler et al. (19) utilized images of MEL and NV to train and evaluate the ResNet50 TL model for examining label noise effects. The input dataset consisted of 804 images of MEL and NV procured from a combination of HAM10000 and ISIC Archive. Accuracy was evaluated for two types: For medical applications, the accuracy attained was 75%, and for biopsy, the accuracy achieved was 74%. The authors observed that the DL approach was extremely superficial and recommended biopsy-verified images to reduce the effect of label noise. Mahbod et al. (20) proposed a three-stage fusion technique combined with image downsampling and skin lesion cropping. The input dataset consisted of 12,927 dermatoscopic images of skin lesions. A CNN model was implemented to classify skin diseases. The research achieved an accuracy of 86.2%. However, the proposed research presented some limitations as significant training time was required for the many implemented sub-models. Han et al. (21) suggested a model for skin lesion classification. The dataset was formed by procuring dermoscopic skin lesion images from various hospitals, with 2,844 images. The RCNN architecture was implemented for classification into two categories based on the type of carcinoma detected, i.e., BCC and SCC. The research achieved an AUC score of 0.91. Masni et al. (22) proposed an analysis of TL models to classify three types of skin lesions. The dataset was taken using the ISIC 2017 dataset and consisted of 2,750 dermatoscopic images of skin lesions. A comparison between InceptionV3, ResNet50, Inception-ResNetV2, and DenseNet201 TL models was presented based on the classification of the dataset into NV, MEL, and AKIEC. The TL models' accuracies were: InceptionV3-−81.29%, ResNet50-−81.57%, Inception-ResNetV2-−81.34%, and DenseNet201–73.44%. Polat et al. (23) presented a CNN design to classify skin lesions into seven classes. The dataset, which consisted of a total of 10,015 images, was used for input. The CNN model attained 77% accuracy. Duggani et al. (24) employed a deep learning approach by proposing and implementing a customized CNN design to classify skin disease. The dataset consisted of 200 images from the PH2 dataset. The CNN design was utilized to categorize the dataset into two types: MEL and NV. The authors observed that the CNN model attained 97.49% accuracy. Khan et al. (25) employed a deep learning approach by proposing and implementing a customized CNN design. The dataset consisting of 10,015 dermatoscopic images of distinct types of skin diseases was employed for the research study. The CNN design was used to categorize the seven types: NV, DF, MEL, AKIEC, BKL, BCC, and VASC. The research achieved 87% accuracy, 86% sensitivity, 87.01% precision, and 86.28% F1 score. Shetty et al. (26) presented research on classifying images into seven distinct forms of skin lesions. The authors observed that a customized CNN model achieved an accuracy of 95.18%. Anand et al. (27) proposed an analysis of the VGG16 model and a modified VGG16 TL model with added multiple fine-tuning layers for skin lesion detection. The input dataset consisted of 3,297 images procured from the internet. Data augmentation techniques were implemented for diversifying the dataset. The models were implemented to classify the images between benign and malignant classes. Several hyperparameters were optimized and compared for better performance. The authors observed that the modified VGG16 TL model achieved 90% accuracy. Anand et al. (28) employed a TL approach by employing an Xception TL model for the detection of skin lesions. The HAM10000 dataset consisting of 10,015 images was utilized as the input dataset. Data Augmentation techniques were implemented on the input dataset for diversification. The Xception TL model classified the input dataset images into seven types of skin diseases and achieved 96.40% results. Aldhyani et al. (29) utilized the DL approach for skin disease detection by proposing and implementing a lightweight dynamic kernel CNN. The HAM10000 was utilized as the input. The proposed CNN model consisted of dynamic-sized kernels, significantly reducing the number of trainable parameters. The authors observed an accuracy of 97.85%, achieved by the proposed CNN model. Nigar et al. (30) designed and proposed an Explainable approach. The dataset employed in the research consisted of 25,331 images from the ISIC 2019. The suggested XAI system was executed to classify dermatoscopic images into eight distinct types of skin lesions.

3 Proposed methodology

This research study proposes a fully automated system of CNN models for ultimately detecting a skin lesion to classify a particular type of skin lesion using datasets developed from the ISIC Archive. This is achieved by dividing the classification of images into three Tasks. Figure 1 represents the flow chart of the suggested research for the complete diagnosis of skin lesions.

The first task involves binary classification of images to ascertain whether skin lesions are in the images of the first dataset or not. The second task involves binary classification of images to classify images of the second dataset based on whether the skin diseases are benign or malignant. The third task involves multiclass classification of benign/malignant skin lesions according to further specific types, as shown in Figure 1. For task 3, seven skin lesion classes are taken as Actinic Keratoses and Intraepithelial Carcinoma/Bowen's Disease (AKIEC), Basal Cell Carcinoma (BCC), Benign Keratosis-like Lesions (BKL), Dermatofibroma (DF), Melanoma (MEL), Melanocytic Nevi (NV),

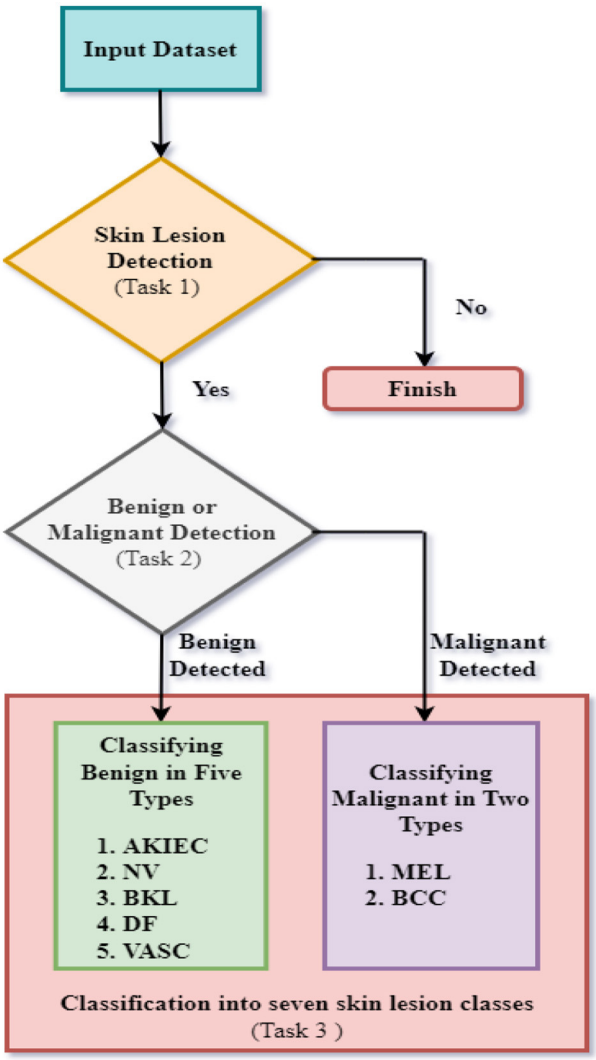

FIGURE 1
Flowchart for proposed methodology of complete diagnosis of skin lesions.

and Vascular Lesions (VASC). The three tasks are accomplished using three distinct CNN models for each task. The proposed CNN designs were trained and tested using images from three distinct datasets formed from the ISIC Archive. First, the classification of images of the first dataset was implemented for the detection of skin lesions utilizing the first proposed CNN architecture. Next, the second CNN design was implemented to categorize images of the second dataset to ascertain whether skin lesions are benign or malignant. Finally, the third CNN model was implemented to classify images into seven specific categories of benign/malignant skin lesions.

The use of three unique CNNs for three separate skin lesion classification tasks has several benefits: It is possible to tune each CNN for a specific task, enabling the customization of architecture and hyperparameter configurations to achieve optimal performance for the given classification problem. The pursuit of this specialism has the potential to enhance accuracy and increase the reliability of forecasts in many tasks. The use of a dedicated CNN for each task enables the model to concentrate on acquiring knowledge pertaining to the distinct characteristics associated with that particular activity while minimizing the influence of other tasks' intricacies. For instance, the CNN may be specifically constructed to differentiate between benign and malignant tumors by only emphasizing characteristics that are suggestive of malignancy. Rather than constructing a singular, intricate model to address various tasks, the use of distinct CNNs enables the development of more straightforward architectures that are more manageable and trainable.

Furthermore, this phenomenon may result in expedited training durations and reduced computational expenditures. The use of separate models for each task facilitates the comprehension of the decision-making process employed by each CNN. This may be of significant use in comprehending the behavior of the model, particularly in medical contexts where the capacity to provide explanations is of utmost importance. The use of distinct CNNs for various tasks may enhance the model's ability to generalize its performance over a wide range of datasets. This is because each network can effectively adapt to the unique intricacies and variations present in the data that are pertinent to its respective job. The use of distinct CNNs enables a modular methodology for the identification of skin lesions. Each model can undergo separate enhancements, updates, or replacements without causing any impact on the other models. This characteristic allows for flexibility in the maintenance and development of the system. The use of distinct CNNs for distinct tasks enables the isolation of errors in a particular model, hence facilitating the identification and resolution of difficulties within the classification process. Furthermore, this approach enables more focused debugging and improved refining of particular models.

3.1 Dataset description

The International Skin Imaging Collaboration (ISIC), with the primary aim of minimizing melanoma mortality through the facilitation of the administration of digital skin imaging, is an international bond between academics and the industry. The ISIC Archive archives readily accessible skin lesion images under the Creative Commons License. Dermoscopic images of specific skin lesions have been the archive's initial emphasis since they are intrinsically regulated due to the use of a specialized capture instrument and lack many of the privacy concerns of medical imaging. The images available through the archive are annotated with ground-truth diagnoses and further clinical metadata. This research study utilized annotated images from the ISIC Archive to form three distinct datasets for each classification task. The datasets contained various images for each task according to the classification tasks. The classes, number of images, and train-test splits for each classification task are presented in the following sub-sections.

The Classification Task 1 Dataset consisted of images labeled with two classes according to Classification Task 1, which involved the detection of skin lesions. Thus, the dataset images were labeled according to whether skin lesions were detected. The dataset

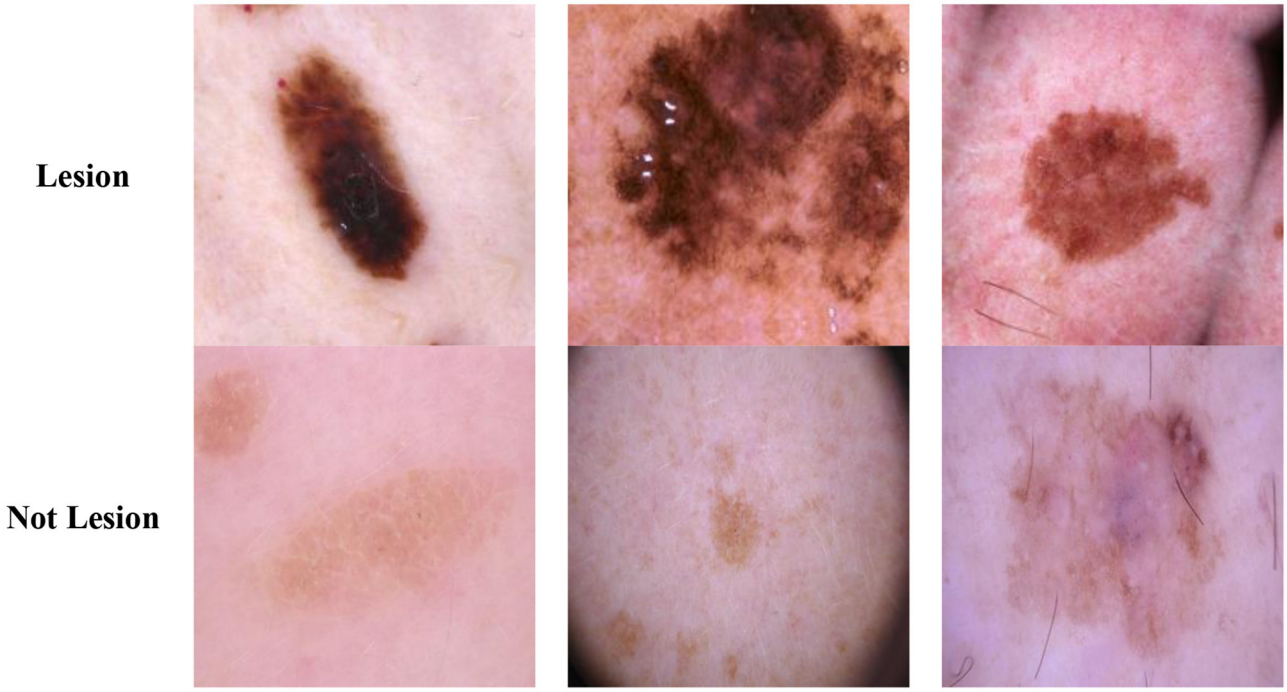

FIGURE 2
Classification task 1: skin lesion detection dataset images.

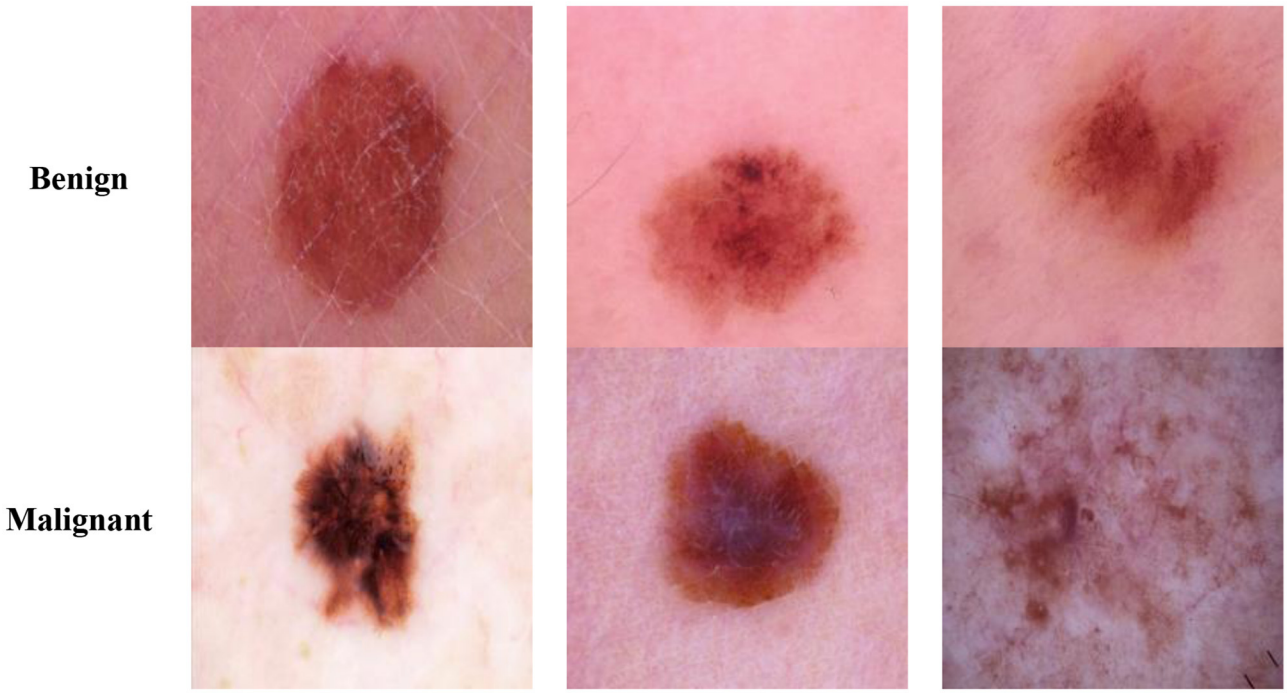

FIGURE 3
Classification task 2: classification of benign and malignant dataset images.

consisted of 17,806 images labeled Lesion and Not lesion. The input images' size was 224 by 224 pixels, and the number of channels was set at 3. The dataset was split into 12,464 images (70%) for the train set, 1,780 images (10%) for the validation set, and 3,561 images (20%) for the test set. Figure 2 displays the class labels for Classification Task 1 and some images from each class.

The Classification Task 2 Dataset consisted of images labeled with two classes according to Classification Task 2 for the

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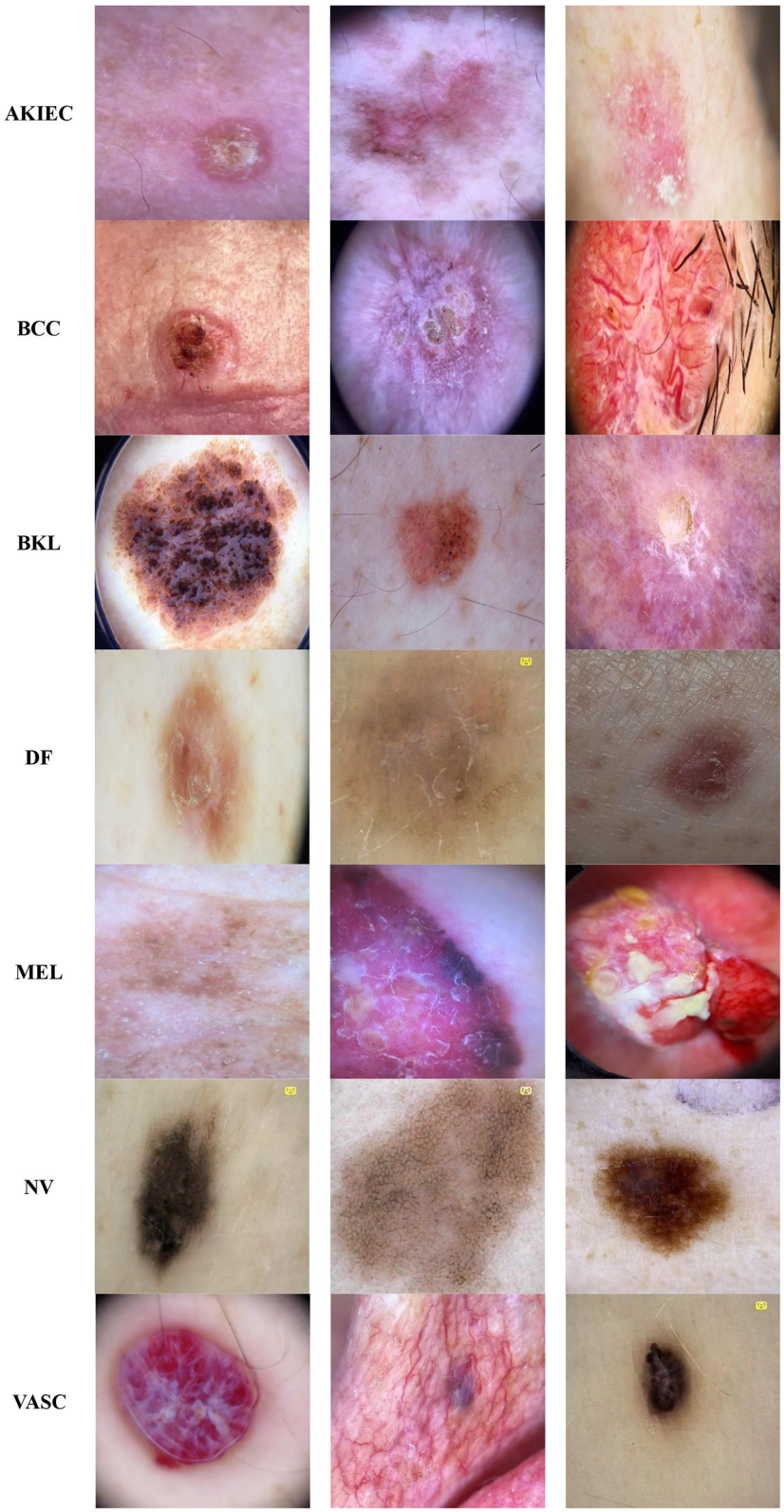

FIGURE 4
Classification task 3: benign/malignant skin lesion classification in seven classes dataset images.

TABLE 1 Number of skin lesion images for each dataset.

Classification task	Classification group	Number of images for each group	Total number of images
Classification 1	Lesion	8,903	17,806
	Not Lesion	8,903	
Classification 2	Benign	1,800	3,297
	Malignant	1,497	
Classification 3	AKIEC	6,696	46,935
	BKL	6,718	
	BCC	6,680	
	DF	6,658	
	MEL	6,692	
	NV	6,709	
	VASC	6,784	

classification of the skin lesions as Benign and Malignant. The dataset consisted of 3,297 images labeled with classes Benign or Malignant. The input images' size was 222 by 222 pixels, and the number of channels was set at 3. The database has been split into 2,307 images (70%) for the train set, 330 images (10%) for the validation set, and 660 images (20%) for the test set. Figure 3 displays the class labels for Classification Task 2 and some images from each class.

The Classification Task 3 Dataset consisted of images labeled with two classes according to Classification Task 3 to categorize the skin diseases into seven categories: AKIEC, BCC, BKL, DF, MEL, NV, & VASC. The dataset consisted of 46,935 images. The input images were 28 by 28 pixels, and the number of channels was 3. The dataset was split into three sets consisting of 30,508 images (65%) for training, 4,693 images (10%) for validation, and 11,734 images (25%) for testing. Figure 4 displays the class labels for Classification Task 3 and some images of skin lesions.

Table 1 represents the various classification groups for each classification task involved in complete skin disease detection. The Classification Groups, Number of images for each group, and the total number of images for specific classification tasks are highlighted for each classification task.

3.2 Data augmentation

Data Augmentation is modifying existing training data to generate new, synthetic training data. To enhance the volume of data available for training a network without collecting extra data, this is frequently employed in ML and DL (31). Data Augmentation provides various advantages, including improved model performance, reduced overfitting, robustness of models, and increased diversity. Data augmentation was performed on the ISIC datasets to improve their diversity. This research study diversifies the dataset by using rotate, zoom, horizontal flip, and vertical flip. This improves the training process of CNN models and enhances their performance. After augmentation, the datasets were split to form sets for training and testing the proposed CNN models. Some examples of the data augmentation techniques utilized in this research study are displayed in Figure 5.

3.3 Proposed CNN models

CNN is a popular DL model. A typical CNN architecture consists of two steps: feature extraction and classification. The CNN model extracts and varies features through five layers: the input, convolution, pooling, fully connected, and classification layers. CNN performs feature extraction and classification by deploying increasingly trainable layers stacked on each other. In the feature extraction phase of a CNN, convolutional and pooling layers are utilized, whereas fully connected classification layers are used in the classification phase. This paper proposed a system of three CNN models for three distinct classification tasks. The grid search technique was used to optimize the hyperparameters of each CNN model.

3.3.1 Proposed CNN model 1 for skin lesion detection

The first CNN model determines whether a patient's skin image contains a skin lesion, as it is designed to detect skin lesions. This classification is referred to throughout this article as Classification Task 1. Figure 6 illustrates the structure of the proposed CNN architecture 1, which includes 60 layers: 1 Input, 19 Convolutions, 19 ReLU, 19 Batch Normalization, 1 Global Average Pooling, and 1 Classification layer. The output layer consists of two neurons because the initial CNN architecture aims to classify an image into two categories. The SoftMax activation function uses the dense layer's input, a 2-D feature vector, to determine the presence or absence of a lesion.

Table 2 shows the model summary of the first CNN architecture. The model summary details the input image size, output image size, and the parameters of 1 Input Layer, 10 Convolutional Blocks, 1 Global Average Pooling, and 1 Dense layer. Convolutional Blocks 1–9 consist of 6 layers each: 1 Conv2D layer, 1 Depthwise Conv2D layer, 2 Batch Normalization layers, and 2 activation layers. Convolutional Block 10 consists of 3 layers: 1 Conv2D, 2 Batch Normalization layers, and 2 activation layers. The model consists of a total of 2,147,522 parameters. The parameters are split into trainable and non-trainable categories consisting of 2,133,826 parameters and 13,696 parameters, respectively.

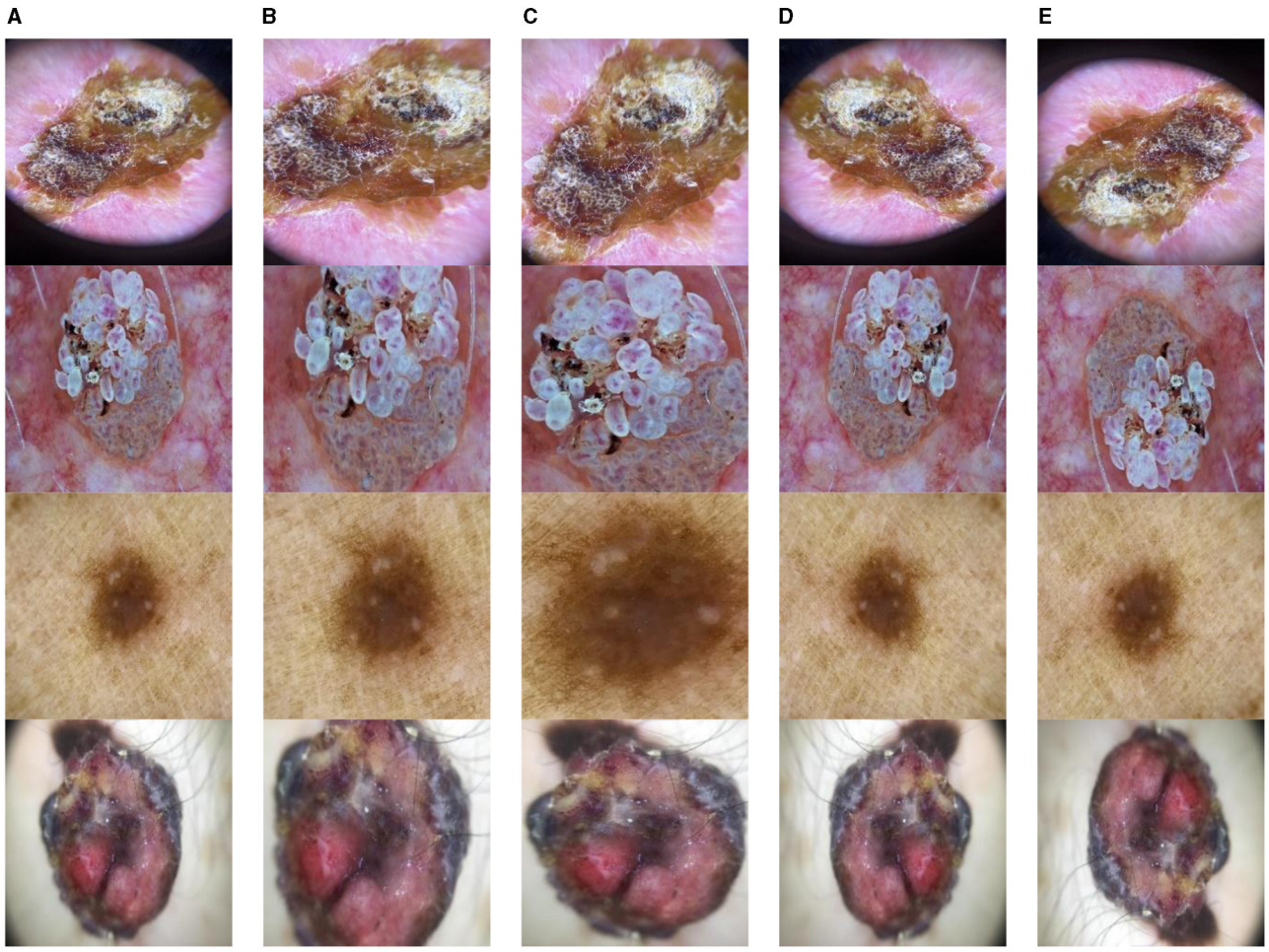

FIGURE 5
Data augmentation **(A)** original image, **(B)** rotate, **(C)** zoom, **(D)** horizontal flip, and **(E)** vertical flip.

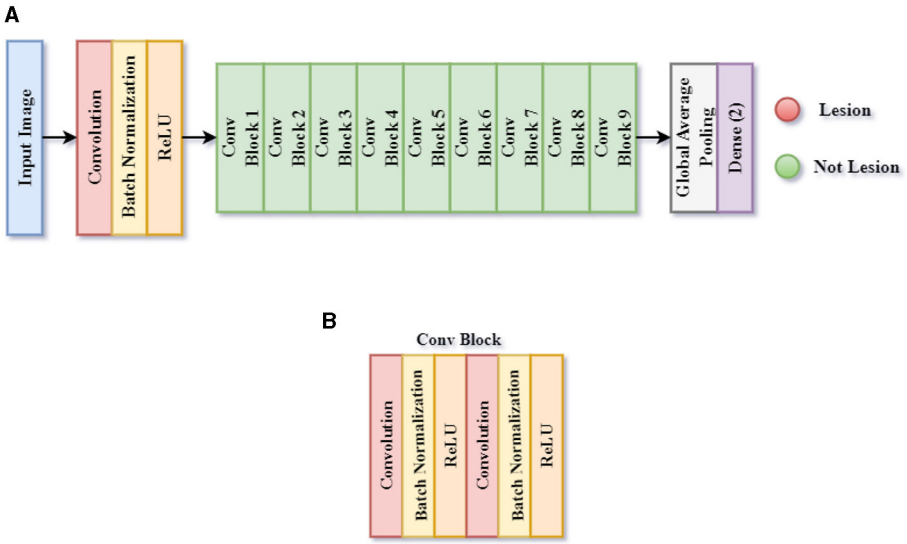

FIGURE 6
Framework of proposed CNN model 1 for skin lesion detection task 1. **(A)** CNN model 1, and **(B)** Conv block.

3.3.2 Proposed CNN model 2 for benign/malignant classification of skin lesions

The lesions can also be classified separately into Benign or Malignant. The third CNN model is used for the implementation of this classification. This classification is referred to as Classification Task 3 throughout the paper. As illustrated in Figure 7, the proposed CNN design for Classification Task 2 is comprised of 10 weighted layers: 1 Input, 4 Convolutional layers, 2 Max Pooling layers, 1 Dense layer, 1 Dropout layer, and 1 classification layer. As the CNN 2 model is simulated for the classification of an image into two classes, the output layer contains two nodes. The SoftMax activation function predicts the final lesion type after receiving a 2-D feature vector as input from the final dense layer.

The model summary of the second CNN design is highlighted in Table 3. The model summary provides information regarding the input image size, output image size, and parameters for 4 Conv2D layers, 2 MaxPooling layers, 1 Flatten layer, and 2 Dense layers. There are 2,881,314 parameters in the architecture. There are no non-trainable parameters, as every parameter is trainable.

TABLE 2 Model summary of proposed CNN model 1 for skin lesion detection.

Layer name	Input image size	Output image size	Number of parameters
Input layer	-	224 × 224 × 3	0
Convolutional block 1	224 × 224 × 3	112 × 112 × 32	1,408
Convolutional block 2	112 × 112 × 32	56 × 56 × 64	3,136
Convolutional block 3	56 × 56 × 64	56 × 56 × 128	10,368
Convolutional block 4	56 × 56 × 128	28 × 28 × 128	18,560
Convolutional block 5	28 × 28 × 128	28 × 28 × 256	37,120
Convolutional block 6	28 × 28 × 256	14 × 14 × 256	69,888
Convolutional block 7	14 × 14 × 256	14 × 14 × 512	139,776
Convolutional block 8	14 × 14 × 512	14 × 14 × 512	270,848
Convolutional block 9	14 × 14 × 512	14 × 14 × 1,024	541,696
Convolutional block 10	14 × 14 × 1,024	14 × 14 × 1,024	1,052,672
Global average pooling	14 × 14 × 1,024	1,024	0
Dense	1,024	2	2,050

3.3.3 Proposed CNN model 3 for classification of benign/malignant skin lesion in seven classes

The third CNN model is implemented for the classification of images into seven classes: AKIEC, BCC, BKL, DF, MEL, NV, and VASC. This classification is referred to as Classification Task 3 throughout the article. As shown in Figure 8, the proposed CNN design to Classify Task 3 consists of 24 weighted layers: 1 Input, 7 Convolutional layers, 7 Batch Normalization layers, 3 Max Pooling layers, 4 Dense layers, 1 Dropout layer, and 1 Classification layer. The output layer includes seven neurons since the third CNN design is intended to classify an image into seven classes. The SoftMax classifier creates the final lesion type prediction, which receives an input of a seven-dimensional feature vector from the last dense layer.

Table 4 presents the model summary of the third CNN design. The model summary details the input image size, output image size, and the parameters of 1 Input Layer, 4 Convolutional Blocks, 1 Flatten, 1 Dropout, 4 Batch Normalization, and 5 Dense layers. Convolutional Block 1 consists of 3 layers: 1 Conv2D, 1 MaxPooling2D, and 1 Batch Normalization layer. Convolutional Blocks 2 and 3 consist of 4 layers: 2 Conv2D, 1 MaxPooling2D, and 1 Batch Normalization layers. Convolutional Block 4 consists of 3 layers: 2 Conv2D and 1 MaxPooling2D layers. The model consists of a total of 1,275,079 parameters. The parameters are split into trainable and non-trainable categories consisting of 1,273,671 parameters and 1,408 parameters, respectively.

4 Experimental setup

Several obstacles have developed in the utilization of CNNs as their application in the discipline of medical imaging analysis has grown. More significant computational expenses are generated

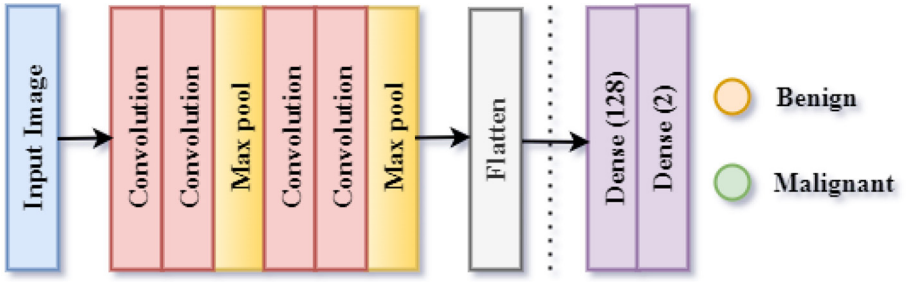

FIGURE 7
Framework of proposed CNN model 2 for benign/malignant lesion classification task 2.

when the designs, which are improved to produce more effective outcomes, become deeper and the input images become of better superiority. Utilizing robust hardware and tuning the hyper-parameters of the existing models are crucial for lowering these computing costs and producing superior outcomes. As a result, the suggested CNN models virtually all have their key hyper-parameters automatically adjusted using the grid search optimization approach. When the search space for the value range is limited, the grid search optimization method is a useful alternative to CNN hyper-parameter optimizations. Grid Search Optimization was therefore implemented in this research study for each classification task for optimizing the hyper-parameters of each of the suggested CNN architectures.

Furthermore, to scientifically validate the study's findings, analyzing the classification parameters to classify image research is essential. If not done properly, then the performance of the classification research remains without evidence and is thus academically insufficient. The performance of each proposed CNN model for the specified classification tasks of skin lesions was evaluated using several methods, such as the Loss Analysis Plot, Accuracy Analysis Plot, and Confusion Matrix.

TABLE 3 Model summary of proposed CNN model 2 for benign/malignant classification of skin lesions.

Layer name	Input image size	Output image size	Number of parameters
Input layer	-	222 × 222 × 3	0
Conv2D	222 × 222 × 3	222 × 222 × 16	448
Conv2D	222 × 222 × 16	220 × 220 × 16	2,320
MaxPooling2D	220 × 220 × 16	110 × 110 × 16	0
Conv2D	110 × 110 × 16	108 × 108 × 8	1,160
Conv2D	108 × 108 × 8	106 × 106 × 8	584
MaxPooling2D	106 × 106 × 8	53 × 53 × 8	0
Flatten	53 × 53 × 8	22,472	0
Dropout	22,472	22,472	0
Dense	22,472	128	2,876,544
Dense	128	2	258

4.1 Hyperparameter optimization using grid search

To identify the ideal set of hyperparameters for proposed CNN models, the Grid Search Optimisation method has been used for hyperparameter optimization. Values for hyperparameters are predetermined prior to the beginning of the process of learning as they cannot be inferred solely from the data (32). Architectures for CNN models are relatively complex and contain many hyperparameters. To enhance the performance of proposed models, two types of hyperparameters are tuned, i.e., Architectural hyperparameters and fine modification hyperparameters. Architectural hyper-parameters include the convolutional layers, pooling layers, fully connected layers, and the activation function. In contrast, Batch size and learning rate, conversely, are referred to as acceptable alterations of hyper-parameters. In grid search, a grid of potential results for the hyperparameters mentioned above is first defined, and the CNN

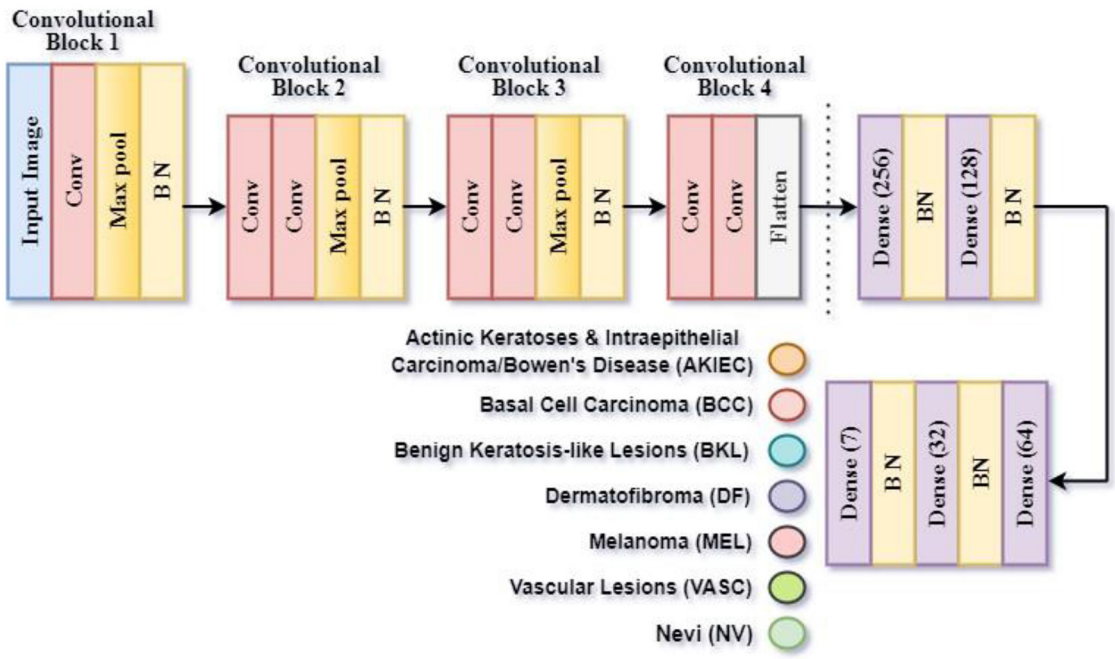

FIGURE 8
Framework of proposed CNN model 3 for classification task 3 of benign/malignant skin lesion classification in seven classes.

TABLE 4 Model summary of proposed CNN model 3 for classification of benign/malignant skin lesion in seven classes.

Layer Name	Input Image Size	Output Image Size	Number of Parameters
Input layer	-	28 × 28 × 3	0
Convolutional block 1	28 × 28 × 3	14 × 14 × 32	1,024
Convolutional block 2	14 × 14 × 32	7 × 7 × 64	55,680
Convolutional block 3	7 × 7 × 64	3 × 3 × 128	221,952
Convolutional block 4	3 × 3 × 128	1 × 1 × 256	885,248
Flatten	1 × 1 × 256	256	0
Dropout	256	256	0
Dense + batch normalization 1	256	256	66,816
Dense + batch normalization 2	256	128	33,408
Dense + batch normalization 3	128	64	8,512
Dense + batch normalization 4	64	32	2,208
Dense	32	7	231

TABLE 5 Optimum hyper-parameters results achieved by grid search of proposed CNN model 1 for skin lesion detection task.

Hyper parameters	Hyper parameter range	Optimized value
Convolution layers	[13–19]	19
Global average pooling layer	[1–4]	1
Fully connected layers	[1–4]	1
Activation function	[ReLU, Softmax, Sigmoid, Leaky ReLU]	ReLU, Softmax
Batch size	[16, 64, 128]	64
Learning rate	[0.0001, 0.01, 0.001, 0.00001]	0.01
Number of epochs	[10, 20, 30, 40, 50]	30

model is then trained with all feasible combinations to ascertain which combination produces the greatest performance.

The stages involved in grid search optimization for CNN models are as follows:

1. Hyperparameter grid formation: for each hyperparameter that is to be optimized, a range of possible values is set.
2. Potential combination generation: all potential combinations of hyperparameters are generated from the range of values in the formed grid.
3. Model evaluation: the proposed model is implemented using each potential combination of the hyperparameters, and its performance is evaluated.
4. Determination of optimized hyperparameter combination: the hyperparameter combination with the best results is determined.
5. Utilization of optimized hyperparameters: the proposed design is retrained and implemented with the optimized hyperparameters derived from the grid search.

TABLE 6 Optimum hyper-parameters results achieved by grid search of proposed CNN model 2 for benign/malignant classification of skin lesions.

Hyper parameters	Hyper parameter range	Optimized value
Convolution layers	[1–4]	4
Max pooling layers	[1–4]	2
Fully Connected layers	[1–4]	2
Activation function	[ReLU, Softmax, Sigmoid, Leaky ReLU]	ReLU, Sigmoid
Batch size	[16, 64, 128]	64
Learning rate	[0.0001, 0.01, 0.001, 0.00001]	0.001
Number of epochs	[10, 20, 30, 40, 50]	30

TABLE 7 Optimum hyper-parameters results achieved by grid search of proposed CNN model 3 for classification of benign/malignant skin lesions in seven classes.

Hyper parameters	Hyper parameter range	Optimized value
Convolution layers	[3–9]	7
Max pooling layers	[1–4]	3
Fully connected layers	[2–5]	5
Activation function	[ReLU, Softmax, Sigmoid, Leaky ReLU]	ReLU, Softmax
Batch size	[16, 64, 128]	64
Learning rate	[0.0001, 0.01, 0.001, 0.00001]	0.001
Number of epochs	[10, 20, 30, 40, 50]	30

The Grid Search Optimization for each classification task has been shown in Tables 5–7. Table 5 shows the optimized hyperparameters derived from the grid search of the first proposed CNN model implemented for the detection of Skin Lesions.

Table 6 shows the optimized hyperparameters derived from the grid search of the second proposed CNN model implemented for the classification of Skin Lesions as Benign or Malignant.

Table 7 shows the optimized hyperparameters derived from a grid search of the third proposed CNN model implemented for the Classification of Benign/Malignant Skin Lesions in seven distinct classes.

The optimized values of hyperparameters derived from the grid search algorithm are finally used to simulate and evaluate the CNN models for different categorization tasks.

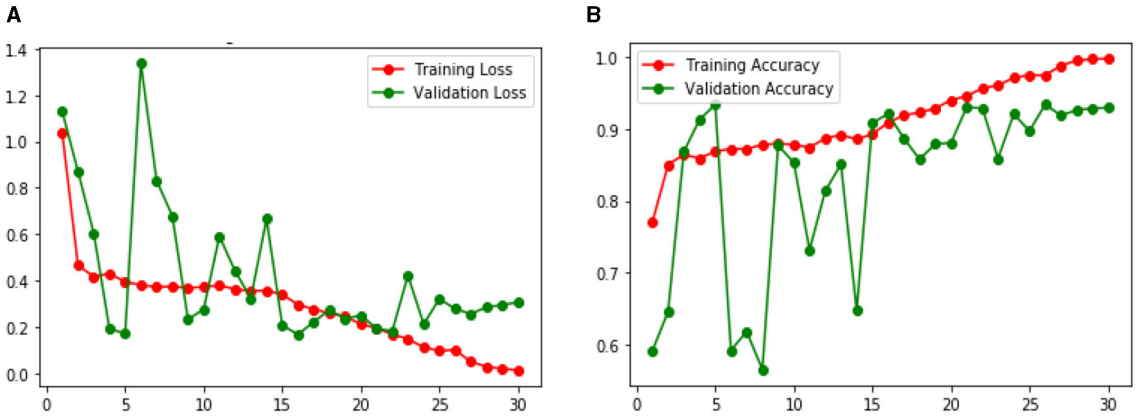

FIGURE 9
Results of proposed CNN model 1 for classification task 1 **(A)** Loss analysis plot, and **(B)** accuracy analysis plot.

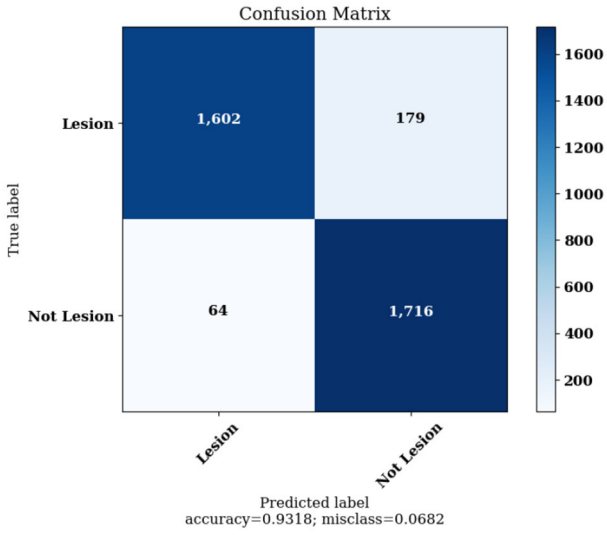

FIGURE 10
Confusion matrix achieved for classification task 1.

4.2 Results

Analyzing the performance of classification research is essential to validate the study's findings scientifically. If not done properly, then the performance of the classification research remains without evidence and is thus academically insufficient. This research evaluates the performance of the CNN models implemented for the three Classification Tasks using Analysis Plots of Loss and Accuracy and Confusion Matrices. These give an overall summary of the performance of the CNN models by providing information regarding learning rate and overfitting during training and performance parameters such as Accuracy, Precision, Recall, and F1 Score during the model implementation on the test sets.

The Loss and Accuracy Analysis Plots are used to determine several parameters observed during the training of the CNN models. The Loss Analysis Plot highlights the loss of a model during the training and validation phase. It is used to observe whether the model had a good learning rate. The Accuracy Analysis Plot highlights the accuracy of a model during the training and validation phase. The gap between the training accuracy plot and validation accuracy plot represents whether a problem of overfitting had occurred.

A table used to assess the efficiency of a classification design is referred to as a confusion matrix or error matrix. It is a multi-dimensional matrix that displays the actual and predicted class labels for each piece of data in a classification task's summary results.

4.2.1 Performance of CNN model 1 for skin lesion detection

Figure 9 shows the Loss and Accuracy Analysis Plots obtained by the first CNN model for Classification Task 1. Figure 9A highlights the loss incurred by the proposed CNN model during the training and validation phase. The training loss was 0.10, and the validation loss was observed to be 0.28. It can be seen that since the slope of the training and validation plots is exponentially decreasing, the model had a good learning rate. Figure 9B highlights the accuracy obtained by the proposed CNN model for the training and validation phase. The training accuracy achieved by the design was observed as 0.98, and the validation accuracy was observed as 0.93. Since the gap between the training and validation accuracy is low, negligible overfitting in the model is represented.

Figure 10 highlights the Confusion Matrix the CNN for Classification Task 1 formed. For classification task 1, the confusion matrix is a two-dimensional matrix that indicates the predictions made by the model for classifying images into two classes, detecting whether the image contains skin lesions or not.

4.2.2 Performance of CNN model 2 for benign/malignant classification of skin lesions

Figure 11 shows the Loss and Accuracy Analysis Plots obtained by the second CNN model for Classification Task 2. Figure 11A

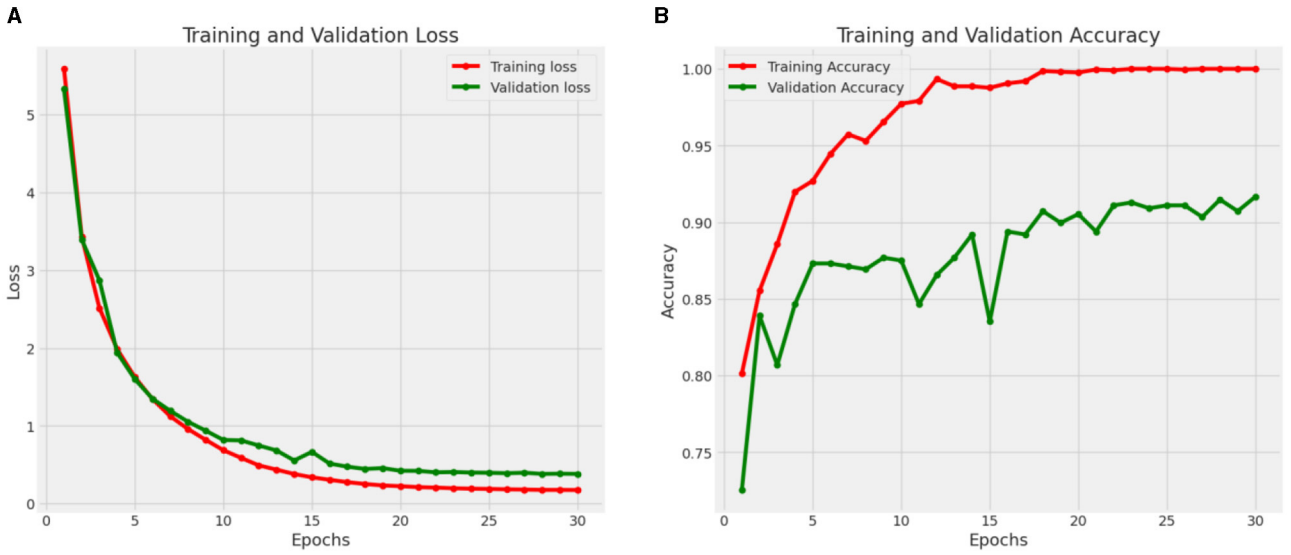

FIGURE 11
Results of proposed CNN model 2 for classification task 2. **(A)** Loss analysis plot, and **(B)** accuracy analysis plot.

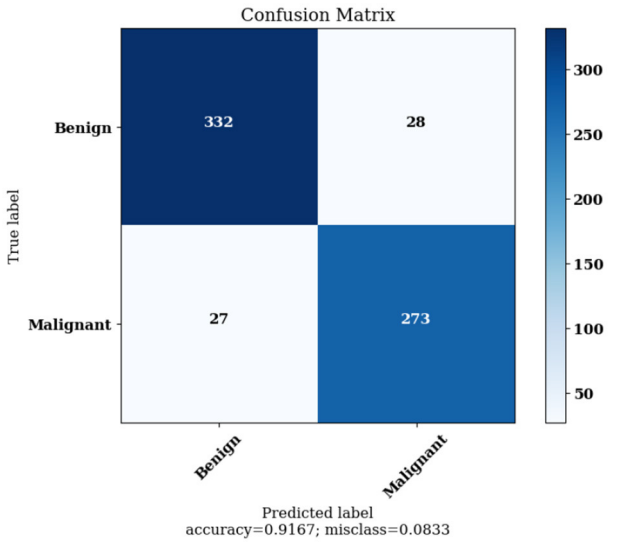

FIGURE 12
Confusion matrix achieved for classification task 2.

highlights the loss incurred by the proposed CNN model during the training and validation phase. The training loss was 0.10, and the validation loss was 0.21. It can be observed that since the slope of the training and validation plots is exponentially decreasing, the model had a good learning rate. Figure 11B highlights the accuracy obtained by the proposed CNN model during the training and validation phase. The training accuracy achieved by the model was observed as 0.98, and the validation accuracy was observed as 0.92. Since the gap between the training and validation accuracy is low, negligible overfitting in the model is represented.

Figure 12 highlights the Confusion Matrix the CNN for Classification Task 2 formed. For classification task 2, the confusion matrix is a two-dimensional matrix that indicates the predictions made by the model for classifying images into two classes, showing whether the lesion detected is benign or malignant.

4.2.3 Performance of CNN model 3 for classification benign/malignant skin lesions in seven classes

Figure 14 shows the Loss and Accuracy Analysis Plots obtained by the third CNN model for Classification Task 3. Figure 13A highlights the loss incurred by the proposed CNN model during the training and validation phase. The training loss was 0.07, and the validation loss was 0.11. It can be seen that since the slope of the training and validation plots is exponentially decreasing, the model had a good learning rate. Figure 13B highlights the accuracy obtained by the proposed CNN model during the training and validation phase. The training accuracy achieved by the model was observed as 0.99, and the validation accuracy was observed as 0.98. Since the gap between the training and validation accuracy is low, negligible overfitting in the model is represented.

Figure 14 highlights the Confusion Matrix the CNN for Classification Task 3 formed. For classification task 3, the confusion matrix is a multi-dimensional matrix that indicates the predictions made by the model for the classification of images into seven classes according to the type of lesion detected. The scale of 0 to 6 on the x-axis and y-axis represents the classes for classification task 3, which are as follows: 0 for AKIEC, 1 for BCC, 2 for BKL, 3 for DF, 4 for MEL, 5 for NV, and 6 for VASC.

The Confusion Matrices displayed in Figures 10, 12, 14 are utilized to analyze specific metrics for each CNN model implemented for the classification tasks. Table 8 represents

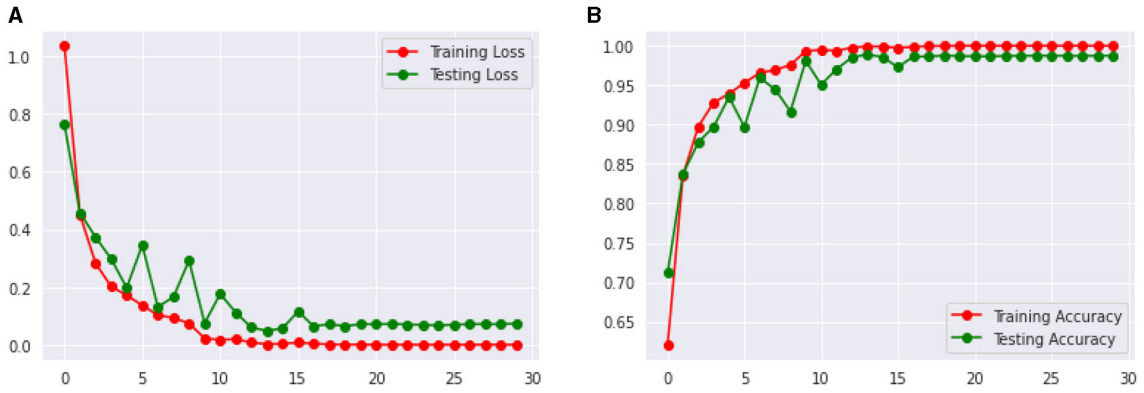

FIGURE 13
Results of proposed CNN model 3 for classification task 3. **(A)** Loss analysis plot, and **(B)** accuracy analysis plot.

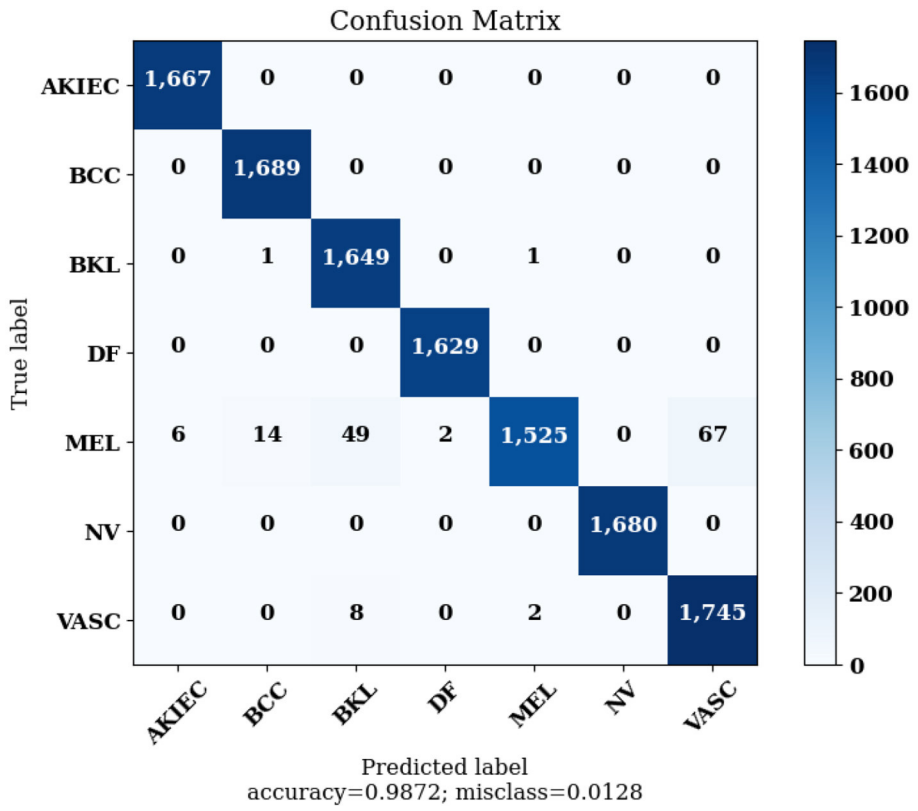

FIGURE 14
Confusion matrix achieved for classification task 3.

Confusion Matrix values for each class of each classification task and the evaluated performance metrics, including Precision, Recall, F1 Score, and Accuracy.

As seen from Table 8, each of the CNN models achieved excellent performance. CNN model 1 simulated the detection of skin lesions and achieved an accuracy of 93.18%. CNN model 2 for the Benign/Malignant Skin Lesions classification attained an accuracy of 91.67%. CNN model 3 for Classification of Benign/Malignant Skin diseases in Seven Classes achieved an accuracy of 98.72%.

4.2.4 Comparative result analysis of hyperparameter optimisation using grid search

To validate the implementation of the Hyperparameter Optimisation using the Grid Search technique employed in this study, Table 9 presents a comparative analysis of the results obtained for the three classification tasks by the CNN models without and with the implementation of the Grid Search technique. A comparison of the aggregate of the performance metrics Precision, Recall, Specificity, F1 Score, and Accuracy is presented for each classification task.

TABLE 8 Performance metrics for detection and classification of skin lesions.

CNN Model	Classes	TP	TN	FP	FN	Precision	Recall/ Sensitivity	Specificity	F1 Score	Accuracy
CNN Model 1	Lesion	1,602	1,716	64	179	0.96	0.91	0.96	0.93	93.18%
	Not Lesion	1,716	1,602	179	64	0.90	0.96	0.90	0.93	
CNN Model 2	Benign	332	273	27	28	0.93	0.92	0.91	0.92	91.67%
	Malignant	273	332	28	27	0.90	0.91	0.92	0.90	
CNN Model 3	AKIEC	1,667	9,917	6	0	1	1	0.99	1	98.72%
	BCC	1,689	9,895	15	0	0.99	1	1	1	
	BKL	1,649	9,935	49	2	0.98	0.99	0.99	0.99	
	DF	1,629	9,955	2	0	1	1	1	1	
	MEL	1,525	1,0059	3	138	0.99	0.92	1	0.95	
	NV	1,680	9,904	0	0	1	1	1	1	
	VASC	1,745	9,839	67	10	0.95	0.99	0.99	0.97	

TABLE 9 Comparison of results for hyperparameter optimization using grid search.

	Without hyperparameter optimisation					Hyperparameter optimisation using grid search				
CNN model	Precision	Recall	Specificity	F1 Score	Accuracy	Precision	Recall	Specificity	F1 Score	Accuracy
CNN model 1	0.88	0.86	0.86	0.87	86.73%	0.93	0.94	0.93	0.93	93.18%
CNN model 2	0.82	0.84	0.81	0.83	83.42%	0.91	0.92	0.92	0.91	91.67%
CNN model 3	0.85	0.84	0.83	0.85	85.61%	0.99	0.98	1	0.99	98.72%

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TABLE 10 Comparison of proposed work with related studies.

References	Classification type	Dataset utilized	Number of images	Technique implemented	Accuracy achieved
Cassidy et al. (14)	AKIEC BCC MEL SCC	Internet	3,753	AlexNet	AKIEC = 92.3% BCC = 91.8% MEL = 94.2% SCC = 95.1%
Liang (15)	AKIEC BCC BKL NV MEL	HAM10000 ISIC Archive	11,444	CNN	$p<0.001$
Dorj et al. (16)	MEL BCC	PH^2 ISIC 2016 Challenge ISIC 2018 Challenge	7,849	Feature Fusion between AlexNet & VGG16	99%
Maron et al. (17)	MEL NV	HAM10000 ISIC Archive	804	ResNet50	75.03%
Polat and Koc (23)	AKIEC BCC BKL DF MEL NV VASC	HAM10000	10,015	CNN	86.5%
Duggani and Nath (24)	AKIEC BCC BKL DF MEL NV VASC	HAM10000	10,015	CNN	95.18%
Khan et al. (25)	Benign Malignant	Internet	3,297	VGG16	89.09%
Shetty et al. (26)	AKIEC BCC BKL DF MEL NV VASC	HAM10000	10,015	Xception	96.40%
Anand et al. (27)	AKIEC BCC BKL DF MEL NV VASC	HAM10000	10,015	Lightweight Dynamic Kernel CNN	97.85%
Anand et al. (28)	AKIEC BCC BKL DF MEL NV VASC SCC	ISIC 2019 Challenge	25,331	XAI	94.47%
Proposed Work	Lesion Not lesion, Benign Malignant, AKIEC BCC BKL DF MEL NV VASC	ISIC Archive	17,806 3,297 46,935	CNN Model 1 CNN Model 2 CNN Model 3	93.18% 91.67% 98.72%

As observed from Table 9, using Grid Search for Hyperparameter Optimisation leads to significantly better results throughout all performance metrics when compared to no implementation of hyperparameter optimization. Using Grid Search leads to consistently high performance metrics thus validating the performance of the models for each classification task further.

4.2.5 Comparison of proposed work with related studies

Table 10 highlights the comparison of the proposed work in this research study. The various studies are compared based on several categories, including Classification Type, Dataset Utilized, Number of Images, Technique Implemented, and Accuracy Achieved.

5 Conclusion and future work

Modern advancements in deep learning have led to the expansion of machine learning research and study beyond feature engineering to architectural engineering. This study presents a system of CNN models for comprehensive skin lesion diagnosis. Three robust CNN architectures were presented for three skin lesion classification tasks involving the classification of a skin lesion, determining whether a lesion is benign or malignant, and classifying the skin lesion by type. Annotated images from the ISIC Archive were utilized to form three distinct datasets for each classification task. For each task, the datasets contained various images according to the classification tasks. Grid Search optimization was implemented in each of the proposed CNN models to optimize the hyperparameters and obtain the best results. The detection of skin lesions was performed with an accuracy of 93.18 percent. In addition, the classification of skin lesions based on whether they were benign or malignant was obtained with an impressive 91.67 percent accuracy. The classification of cutaneous lesions into seven distinct categories was accomplished with a high degree of precision (98.72%). The results and performance of the proposed CNN models demonstrate the effectiveness of deep-learning approaches for Skin lesion classification. This research study proposes CNN models that can be used to aid dermatologists with initial skin lesion classification screening. Although the primary emphasis of the study was on CNN models, it is suggested that future research should consider investigating more sophisticated models, such as Transformers or hybrid architectures that integrate CNNs with Recurrent Neural Networks (RNNs) or attention techniques. The designs mentioned above have shown potential in several fields and might potentially enhance the precision and resilience of skin lesion data categorization. The integration of other data sources, such as histopathology pictures, patient medical history, or genetic information, has the potential to augment the efficacy of the model by offering a comprehensive perspective on the patient's medical state. The use of a multimodal approach has the potential to enhance the precision and customization of diagnostic instruments. Future research endeavors may prioritize the adaptation of these models to facilitate their real-time implementation inside clinical environments. Potential areas of focus may include the creation of interfaces that are intuitive and easy to use for dermatologists, as well as the incorporation of pre-existing medical imaging technologies. The validation of the efficacy of these models in real-world contexts via the implementation of clinical trials is crucial for the successful shift from research to practical application. Future research endeavors may prioritize the adaptation of these models to facilitate their real-time implementation inside clinical environments. Potential areas of focus may include the creation of interfaces that are intuitive and easy to use for dermatologists, as well as the incorporation of pre-existing medical imaging technologies. The validation of the efficacy of these models in real-world contexts via the implementation of clinical trials is crucial for the successful shift from research to practical application. The use of explainability approaches such as Grad-CAM or SHAP has the potential to improve the interpretability of CNN models, hence enhancing their reliability and facilitating their integration into clinical practice. Implementing this approach would enable healthcare practitioners to comprehend the underlying rationale behind the model's predictions, hence enhancing their trust in the outcomes.

Data availability statement

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

Author contributions

RP: Writing – original draft, Methodology, Resources, Writing – review & editing. NS: Writing – review & editing, Software. SG: Writing – review & editing, Investigation, Methodology, Project administration. DG: Investigation, Validation, Writing – original draft. SJ: Methodology, Supervision, Writing – review & editing. SM: Funding acquisition, Resources, Software, Visualization, Writing – review & editing. HQ: Data curation, Funding acquisition, Methodology, Project administration, Resources, Writing – review & editing. MA: Validation, Writing – review & editing. AK: Validation, Writing – review & editing.

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Conflict of interest

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

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Breaking barriers: enhancing cancer detection in younger patients by overcoming diagnostic bias in primary care

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Introduction

The issue of diagnostic bias within primary care has profound implications for the early detection of cancer, particularly among younger patients. Diagnostic bias refers to the preconceived notions and assumptions that influence a clinician's judgment, potentially leading to misdiagnosis or delayed diagnosis (1). Early diagnosis of cancer is critical for effective treatment and improved prognostic outcomes, making the recognition and mitigation of diagnostic biases an essential component of primary care practice.

Cancer incidence and mortality in adults under 50 years of age has been rising globally in the decades since 1990, especially in more highly-developed countries (2). This trend has occurred in the UK, and 9% of new cancer cases are diagnosed in those aged 25–49 (a rise in incidence of 22% from 1993 to 2019, total incidence 164.6 per 100,000 25–49 year olds in 2019), predominantly affecting women (Tables 1, 2) (3). Whilst this trend may partially be due to increasing access to investigations and improved diagnostic capabilities, it has been suggested that the rising incidence is also partly attributable to the oncogenic effects of rising obesity, rising alcohol consumption, and new dietary and environmental exposures (4).

Primary care physicians are often the first point of contact for patients, positioning them uniquely to detect early signs of cancer. However, the age-related bias that younger patients are less likely to have serious conditions such as cancer can lead to significant delays in diagnosis (1, 5). This is especially concerning given that certain cancers in young patients can be more aggressive and progress rapidly, such as in breast cancer (6). Therefore, the main argument posited in this view point is that primary care physicians must actively work to overcome diagnostic biases that impede the early detection of cancer in younger patients.

Diagnostic bias in younger patients

Diagnostic bias toward younger patients has the potential to lead to significant delays in identifying serious conditions such as cancer. Interviews with young adults with cancer, revealed that in many cases the patient and/or the clinician assumed it unlikely they would have cancer due to their age, resulting in delayed diagnosis in most cases (7). This bias is even noted in cancer investigation clinical guidance, with many guidelines having strict age cut-offs for investigating certain symptoms, such as under the UK's 2-week wait pathways (although some do contain overriding caveats for serious clinician

TABLE 1 Cancer incidence rates per 100,000 population per year, subdivided by age group, in males and females aged 25–49 in the UK, from 2017–2019.

Age	Male	Female
Cancer incidence rate per 100,000 population per year		
25–29	47.1	70.3
30–34	67.0	119.7
35–39	90.7	177.4
40–44	126.9	268.6
45–49	215.4	418.0

TABLE 2 Percentages of different types of cancer as a proportion of the total incidence of new cancer diagnoses, in males and females aged 25–49 in the UK, from 2017–2019 (data from Cancer Research UK; N.B. all data excludes non-melanoma skin cancer) (3).

Male	Female
Proportion of cancer incidence per type in 25–49 Year Olds	
Testicular cancer 14%	Breast cancer 43%
Bowel cancer 11%	Melanoma 9%
Brain, central nervous system, or other intracranial cancer 10%	Cervical cancer 8%
Melanoma 10%	Thyroid 6%
Head and neck cancer 7%	Brain, central nervous system, or other intracranial cancer 6%
Other types of cancer 52%	Other types of cancer 32%

concern) (8). Younger individuals presenting with atypical symptoms can be presumed by clinicians to have benign conditions (9), a presumption likely rooted in the significantly lower statistical prevalence of cancer within this demographic, (5, 10)something elsewhere termed epidemiological optimism bias (11). This bias is further exacerbated by the tendency of some primary care physicians to prioritize more common and less severe diagnoses (6). Studies have demonstrated that general practitioners are less likely to suspect malignancy in younger patients, which can result in delays in diagnosis and treatment (10, 12).

Research indicates that when younger patients present with symptoms such as unexplained weight loss, persistent pain, or unusual lumps, these signs are often attributed to benign causes like stress, infections, or minor injuries. For instance, a study by Dommett et al. (10) found that the likelihood of cancer being initially misdiagnosed in younger individuals was substantially higher compared to older adults. This misdiagnosis often leads to multiple consultations and a significant delay before appropriate investigations are conducted.

A notable example is the misdiagnosis of Hodgkin lymphoma in younger patients, which often presents with non-specific symptoms such as fatigue, fever, and lymphadenopathy. A delay in recognizing these symptoms as potential indicators of cancer can severely impact prognosis (10, 13). Similarly, younger patients with colorectal cancer often have a delay in diagnosis (14), due to both patient and doctor delay, and in some cases can also receive misdiagnosis as common benign conditions, such as hemorrhoids (15).

The tendency to overlook serious conditions in younger patients highlights the urgent need for heightened awareness and consideration of cancer as a differential diagnosis. Studies such as those by Lyratzopoulos et al. (16) have underscored the importance of considering a wider range of potential diagnoses to prevent delays that can compromise treatment outcomes. By recognizing and challenging these biases, we hope primary care physicians can improve diagnostic accuracy and ensure more timely intervention, ultimately enhancing patient care and survival rates.

Importance of differential diagnosis and appropriate investigation

The necessity of considering cancer as a potential diagnosis in younger patients cannot be overstated. When cancer is not included as a differential diagnosis, critical time may be lost, leading to more advanced disease stages at the time of diagnosis. This delay can diminish the efficacy of treatment and worsens patient prognosis, making early and accurate diagnosis paramount (10, 11, 17). For example, a study by Swann et al. (18) reflects that delayed cancer diagnosis in younger patients often results in more aggressive disease progression and reduced survival rates. Conducted as a clinical audit in English general practices, data was collected on 17,042 patients newly diagnosed with cancer in 2014, noting that diagnostic delays occurred in 22% of cases due to patient, clinician, or system factors.

The thoroughness of the diagnostic process is crucial in mitigating these delays. Primary care physicians must adopt a comprehensive and systematic approach to evaluating symptoms, irrespective of the patient's age. This involves maintaining a high index of suspicion and conducting appropriate investigations even when initial symptoms are non-specific. As noted by Black et al. (19), implementing a structured diagnostic protocol can enhance early detection rates and improve clinical outcomes.

Vigilance in identifying potential cancer signs is imperative. Whilst of course the majority of presentations in primary care are not due to cancer, we would propose a dual approach of working toward a most likely diagnosis, whilst also considering serious differential diagnoses. For instance, non-specific symptoms such as abdominal pain, or unexplained weight loss, should prompt consideration of malignancy and inclusion of appropriate investigations regardless of patient age and whether malignancy is the most likely diagnosis. The integration of decision support tools and evidence-based guidelines in primary care practice can aid clinicians in making more informed diagnostic decisions (20, 21, 27). Additionally, a proactive stance, as recommended by O'Sullivan et al. (22), involves routine updates to clinical guidelines and continuous professional development to keep abreast of emerging trends in cancer presentation and investigation.

Beyond challenging diagnostic biases to improve clinician recognition of potential cancers in younger patients, there must be better support for clinicians in then making further decisions about investigations. An investigation can be judged in terms of its appropriateness, which is the balance of risk and benefit

of any investigation for a specific patient (23). Unfortunately, there is generally a lack of research into the appropriateness of investigations specifically for cancer in younger people presenting to primary care (24). Changing this is vital to better inform guidelines and decision support tools, so that clinicians are well supported in making decisions about the investigations needed to diagnose cancer.

Apart from the potential benefit of an accurate diagnosis, there are innumerable risks of an investigation a clinician will be weighing up, such as: false reassurance and patient disengagement following a false negative result; patient anxiety and further investigations resulting from either false positive results or non-symptomatic incidental findings; and the risks of direct harm from any investigation, for example radiation exposure. More broadly, clinicians will also be considering the wider implications of any investigation, including the costs to the healthcare system and the risk of lengthening waiting times for investigations for other patients. These risks are especially pronounced in younger patients presenting to primary care, as the vast majority of presentations, will not be due to cancer. To make more confident decisions about investigations, clinicians must be given enhanced guidelines for managing investigations for potential cancer in younger people, as well as better data to back-up their decisions. This research and guidance should also account for possible lead-time bias, which would be the potential for any increase in investigation in younger people for cancer, to lead to earlier detection but not necessarily truly enhanced survival (25).

Training and awareness programs

The implementation of comprehensive training and awareness programs for general practitioners (GPs) is critical in addressing diagnostic biases and improving the accuracy of cancer detection in younger patients. Such programs are designed to enhance clinicians' awareness of their biases, be they conscious or unconscious, and equip them with the necessary skills to recognize atypical presentations of cancer. These educational initiatives can significantly alter diagnostic practices and improve patient outcomes (Table 3). An excellent example of this is Bowel Cancer UK's "Never Too Young" initiative (26).

Effective training programs focus on several key areas. Firstly, they emphasize the importance of a thorough and systematic approach to diagnosis, encouraging GPs to consider a broad differential diagnosis that includes malignancies, regardless of the patient's age (19). According to a study by Walter et al. (28), training that incorporates case-based learning and simulation exercises can improve diagnostic accuracy by providing GPs with practical experience in identifying cancer symptoms in younger patients. These programs also highlight the significance of early detection and the potential consequences of delayed diagnosis, reinforcing the need for vigilance and overcoming diagnostic bias in clinical practice.

Furthermore, awareness initiatives that target diagnostic bias can help clinicians recognize and mitigate their own preconceived notions. A study by Staal et al. (29) examined the importance of fostering a broad differential diagnostic approach, as narrowing the focus prematurely can overlook potential key diagnoses. Incorporating reflective practice, where physicians regularly review and critically analyze their diagnostic decisions, can foster a culture of self-awareness, openness and continuous improvement.

In addition to formal training, ongoing professional development and access to updated clinical guidelines are essential. Regular workshops, educational courses, and peer-reviewed journals help keep GPs up to date with the latest evidence-based practices and emerging trends in cancer diagnosis. For instance, the integration of decision support tools, as recommended by Schmidt et al. (30), can assist GPs in making more informed decisions by providing contemporary guidance based on current clinical data.

Discussion

The necessity to overcome diagnostic biases in primary care to enhance early cancer detection in younger patients has been examined in the preceding sections. The central points underscored the detrimental impact of age-related biases, the importance of including cancer in differential diagnoses for younger patients, and the vital role of training and awareness programs (1, 10). Addressing these biases has significant implications for clinical practice, patient outcomes, and the broader healthcare system.

One of the primary implications for practice is the potential improvement in early cancer detection rates among younger patients (17). Early diagnosis is crucial as it often leads to better prognostic outcomes and more effective treatment options (5). By ensuring that cancer is considered as a possible diagnosis irrespective of patient age, primary care physicians can help mitigate the risks associated with delayed diagnosis (19, 21). Moreover, addressing diagnostic biases can enhance the overall quality of patient care. When physicians adopt a more inclusive diagnostic process, they are likely to conduct more thorough evaluations, thereby improving the accuracy of their diagnoses (20, 22). This comprehensive approach not only benefits the patients by providing timely and appropriate care but also reinforces trust in the healthcare system. To actively engage primary care physicians in mitigating diagnostic biases, ongoing education and awareness-raising must be emphasized. Professional development programs that focus on recognizing and overcoming diagnostic biases should be mandated (22).

Furthermore, implementing decision support algorithms in primary care settings can significantly aid in reducing diagnostic errors. Algorithms can provide evidence-based guidance and highlight potential malignancies based on presenting symptoms, regardless of patient age. The use of artificial intelligence (AI) in primary care is one area that may see future expansion and work alongside this. AI tools can analyze large datasets to identify patterns that may not be immediately apparent to human clinicians, which could offer enhanced diagnostics and in the future (31). However, this is dependent on the specifics of any AI development and implementation, and there are concerns being raised of AI amplifying and entrenching the existing human diagnostic biases of those designing and developing it (32, 33).

Primary care settings should also advocate for policy changes that support regular training and the integration of diagnostic support tools. Policymakers and healthcare administrators need

TABLE 3 Summary of key strategies to mitigate diagnostic bias in cancer detection among younger patients.

Strategy	Description	Expected outcome
Comprehensive diagnostic protocols	Implementation of structured diagnostic protocols based on evidence, including age-specific guidelines to reduce age-related biases in diagnosis.	Improved early detection rates, diagnostic accuracy, and appropriateness of diagnostic procedures.
Training and awareness programs	Education and training to enhance clinicians' awareness of biases and equip them with skills to recognize atypical cancer presentations. This includes case-based learning and simulation exercises.	Increased clinician awareness, reduced diagnostic errors, and improved management of atypical cases.
Patient-centered care	Extended consultation times, shared decision-making, improved communication channels, and greater patient engagement in their diagnostic journey.	Enhanced patient satisfaction, trust, and engagement, leading to more accurate and timely diagnoses.
Decision support tools	Integration of AI and other decision support tools to provide real-time diagnostic guidance, with recommendations grounded in solid evidence of net clinical benefit.	Reduction in diagnostic errors, improved decision-making processes, and safer diagnostic practices.
Multidisciplinary teams	Collaboration with specialists such as oncologists, radiologists, and pathologists to provide a more comprehensive and evidence-based diagnostic approach.	Reduced diagnostic errors, holistic evaluation of potential cancer diagnoses, and improved outcomes.
Empathetic communication	Training in empathetic communication to build stronger patient-provider relationships, with emphasis on active listening and validating patient concerns.	Increased patient trust, adherence to diagnostic procedures, and improved diagnostic outcomes.
Diagnostic appropriateness tools	Utilization of resources such as the ACR Appropriateness Criteria, NICE Guidelines, and similar evidence-based tools to ensure diagnostics align with clinical indications.	Reduced overdiagnosis and overtreatment, optimal allocation of healthcare resources, and fewer delays.
Reflective practice and audits	Regular audits of diagnostic practices and reflective exercises to evaluate and address potential biases in clinicians' diagnostic approaches.	Continuous improvement in diagnostic quality and adherence to best practices.

to allocate resources (both in terms of finances and clinician time) toward these initiatives, recognizing their long-term benefits in improving patient outcomes and reducing healthcare costs associated with late-stage cancer treatments (28), alongside the important moral imperative to challenge factors that disadvantage younger people with cancer. Collaborations with academic institutions, professional organizations, and charities, can help facilitate the development and dissemination of effective training and policy changes (26, 27, 34, 35).

Future research should focus on several key areas of cancer diagnosis in younger people. Firstly, it is vital research looks to further develop and validate diagnostic algorithms that are tailored to younger patient populations, so that clinicians can be better supported in their decision making. Studies should also investigate the effectiveness of different training methodologies in reducing diagnostic biases and improving early detection rates (13, 18, 19, 36, 37). Emerging population-based evidence supports this trend as particularly urgent. Sifaki-Pistolla et al. (38) demonstrated a significant increase in the incidence of colorectal cancer among age groups below 50 years during the past 30 years in the Greek population, while further projection indicated that there is also a trend to be projected. These findings set the challenge for updating the guidelines by putting an accent on young age groups early in the course of interventions.

Additionally, research on patient outcomes following the implementation of bias reduction strategies can provide valuable insights into the practical benefits of these initiatives. There is a broader picture here as well, which has innumerable areas where future research would be helpful, including research looking to understand and intervene in patient factors related to delayed presentation in younger people with cancer, as well as research examining the underlying reasons for the rising incidence of cancer diagnosis in younger people. Besides, cultural and behavioral factors play an important role in the influence of delays in diagnosis. Oikonomidou et al. indicated that in rural Greece, patients often refused diagnostic procedures such as endoscopy due to fears, misconceptions, and competing life priorities. These barriers underline the need for culturally sensitive strategies to enhance compliance and early detection (39).

Patient-centered care strategies

Addressing diagnostic biases in primary care not only requires systemic and educational interventions but also necessitates a shift toward more patient-centered care strategies. These strategies place the patient at the heart of the diagnostic process, ensuring that their concerns and symptoms are thoroughly evaluated and addressed. One effective patient-centered strategy is the implementation of extended consultation times for complex cases, allowing GPs to conduct more comprehensive histories and examinations, and consider a wider range of differential diagnoses. Research by Epstein et al. (34) suggests that longer consultation times are associated with improved diagnostic accuracy, particularly in cases presenting with atypical symptoms.

Another crucial aspect of patient-centered care is the active involvement of patients in their diagnostic journey. This can be achieved through shared decision-making, where patients are encouraged to participate more actively in discussions about their symptoms, investigations, and differential diagnoses. Providing patients with detailed information about their symptoms can empower them to advocate for their own health. A study by Charles et al. (35) found that patient involvement in the diagnostic process leads to higher satisfaction and better health outcomes. Concurrently, improving communication channels between GPs and patients is essential. Timely follow-ups and open lines of communication can help in monitoring the progression of symptoms and making appropriate adjustments to the diagnostic approach. Implementing electronic health records (EHR) with patient portals can facilitate this communication.

Patient education is a critical public health and policy component of patient-centered care. Educating patients about the signs and symptoms of cancer, regardless of their age, can raise awareness and prompt earlier medical consultations. Community outreach programs and educational campaigns, as highlighted by Young and Robb (36) have been shown to improve public awareness of cancer symptoms, which can lead to more timely presentation and diagnosis.

Integrating multidisciplinary teams into primary care can also enhance patient-centered care. Collaboration with specialists such as oncologists, radiologists, and pathologists can provide a more comprehensive approach to diagnosis and treatment planning (35–37).

Lastly, fostering a supportive and empathetic clinical environment is paramount. Primary care physicians should be trained in empathetic communication, which involves actively listening to patients, validating their concerns, and expressing genuine care and understanding. Empathetic interactions have been shown to build stronger patient-provider relationships, increase patient trust, and improve adherence to recommended diagnostic procedures (37).

Conclusion

Addressing diagnostic biases in primary care is paramount for improving the detection of cancer in younger patients. Overcoming these biases requires a multifaceted approach, including comprehensive training programs to enhance clinical awareness, the integration of decision support tools, and systemic changes to support continuous professional development. Furthermore, adopting patient-centered care strategies, such as extended consultation times, shared decision-making, and improved communication, can significantly enhance diagnostic accuracy and patient outcomes. By challenging diagnostic biases, and fostering an environment of vigilance and empathy, we hope primary care physicians can better identify and diagnose cancer in younger patients, ultimately leading to more timely and effective treatments. This proactive and inclusive approach not only benefits patients but also wider healthcare systems.

Author contributions

WJ: Conceptualization, Data curation, Investigation, Resources, Validation, Visualization, Writing – original draft, Writing – review & editing. DH: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Resources, Validation, Visualization, Writing – review & editing.

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Overview of female healthcare providers' outlooks on cervical cancer screening: a narrative review

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Background: Cervical cancer is the second most frequent gynecologic cancer. Uniquely, it is easily preventable and treatable cancer if identified early. The insights of healthcare providers about cervical cancer screening have a crucial role in prevention and treatment. However, there has been limited literature on the providers' perspectives on cervical cancer screening.

Objective: This review narrated the female healthcare providers' (FHCPs') outlooks on cervical cancer screening in terms of risk perceptions, awareness, knowledge, attitude, practice, and possible barriers.

Methods: A thorough literature search was conducted to identify studies conducted on female healthcare providers' overview of the perceived risk of cervical cancer, cervical cancer screening awareness, knowledge, attitude, and practice, as well as barriers to cervical cancer screening. Databases such as PubMed, Medline, Embase, Virtual Health Library, and Google Scholar were used to search for articles.

Results: Accordingly, this review identified that female healthcare providers have a low perceived risk of the disease, poor awareness and knowledge, unfavorable attitudes, and low uptake of screening practices. Furthermore, this review highlights the obstacles to cervical cancer screening acceptance, such as service inaccessibility, a lack of training and education, and fear of the procedure and results.

Conclusion: This narrative review described the variable distribution of the FHCPs' perceived risk of acquiring cervical cancer (CC). Poor knowledge and screening practices were observed. Moreover, the barriers to cervical cancer screening uptake were described. Given that healthcare providers are on the frontlines (act as role models) in increasing the community's cervical cancer

screening uptake, we suggest concerned bodies increase screening access and implement staff training programs. In addition, further mixed studies should be considered to deeply understand the possible attributes ingrained in individual and social belief systems.

KEYWORDS

cervical cancer, screening, knowledge, barriers, female healthcare providers, narrative review

Introduction

Globally, approximately 9.2 and 4.4 million new cancer cases and deaths were recorded in the female population in 2020, respectively. Cervical cancer (CC) was found to be the most commonly diagnosed gynaecologic cancer and the second leading cause of death in the same year, following only breast cancer (1). Additionally, CC gravely disturbs the survivor's quality of life (2).

In comparison to that in technologically developed countries, the burden of CC is higher in developing countries (1, 3). Poor regions of the world, including Sub-Saharan Africa (SSA), were particularly hard hit by CC, with 90% of cases reported (4). According to GLOBOCAN 2020, CC accounted for approximately 5,338 deaths in Ethiopia (5). In the same country, it was also the most common cause of cancer death in most reproductive-age women (15–44 years) (6).

CC is mostly caused by the human papillomavirus (HPV) (7). Globally, approximately 70% of all CC cases are caused by the high-risk (oncogenic) strains, HPV-16 and HPV-18, and the rest of the cases are caused by strains such as 31, 33, 45, 52, and 58 (4, 8, 9). According to the American Cancer Society's guidelines, this cancer-causing virus can be prevented by strategies such as risk reduction, being vaccinated, and undergoing screening timely (10).

CC is a tumour that can be easily prevented and treated if detected early (8). In resource-poor settings, HPV vaccination and screening are effective and profitable options for eliminating CC (11). Cervical cancer screening (CCS) can easily detect precancerous cells. The HPV test, the Pap test, and visual inspection with acetic acid are all methods for detecting CC (12). Screening is recommended for all women aged 21 to 65 years. According to the American Academy of Family Physicians and the U.S. Preventive Services Task Force, the interval for CCS is every 3 years for women aged 21 to 29 and every 5 years for women aged 30 to 65 years (13).

Although it is a preventable cancer type, approximately one-half of women with CC had not undergone screening before diagnosis (13). Remarkably, screening and case treatment are underutilized in resource-limited settings where CC accounts for 90% of case fatalities (4).

Abbreviations: CC, cervical cancer; CCS, cervical cancer screening; FHCPs, female healthcare providers; LMIC, low- and middle-income country.

The World Health Organization (WHO) set a 90-70-90 target for resourced-limited countries by 2030, with the goal of reaching 90% HPV vaccination of girls by the age of 15, 70% HPV screening by the age of 35, and 90% treatment of women diagnosed with the disease by the age of 45 (14).

Healthcare providers are the major sources of health information for clients and the general public (15, 16). According to a study by F. Kimondo, H. Kajoka, M. Mwantake, et al., approximately 80% of CCS was conducted by healthcare providers (17). Healthcare providers are pioneers whose beliefs, attitudes, and approaches linearly affect their clients' intention and utilization of the service they provide. They have a professional obligation to educate, motivate, and promote screening and other preventative measures to their clients. They are the clients' main sources of information about risk factors, prevention, and treatment of CC (18–21). Thus, recognizing their awareness, knowledge, attitude, and barriers to screening has a fundamental role in the prevention and management of CC. This review narrates the female healthcare providers' (FHCPs') outlooks on cervical cancer screening.

Methods

We conducted an overview of the literature, which is one type of the three narrative literature reviews identified by B. Green, C. Johnson, and A. Adams (22). Three authors (WG, AD, and FB) executed a thorough literature search for 1 week (from February 2 to 18, 2022) using advanced search strategies for all important studies published up to the last date of the search. The search included different databases such as PubMed, Medline, Embase, and Virtual Health Library. Additionally, we rigorously searched Google Scholar and government databases to access reports and unpublished studies. We connected the search terms such as "female", "woman", "Health extension worker", "Healthcare provider", "healthcare Professional", "Healthcare worker", "physician", "doctor", "nurse", "midwife", "radiologist", "pharmacist", "dieticians", "medical" "laboratory technician", "dentists", "physiotherapists", "optometrist", "occupational therapist", and "physician assistant" using Boolean operators including OR and AND. After completion of searches, we retrieved and saved all the search results in Mendeley Library.

Article selection criteria

In this review, we included all the global literature (regardless of geography and publication period) of studies that were conducted on female healthcare providers' overview of the perceived risk of CC, CCS awareness, knowledge, attitude, and practice, as well as barriers to cervical cancer screening. We excluded from this review the articles not accessed in full length and those published in languages other than English.

Quality assessment

Four authors (WG, AWD, GND, and EE) conducted a quality check for the retrieved articles based on their relevance to our predetermined topics of interest, whether the outcome was appropriately identified, and methodological thoroughness.

Results and discussion

Perceived risk of the disease

All the articles that assessed FHCPs' perceived risk of disease were on studies conducted in the South and Southeast Asian countries. For instance, in Singapore, 98% of female nurses had a perceived risk of CC, which is tied to adequate knowledge of the cancer (23). According to a study from Chennai, India, approximately 42% of FHCPs did not perceive that they were at risk for CC. Likewise, approximately 20% of providers had no intention to be screened (24). In a study conducted in Malaysia, a low perceived risk of CC is a barrier to screening (25). The perceived risk variations between populations from different countries could be due to personal beliefs, religion, perceptions, attitudes, and levels of knowledge about the disease.

Awareness and knowledge of cervical cancer screening

The providers' adequate CCS awareness could enhance the clients' screening practice. Incompatible with this fact, the majority of the literature shows poor awareness among FHCPs. For instance, a study conducted by A. Med., D. Hastanesi, A. Hekimli, et al. revealed low awareness of CCS among FHCPs (20). A study conducted in Malaysia also showed FHCPs' low awareness of CCS (25). Moreover, FHCPs' low CCS awareness was observed in Ethiopia, one of the SSA countries (26, 27). Contrary to this, a study conducted by S. Sudharshini, V. Anantharaman, and A. Chitra found a higher level (95%) of CCS awareness among FHCPs (24). The variability in the providers' awareness may be linked to curricular variations and training availability. Hence, a mixed-approach study is suggested to explore such attributes of awareness.

Unlike that of the clients, healthcare practitioners' inadequate knowledge has a far-reaching influence on the entire community. To improve screening behavior, women's understanding of the risk factors, causes, early indications, and treatment choices for CC is critical (28). Undoubtedly, in the case of healthcare providers' inadequate knowledge, it is difficult to empower the community's screening behavior and awareness. In this review, healthcare providers had limited knowledge of CCS. A study conducted by B. Obeidat, Z. Amarin, and L. Alzaghal identified FHCPs' poor awareness of screening in Jordan (29). A study conducted in Saudi Arabia revealed that only 4% of FHCPs had a good level of knowledge (30). In a study from Nigeria, approximately 71% of FHCPs had poor knowledge of CCS (31). A study conducted in Ethiopia found more than one-half of FHCPs had poor knowledge (27). Similarly, in a study conducted in Turkey and Jordan, more than one-half of the participants had poor knowledge (18, 20). A study conducted on nursing staff in India revealed that 77% of participants knew about CCS (32). In contrast, in a study conducted in Albania, more than three-fourths of FHCPs had sufficient knowledge of CCS (33). These variable distributions of providers' screening knowledge could be associated with exposure to capacity-building training and academic curricular variations.

Attitudes toward cervical cancer screening

Providers' attitude toward screening is another important factor in increasing the awareness and practice of individual clients. In a research conducted in Saudi Arabia, approximately three-quarters of FHCPs believed that screening is useful in preventing CC (30). A study conducted in Ethiopia found that only one-quarter of FHCPs supported CCS (27). Generally, we found too little literature on this specific topic of interest. Hence, further quantitative and qualitative research on this population is necessary to construct strong evidence.

Cervical cancer screening practices

Evidence about CCS practice FHCPs was reviewed from 10 articles. A study from Jordan found that 80% of FHCPs had never been screened (29). In Singapore, less than one-half of nurses had never undergone CCS (23). A study from Chennai, India, revealed that 82% of FHCPs have never undergone screening for CC (24). A. Med., D. Hastanesi, A. Hekimli, et al. also identified healthcare providers' poor screening practices (20). In Saudi Arabia, only one-fourth of FHCPs have been screened (30). A study conducted by M. Urasa and E. Darj showed that 85% of participants had not undergone screening at all, and the majority did not even know the intervals of CCS (34). Similarly, a survey from India found that 85% of nurses had never been screened (32). A survey conducted in South-South Nigeria revealed that 89% of healthcare workers had never been screened (31). K. Fatjona, G. Theodhosi, Y. Bilushi, et al.

revealed that more than three-fourths of FHCPs had not ever practiced CCS (33). Moreover, approximately 91% of FHCPs had not undergone screening in Ethiopia (27). In general, most articles reviewed in this study showed poor CCS practice among FHCPs, where more than three-fourths had not undergone screening. This screening practice gap may be explained by different underlying factors, including privacy issues (being screened by a staff member), fear of procedures and positive results, poor risk perception, and attitudes toward the disease.

Barriers to cervical cancer screening

In this review, evidence is gathered on the inaccessibility of services, fear of the procedures and results of screening, and lack of health education and training as factors that hinder FHCPs from screening.

Inaccessibility of services

CC commonly affects women who live in low- and middle-income countries (LMICs) that are deprived of resources for prevention and treatment (35). The current review supports this fact. All articles that explored inaccessibility as a constraint for screening were identified to be from LMICs. Accordingly, a qualitative study from Malaysia explored the lack of resources as a main barrier to screening uptake (25). A study conducted in Jordan showed that more than one-half of FHCPs had not been screened due to a lack of screening services (29). N. Haweissa, J. Lim, and T. Su identified that limited accessibility was due to the expensive cost of screening Libya (19). This problem is exceptionally high in Sub-Saharan Africa (35). The absence of screening kits and inadequate rooms in facilities were stated as barriers to CCS as indicated by evidence from Ethiopia (21, 27, 36). Another study conducted in Ethiopia revealed that a lack of screening materials and infrastructures hinders users from screening utilization (26).

Lack of health education and training

Poor health information affects the disease prevention and treatment behavior of an individual (37). In Tanzania, M. Urasa and E. Darj found that approximately 85% of participants reported the need for health education in their workplace (34). Lack of in-service training has been identified as a factor affecting screening knowledge. In Albania, insufficient staff training was reported as a hindering factor for screening service uptake by healthcare providers (33). In a study conducted in Ethiopia, only 16% of participants have undergone in-service training (36). This fact is also supported by our previous study (27). The studies from Jordan and Ethiopia showed that the likelihood of screening uptake of healthcare providers was higher among those who have undergone training (27, 29).

Fear of the procedure and screening result

The client's perception of pain during the screening procedure, according to evidence, hinders them from screening (38). According to the findings of S. Sudharshini, V. Anantharaman, and A. Chitra, FHCPs had not undergone screening due to embarrassment and diffidence (24). C. Yong, L. Hong, K. Lee, and colleagues hypothesized that participants found screening painful and distressing (25). Moreover, a study conducted in Singapore showed that nurses' false perception of pain was a reason for non-utilization of screening (23). According to a study conducted in Tanzania, 9.5% and 7.3% of nurses denied being screened due to fear of the procedure and the results, respectively (34). Moreover, G. Eze, I. Obiebi, and I. Umuago identified fear of screening procedures as a reason for not undergoing screening (31).

Limitations

This review sheds light on the scientific understanding of CCS from the providers' perspective, particularly from female healthcare providers, which has been poorly researched in the field. However, since we conducted a narrative review that did not strictly follow a systematic process, it may lack methodological rigor and reproducibility. Hence, we suggest that researchers in the field consider systematic reviews, meta-analyses, and qualitative approaches to exploring deep personal and societal beliefs.

Conclusion

Factually, the majority of scientific communities and clinicians have been working on boosting the CCS insights of the users. We thought that the providers' own insight and practice are fundamental to boosting the user's knowledge, attitude, and screening practice. This narrative review described the variable distribution of the FHCPs' perceived risk of acquiring CC. Unexpectedly, poor knowledge and screening practices were observed among the FHCPs. In addition, the review also presented barriers to CC screening uptake among FHCPs, including service inaccessibility, a lack of training and education, and fear of screening methods and screening results. Given that healthcare providers are on the frontlines (act as role models) in increasing the community's CCS uptake, we suggest concerned institutions increase screening access and implement staff training programs. In addition, further mixed studies should be considered to deeply understand the possible attributes ingrained in individual and social belief systems.

Author contributions

WG: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Project administration, Resources, Validation, Visualization, Writing – original draft, Writing –

review & editing. AD: Formal Analysis, Project administration, Resources, Visualization, Writing – original draft, Writing – review & editing. FB: Resources, Supervision, Visualization, Writing – original draft, Writing – review & editing. SA: Data curation, Validation, Writing – original draft, Writing – review & editing. LF: Data curation, Resources, Supervision, Validation, Writing – original draft, Writing – review & editing. AD: Data curation, Investigation, Methodology, Writing – original draft, Writing – review & editing. GD: Investigation, Resources, Supervision, Writing – original draft, Writing – review & editing. GK: Data curation, Methodology, Project administration, Writing – original draft, Writing – review & editing. EE: Data curation, Resources, 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.

Publisher's note

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Oregon primary care providers as a frontline defense in the War on Melanoma™: improving access to melanoma education

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Melanoma is one of the deadliest forms of skin cancer but is typically cured with surgical excision when detected early. As an access point to medical care, primary care providers (PCP) play an integral role in early skin cancer detection. However, limited time for examinations and dermatologic training may present barriers to effective skin examination in the primary care setting. As a facet of Oregon Health & Science University's War on Melanoma™ (WoM), our multi-pronged outreach initiative aims to provide PCPs across Oregon with free, convenient, and effective melanoma education. The WoM PCP education campaign was disseminated starting in May 2019 through primary care networks throughout the state of Oregon to 12,792 PCPs, and education was delivered across several platforms: online multimedia tools, large group didactics, individualized practice-based sessions, and in-person distribution of materials to clinics. To date, 829 PCPs have participated in the online Melanoma Toolkit for Early Detection curriculum, 1,874 providers

have attended CME didactics, and 9 clinics have received facilitated meetings by Oregon Rural Practice-based Research Network. Eighty-three clinics (comprising 770 providers) were visited on-site and provided educational materials, and more than 150 PCPs have received a free smartphone dermatoscope to aid in skin examination and e-consultation. OHSU's WoM has successfully implemented a multifaceted approach to provide accessible melanoma education to PCPs across the state of Oregon. As a result, we hope to encourage appropriate skin examination in the primary care setting and improve PCPs' diagnostic accuracy and confidence in pigmented lesion evaluation.

KEYWORDS

melanoma, skin cancer, primary care, family medicine, education, CME, early detection, prevention

1 Introduction

Melanoma remains one of the deadliest skin cancers. However, early detection of melanoma can significantly improve survival rates and reduce the need for more aggressive treatment options (1). According to the National Cancer Institute (NCI) Surveillance, Epidemiology and End Results (SEER) data for 2013–2019, the average 5-year survival rate was 99.6% (CI 99.3–99.8%) for patients with localized cutaneous disease at diagnosis, and only 35.1% (CI: 33.8–36.4%) for patients with distant disease at diagnosis (2).

1.1 Differential access to dermatologic care and the role of PCPs in melanoma detection

States with a greater density of practicing dermatologists have been shown to be associated with lower mortality to incidence ratios for melanoma (3). However, the distribution of dermatologists in the United States favors urban and coastal regions, leaving rural and underserved areas vulnerable. Additionally, studies based on Cancer Registry data have reported higher incidence and mortality for melanoma in rural areas of the United States (4, 5). In the state of Oregon, there are 110.7 primary care physicians per 100,000 persons, ranking 9th in the United States (6). The ratio of primary care providers (PCP) to dermatologists is even greater when advanced practice practitioners and complementary/alternative medicine providers are classified as PCPs. Based on accessibility, patients are more likely to visit their PCP regularly than a dermatologist. A population-based survey study of 216 melanoma patients showed that 87% of participants had established PCPs while only 20% had a regular dermatologist (7). Thus, PCPs have the opportunity to play an integral role in skin cancer early detection. However, while 63% of participants in the aforementioned study had seen their PCP in the year prior to melanoma diagnosis, most had not received a skin examination (7). Additionally, based on National Health Interview (NHIS) data, only 8% of patients who had seen their PCP in the past year received a skin examination (8). Importantly, a study conducted in Schleswig-Holstein, Germany, the Skin Cancer Research to Provide Evidence for Effectiveness of Screening in Northern Germany (SCREEN) project, showed that PCP training and education in skin cancer detection was associated with a reduction in melanoma mortality (9).

1.2 Challenges associated with conducting skin examinations in the primary care setting

Barriers to PCPs implementing skin examinations include limited appointment time to address all patient concerns, inadequate dermatologic education and training, and insufficient data to support routine skin cancer screening by clinicians per the US Preventive Services Task Force (USPSTF) (10–12). Based on electronic health record data, the average primary care visit is 18.0 min (SD = 13.5 min) despite patients often presenting with multiple concerns that may be deemed of higher priority and require extensive counseling (13). This leaves very little time to conduct a full body skin examination, especially when considering the additional time needed for a patient to undress. Even if time was not a factor, many PCPs have limited formal training on skin examination, optimal biopsy methods, or interpretation of dermatopathology reports. The American Academy of Family Physicians (AAFP) includes the performance of skin cancer screening examinations as well as recognition and management of skin cancer in the recommended curriculum guidelines for family medicine residents (14). However, due to the lack of a standardized educational program and universally agreed upon clinical competencies, many residency programs do not provide formal instruction on skin cancer screening and management (10, 15). Only recently has an expert consensus statement been released on proficiency standards for dermoscopy education in primary care (16). Additionally, PCP-oriented skin cancer screening education typically teaches providers to "triage and refer," but a new educational intervention offering two levels of proficiency "triage and refer" and "diagnose and manage" found that family medicine resident participants demonstrated significant improvement in knowledge and self-efficacy following the training (17). Additionally, it may be unclear to PCPs which patients are appropriate for skin cancer screening. The USPSTF guidelines state that there is insufficient evidence to recommend visual full body skin examination to screen for skin cancer in asymptomatic adolescents and adults; however, this recommendation does not apply to patients with a suspicious skin lesion or those who have elevated risk of skin cancer (11, 12, 18).

1.3 Barriers and facilitators in engaging PCPs in continuing medical education

Engaging PCPs in continuing medical education (CME) has unique challenges. Among Hong Kong providers, over 90% of physicians agree that continuous professional development is important in updating knowledge and skills, only 30.7% of non-specialists (compared to 65.4% of specialists) favor continuous professional development to be a requirement for licensure renewal (19). For PCPs, the main barriers to participating in CME non-essential to board licensure include lack of time, perception of work overload, and motivational factors (20). Additionally, dermatologic CME may be deemed less relevant to their daily practice compared to other topics. According to Reis et al., specific to online CME, a lack of digital competence and infrastructure may impede participation. Convenient schedule and location, relevant content, and incentives for participation may improve engagement in CME (19). A survey study conducted in 2018 reported that factors identified as most important in selecting CME activities were topic, quality of content, availability of CME credit, and clinical practice focus (21). Participants in O'Brien Pott et al.'s survey study also reported that they would be most likely to engage in live, online, point-of-care, and print-based CME activities. A meta-analysis aiming to establish the impact of CME interventions on physician knowledge, performance, and patient outcomes, concluded that multifaceted educational programs, longitudinal workshops, interactive small groups, and case discussion interventions delivered to single discipline participant types had the most significant effect sizes (22).

1.4 Objective

As a facet of Oregon Health & Science University's (OHSU) War on Melanoma™ (WoM), our multi-pronged outreach initiative aims to provide PCPs across Oregon access to convenient and effective melanoma education at no cost.

2 Methods

The institutional review board at Oregon Health & Science University approved this educational study (STUDY00019372) and waived informed consent for survey participants. Our WoM PCP education campaign was disseminated through the primary care networks of the Oregon Medical Board (OMB), Oregon Medical Association (OMA), Oregon Communication Health Information Network (OCHIN), Oregon Rural Practice-based Research Network (ORPRN), University of Oregon (UO), OHSU's PCP counsel, Quest Diagnostics, and Castle Biosciences. Education was delivered across several platforms: online multimedia tools,[1] large group didactics sessions (SAL, EGB, AV), individualized practice-based sessions (SAL, VS), in-person distribution of materials to clinics (Castle Biosciences, VS, and ORPRN), and social media promotions (Quest Diagnostics, University of Oregon). It is important to note that no financial benefits accrued to any group or for-profit company as a part of this distribution. No incentives were offered to increase use of any products offered by these organizations.

2.1 Online multimedia tools

WoM hosts a variety of free comprehensive online resources to appeal to different learning styles and preferences. The Melanoma Toolkit for Early Detection (MTED) aims to equip non-dermatology providers with the skills necessary to confidently recognize pigmented skin lesions that are concerning for melanoma (23). The course encompasses a suite of 6 educational modules, featuring recorded discussions conducted by expert dermatologists on the identification of skin cancers. The self-paced modules are expected to take approximately 0.5 h each for a total of 3 h needed for completion. Participants who successfully completed the course were eligible to receive 3 continuing medical education (CME) credits. Additionally, the online resources offer video tutorials on efficient skin examination and biopsy techniques, electronic medical record tools to identify and stratify at-risk patients, billing tools, and unbranded patient education materials (see footnote 1). This innovative "toolkit" design grants participants the flexibility to engage in the complete curriculum or only specific sections most pertinent to their practice and proficiency (SAL, EGB, ERS).

2.2 Large group didactics and case-based sessions

Study investigators (SAL, EGB, and AVD) led in-person and virtual CME didactics at statewide PCP meetings. Optional surveys were administered following the CME didactic sessions. Additional study team members (AW and JL) hosted monthly case-based dermoscopy webinars tailored for PCPs.

2.3 Individualized practice-based sessions

ORPRN is "a statewide network of primary care clinicians, community partners, and academicians dedicated to studying the delivery of health care, improving the health of Oregonians and reducing rural health disparities." ORPRN representatives facilitated meetings with primary care providers to discuss their current skin examination practices and provide a tailored introduction to our comprehensive educational resources. The presentations generally lasted 30–60 min and took place in-person or via Zoom. The facilitators provided samples of patient-and staff-facing materials.

2.4 Onsite clinic visits and distribution of materials

A study facilitator (VS) conducted onsite visits to primary care clinics across the state to discuss the importance of melanoma screening, distribute educational materials, introduce providers to our comprehensive online multimedia tools, and demonstrate the use of a free smartphone dermatoscope (Sklip, Sklip Inc., Lake Oswego, OR, USA). Clinic sites were selected based on greatest outreach potential,

1 https://www.ohsu.edu/war-on-melanoma/melanoma-early-detection-toolkit

which was defined by high population density, areas containing many primary care practices, and practices with a large number of clinicians. On average, the study facilitator spent 20 min at each clinic site visited. Representatives from Castle Biosciences also distributed educational materials and smartphone dermatoscopes to their PCP network during in-person visits. Additional smartphone dermatoscope attachment devices were also shipped through the United States Postal Service or delivered in-person by various WoM team members and affiliates.

3 Results

3.1 Large email, newsletter, and digital based communications

Since the program launched in May 2019, 12,792 PCPs were solicited by WoM through targeted email campaigns in collaboration with Oregon healthcare accreditation boards, to participate in the PCP curriculum (Table 1). Over 30,000 digital newsletters and 12,000 printed newsletters were sent out. In addition, an email campaign in collaboration with OCHIN was disseminated to 1,704 PCPs, and the open rate was 21.8% ($n = 363$). Finally, a total of 79,924 impressions (message views) were delivered to healthcare providers through collaboration with the Quest Diagnostic PCP network. See supplementary material for example of messages delivered.

3.2 Online multimedia tools

Across the state, 829 PCPs have participated in the MTED curriculum. From 2019 to 2022, primary care-related content on OHSU's WoM website has been viewed a total of 9,951 times by 7,450 unique users (Table 2).

3.3 Large group didactics and case-based sessions

Over 10 CME lectures were led by melanoma experts across the state with a total of 1,874 PCP attendees. The post-lecture survey results are detailed in Table 3. Statements were rated on a scale of 1–5 with 1 = strongly disagree, and 5 = strongly agree. On average, attendees who completed our optional post-lecture survey agreed (mean response >3 on a 5-point scale) that the presentations were relevant to their practice, will influence their clinical practice, and that content was conveyed effectively. In-person large group CME didactics provided by melanoma experts offered a deeper dive into melanoma detection, but participants identified key areas that could be improved. Many post-survey respondents voiced the need for additional clinical and dermoscopic images of melanoma to hone their triage and diagnostic skills. Comments also mentioned a lack of interest in detailed information regarding melanoma management and the desire for additional practical tips for PCPs.

3.4 Individualized practice-based sessions

Of the 61 clinics the ORPRN team attempted to contact, 9 clinics (15%) opted to host a practice facilitator for a tailored introduction to MTED with approximately 69 participants. Four of the participating clinics were located in frontier locations, 2 in rural locations, 1 in a rural/urban location, and 2 in an urban location. Five clinics opted to receive educational materials (1 frontier, 3 rural, and 1 rural/urban). Eight clinics declined any engagement. Thirty-six clinics failed to respond to ORPRN regarding WoM's PCP education initiative.

3.5 Onsite clinic visits and distribution of materials

From May 2022 to June 2022, 83 clinics were visited onsite in (number of cities and number of counties) and provided educational materials, impacting 770 providers (Table 4). More than 150 PCPs have received free smartphone dermatoscopes to date, with user instructions and resources for triage with a dermoscopy expert at our institution.

4 Discussion

Beginning in May 2019, OHSU's WoM implemented a broad, multifaceted, education-based outreach program to PCPs across the state of Oregon. The program consists of online multimedia tools, large group didactics, individualized practice-based sessions, and on-site clinic visits, to offer free, accessible melanoma educational programming. The outreach was accomplished through collaboration with Oregon Medical Board (OMB), Oregon Medical Association (OMA), Oregon Communication Health Information Network (OCHIN), Oregon Rural Practice-based Research Network (ORPRN),

TABLE 1 Credentials of PCPs contacted through the healthcare accreditation boards of Oregon.

Credentials	Number of PCPs contacted (%)
Physician (MD/DO)	4,680 (36.6%)
Physician's Assistant/Associate (PA)	1,594 (12.5%)
Nurse Practitioner (NP)	3,274 (25.6%)
Chiropractor (DC)	1,960 (15.3%)
Naturopathic Doctor (ND)	1,284 (10.0%)
Total	12,792

TABLE 2 Website analytics report for the War on Melanoma PCP toolkit landing page stratified by year.

Year	Page Views	Unique users	Avg time on page (min:sec)	Avg engagement rate*
2019	2,909	2,099	05:25	81.1%
2020	2,779	1,981	06:06	81.0%
2021	1,525	1,165	03:35	76%
2022	2,738	2,205	05:06	92.1%
Overall	9,951	7,450	05:18	82.5%

*Engagement rate is defined by the number of users who click on a link within the webpage.

TABLE 3 CME didactics post-survey results.

Statement	Average rating (scale of 1-5[a])	Number of responses
This presentation was relevant to my practice	3.58	615
I will make changes in patient care based on the information presented	3.41	575
The content of the presentation was conveyed effectively	3.50	610

[a]1 = strongly disagree, 2 = somewhat disagree, 3 = neutral, 4 = somewhat agree, 5 = strongly agree.

TABLE 4 Locations of clinics visited onsite[a].

City	Population in 2022[b]	Proportion of Oregon's total population[c], %	Clinics visited, *n* (%)
Salem, OR	179,605	4.2%	11 (13.3%)
Medford, OR	88,357	2.1%	7 (8.4%)
Corvallis, OR	59,434	1.4%	4 (4.8%)
Grants Pass, OR	39,993	0.9%	6 (7.2%)
McMinnville, OR	34,515	0.8%	7 (8.4%)
Newberg, OR	25,767	0.6%	4 (4.8%)
Klamath Falls, OR	22,501	0.5%	9 (10.8%)
Ashland, OR	21,642	0.5%	7 (8.4%)
Hermiston, OR	19,973	0.5%	5 (6.0%)
Pendleton, OR	16,894	0.4%	6 (7.2%)
La Grande/Elgin, OR	15,182	0.4%	7 (8.4%)
Ontario, OR	11,845	0.3%	7 (8.4%)
Baker City, OR	10,178	0.2%	3 (3.6%)
Total	545,886	12.7%	83 (100.0%)

[a]Sites visited by VS.
[b]Population data reported by Portland State University's Population Research Center.
[c]The certified estimate of Oregon's population in 2022 was 4,281,851.

OHSU's PCP counsel, and with two industry collaborators. ORPRN is a provider network dedicated to improving the health of rural Oregonians through education and research (24). OCHIN, a health information network, shares a similar goal of health equity through innovative solutions (25). Both of these networks are involved in research and well-funded by state and federal sources.

Our education initiative achieved good geographic distribution across the state (Figure 1), and the variety of tools available in the educational toolkit permitted learners to self-select the learning methods that are best suited to their practice, schedule, and learning style.

Map of the State of Oregon, with density of primary care providers (PCP) by practice zip code. Gray indicates there are zero PCP practice addresses listed in each zip code. Gray-blue gradient indicates the number of PCP with practice addresses listed in each zip code. Green shading indicates that a given zip code contains greater than zero PCPs participating in the curriculum. Yellow map markers indicate locations of clinics or hospitals that received in-person presentations and invitations to participate in the curriculum (Map created with Datawrapper).

4.1 Online multimedia tools

Providing meaningful education in a time efficient manner is crucial to engaging busy healthcare providers, and the flexible "toolkit" design of our web-based resources allowed participants to engage in the content most relevant to their pre-existing knowledge base.[2] A previous study confirmed that healthcare providers were highly likely to engage in online CME because learning could be done when clinicians had time and at their own pace (21).

The 2019 MTED pilot study demonstrated a promising 6 percentage point average improvement in identifying benign and malignant lesions (95% CI: 3.5 to 8.6, $p < 0.001$ paired t-test; averages of 82.9% on the pretest to 89.0% on the post-test), accompanied by a 44.2% improvement in diagnostic confidence (95% CI 29.3 to 59.0%, $p < 0.001$, McNemar's test) following completion of the online training modules (23). A larger sample size of participants who completed both pre-and post-surveys is required for additional quantification of the online training's impact on PCP triage accuracy. Additional longitudinal assessment of in-clinic behavior changes would also be helpful in assessing the full impact of our online resources.

One limitation of the online education platform that we utilized was the lack of available user engagement analytics software. Analytics software would have allowed us to determine which topics, if any, were the most utilized. This would have also potentially provided

2 https://www.ohsu.edu/war-on-melanoma/melanoma-early-detection-training

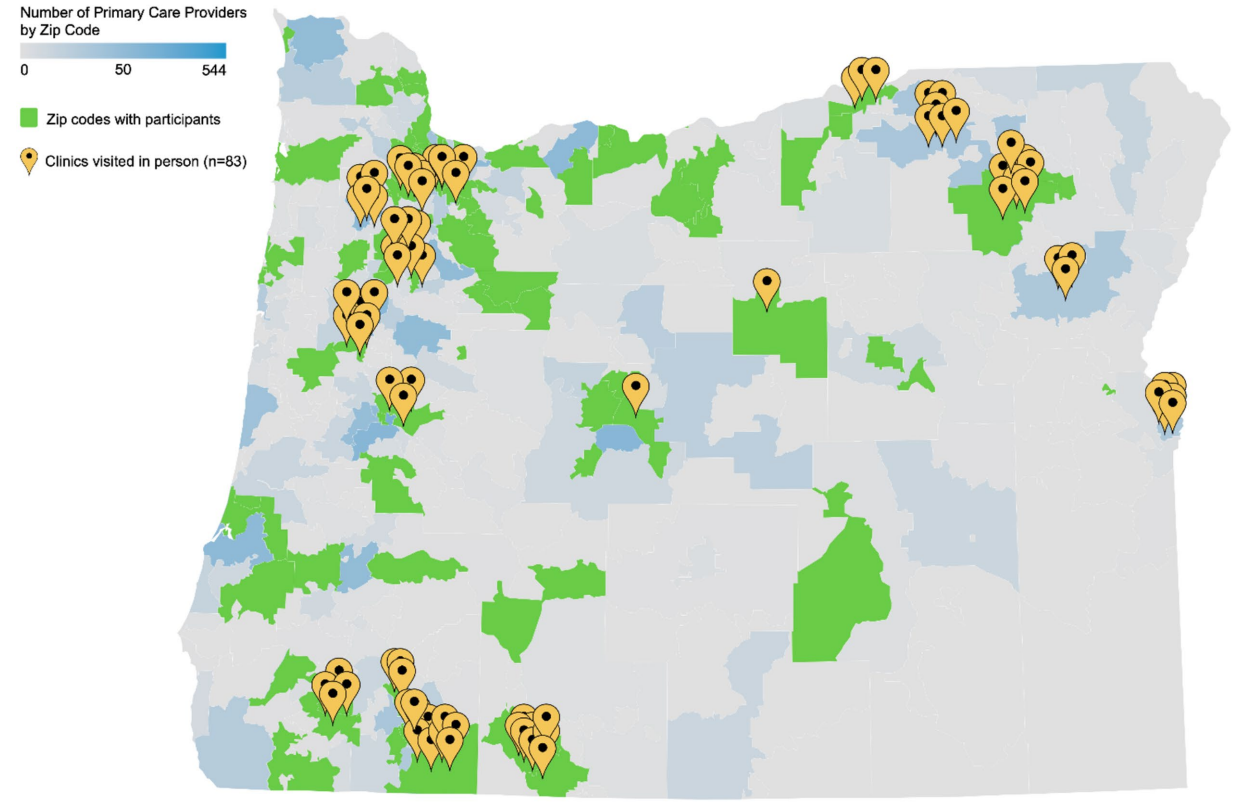

FIGURE 1
Primary care outreach density/distribution.

participant demographic data, thereby allowing us to identify groups who were not effectively reached that may benefit from additional outreach and education.

4.2 Large group didactics and case-based sessions

Healthcare providers who participated in the INFORMED curriculum expressed a need for more detailed skin cancer detection instruction and assistance with challenging patient cases (26). These challenges of online education can be addressed through live instruction with pigmented skin lesion experts. A 2018 survey of 500 healthcare providers revealed a preference for live CME, mainly because they felt topics were best taught using this modality (21). However, it should be noted that the effectiveness of lectures may be limited to auditory learners (27). An alternative method, case-based learning, which links theory and practice, has reportedly been preferred by 84% of medical students over traditional lectures, and has shown improvements in motivation, satisfaction, and engagement (28, 29). It is unknown whether these data discrepancies are related to generational preferences. Regardless, live large group didactics and dermoscopy webinars may serve as a beneficial supplement to online educational methods or previous knowledge.

Monthly live case-based, discussion-oriented dermoscopy webinars tailored for PCP audiences allowed for spaced repetition and also a safe space to ask pigmented lesion experts questions about challenging cases encountered during patient care in the real world. These webinars were scheduled during the noon lunch hour on Fridays to maximize attendance, which resulted in an estimated 75 providers participating throughout the course.

One important learning point was recognizing the importance of having a diverse selection of modalities for education. Some providers preferred in-person training experiences, while some only participated in online options. While in-person training may be preferred, it is limited by its resource-intensive nature. Future efforts will involve consideration of achieving a finer balance in allocating resources to increase access to in-person training modalities.

4.3 Individualized practice-based sessions

The need to improve access to melanoma care in rural areas was highlighted in a study demonstrating that patients in rural zip codes had higher melanoma prevalence and travelled much greater distances for treatment compared to patients residing in urban areas (30). ORPRN's purpose is to address these disparities, and it is one of the most successful programs of its type in the United States. Their mission is to improve health outcomes and equity for persons across the state of Oregon (24). ORPRN's outreach efforts for the WoM project concentrated on PCPs in rural and frontier regions of Oregon due to the scarcity of dermatologists in these communities. While only 9 out of 61 clinics that we contacted engaged in a practice-based session, this engagement rate is similar or outperforms other

initiatives led by ORPRN per their representatives. Although this is typical, we need to find strategies to increase participation (opportunities for follow-up etc).

Reasons cited for declining a practice-based session included staffing shortages, impending EMR changes, and limited capacity to engage in additional quality improvement work. Limited time availability is the common theme across these declinations, making it challenging to overcome. It may be possible to improve participation with increased incentive if resources are available. Even with personalized outreach, these results highlight the barriers faced by rural and frontier healthcare providers in engaging in CME. Contacted clinics acknowledged the importance of melanoma education, and no clinics indicated that they had been approached to engage in melanoma education previously. Other underlying barriers that are difficult to address are negative attitudes in individuals we are attempting to reach, and potential "burn out" from high stress environments. While the participation rate was less than optimal, we now further understand barriers to participation and will implement strategies to overcome these in future outreach efforts.

4.4 Onsite clinic visits and distribution of materials

The primary aim of employing "door-to-door" canvassing as one of our outreach methods was to reach clinics and providers that may otherwise miss or ignore other types of communication. In 2022, Litmus found that people spend just 9 s, on average, looking at an email (31). However, our team members report spending an average of 20 min at each clinic site visited reviewing educational resources. A study regarding door-to-door surveys concluded that this method is valuable in certain research contexts, especially when spending time in a community, conducting observations, and building relationships are central to the overarching goal (32). It should be noted that the success of this method of outreach is highly dependent on individual interpersonal skills and expertise in the topic being shared (33).

In addition to providing information about our educational resources, onsite clinic visits also included a demonstration of a smartphone dermatoscope that PCPs could obtain for free. Dermoscopy improves the diagnostic accuracy for melanoma compared to "naked-eye" visualization alone; however, the high cost of dermatoscopes limits their use by non-dermatology providers (34–37). Furthermore, the diagnostic accuracy from the use of dermoscopy is highly user-dependent, as additional intensive training for pattern recognition of features and routine practice using this technique is required for proficiency. By providing smartphone dermatoscopes to PCPs at no cost as well as in-person training, we attempted to improve their skin examination capabilities and equip them with a tool to quickly capture high-resolution images of skin lesions for inclusion in EMR documentation and e-consultations with dermatologists.

4.5 Conclusion and future directions

OHSU's WoM has launched a robust melanoma education program that is accessible to PCPs across the state of Oregon (38). Individual components of the program were evaluated for integration into the community. While it was not possible to cross-compare different aspects of our program to identify the most effective means of increasing PCP melanoma early detection, long-term impact of the education effort will be assessed through cancer registry data and all-payer all-claims databases. As part of the WoM campaign, we have coupled the outreach to PCPs with a statewide public education campaign encouraging the general population to check their own skin and direct any concerns to their provider for evaluation (38, 39). We hypothesize that a coupled approach will maximize melanoma early detection in Oregon and that this can be translated to other states. Future investigations will also implement new strategies to reach PCPs throughout Oregon. This strategy will effectively deliver education and resources and increase their ability to detect melanoma before it becomes highly morbid or lethal. These data will provide valuable insights into the role of PCPs in the early detection of melanoma and the impact of the WoM program.

Data availability statement

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

Author contributions

ABe: Writing – original draft, Writing – review & editing. JN: Writing – original draft, Writing – review & editing. AV-D: Writing – original draft, Writing – review & editing. EB: Writing – original draft, Writing – review & editing. VO: Writing – original draft, Writing – review & editing. ESt: Writing – original draft, Writing – review & editing. JT: Writing – original draft, Writing – review & editing. EL: Writing – original draft, Writing – review & editing. VS: Writing – original draft, Writing – review & editing. SX: Writing – original draft, Writing – review & editing. MBa: Writing – original draft, Writing – review & editing. ABa: Writing – original draft, Writing – review & editing. MBe: Writing – original draft, Writing – review & editing. CC: Writing – original draft, Writing – review & editing. DC: Writing – original draft, Writing – review & editing. KD: Writing – original draft, Writing – review & editing. KE: Writing – original draft, Writing – review & editing. LF: Writing – original draft, Writing – review & editing. EF: Writing – original draft, Writing – review & editing. AG: Writing – original draft, Writing – review & editing. HJ: Writing – original draft, Writing – review & editing. MJ: Writing – original draft, Writing – review & editing. PK: Writing – original draft, Writing – review & editing. JLe: Writing – original draft, Writing – review & editing. JLu: Writing – original draft, Writing – review & editing. DM: Writing – original draft, Writing – review & editing. SM-K: Writing – original draft, Writing – review & editing. KN: Writing – original draft, Writing – review & editing. RP: Writing – original draft, Writing – review & editing. SP: Writing – original draft, Writing – review & editing. AR: Writing – original draft, Writing – review & editing. SSa: Writing – original draft, Writing – review & editing. ES: Writing – original draft, Writing – review & editing. SSw: Writing – original draft, Writing – review & editing. ST: Writing – original draft, Writing – review & editing. MW: Writing – original draft, Writing – review & editing. KW:

Writing – original draft, Writing – review & editing. OW: Writing – original draft, Writing – review & editing. AW: Writing – original draft, Writing – review & editing. SL: Writing – original draft, Writing – review & editing.

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Conflict of interest

All financial, commercial or other relationships that might be perceived by the academic community as representing a potential conflict of interest must be disclosed. If no such relationship exists, authors will be asked to confirm the following statement: The authors declare that the research conducted and presented in this manuscript was performed by non-commercial partners, except for Castle Biosciences and Quest Diagnostics. Castle Biosciences made an unrestricted donation to the OHSU Foundation that was used to fund part of the marketing outreach to the community, and both Castle Biosciences and Quest Diagnostics included promotion of the PCP Toolkit and MTED in their marketing outreach, independently of marketing of their products. Alexander Witkowski and Joanna Ludzik received no compensation for this study or for the Sklip devices, but are co-founders of Sklip, which was distributed to primary care providers in this study. A conflict-of-interest management plan is in place to help ensure that this research is not affected by these financial interests. Alexander Witkowski and Joanna Ludzik were not involved in data collection or analysis. The datasets generated and analyzed for this study can be made available upon request to the corresponding author.

Publisher's note

Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fmed.2025.1427136/full#supplementary-material

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Examining barriers and facilitators to implementing evidence-based genetic risk-stratified breast cancer screening in primary care

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Introduction: While there is strong evidence supporting family cancer history screening as a tool for risk-stratified cancer screening, challenges in implementation remain. Many efforts tend to focus solely on the high-risk pathway neglecting the entire patient population. This study aims to capture primary care providers' perspectives on implementing genetic-informed, risk-stratified mammography screening guidelines.

Methods: Semistructured interviews were conducted involving 14 providers and 5 practice leaders across 2 Georgia healthcare systems between November 2020 and May 2021. Interviews assessed the barriers and facilitators at patient, provider, and system levels using the Consolidated Framework for Implementation Research. Thematic analysis was conducted using MAXQDA, and Fishbone analysis was applied to summarize the results.

Results: Barriers and facilitators differed between high- and low-risk pathways. For high-risk pathways, barriers included limited provider knowledge and unclear referral protocols, while facilitators included established relationships between providers and genetic professionals and effective electronic health record systems. For low-risk pathways, barriers centered on provider acceptance, guideline inconsistency, and risk communication challenges.

Conclusion: Effective implementation of risk-stratified breast cancer screening requires tailored strategies to address pathway-specific barriers. Integrating ongoing education, clinical decision support, and workflow alignment may enhance program adoption.

KEYWORDS

cancer screening, family history and cancer, mammogram, public health genomics, CFIR

Introduction

The U.S. Preventive Services Task Force (USPSTF) endorses family history-based screening as a frontline public health strategy to risk-stratify populations for tailored cancer prevention services (also known as precision public health) (1). With hereditary breast and ovarian cancer (HBOC), brief screening tools have been validated for identifying the 5%−10% of women who should be referred for genetic counseling and testing. Those with *BRCA* mutations can receive tailored life-saving prevention and treatment options (1). However, using these family history screenings will result in 85%−90% of women finding out they are not at risk for HBOC. These women, in turn, meet the criteria for initiating mammogram screening at age 40 and continuing biennial screenings thereafter. Strong evidence now supports risk-stratified screening regimens as the veritable "win–win," affording early cancer detection and reducing patient burden and health care costs (2).

Controversy persists regarding the appropriate age to begin mammography screening and the best screening interval for women with an average risk for breast cancer (3). Specifically, the USPSTF, the American Cancer Society (ACS), and the American College of Radiology (ACR) each have different screening guidelines (4). Although mammography is widely acknowledged to be a critically important tool for breast cancer screening, its use can have adverse effects, including the possibility of false-positive results, which can cause anxiety and psychological stress and expose women to unnecessary treatment, pain, and side effects (5, 6). In addition, racial disparities in screening mammography use are evident in Black and Hispanic populations (7, 8). For these women, the pursuit of unwarranted mammography presents substantial logistical challenges and increased demand for limited resources. While we must ensure access to mammography screening, risk-stratified recommendations would mitigate an inappropriate demand for limited resources.

There are various challenges in implementing risk-stratified screening guidelines. Mammography screening practices operate within complex health system structures, including provider and patient behaviors. Our pilot work showed that patients struggle to distinguish between inherited vs. sporadic breast cancer risk (9). Additionally, providers fear that deviating from a single community-standard care pathway for screening would increase the risk of medical malpractice claims (10). Although electronic health record (EHR) prompts can help bridge care gaps (such as those related to screenings and immunizations), the logic behind them may be unclear or based on outdated recommendations. These factors can interact [for e.g., populations with low trust in medical systems may view that varied screening intervals are not based on risk but rather on providers refusing to offer necessary care (11)]. Successfully adopting risk-based guidelines requires prospectively identifying barriers to a seamless workflow integration and strategies for increasing patient and provider buy-in (12).

The overarching goal of this study is to characterize provider perceptions of facilitators and barriers to implementing genetic-informed risk-stratified mammography screening in primary care practices in Georgia. The specific aims are to (1) explore health care providers' awareness and perceptions of the genetic-informed risk-stratified mammography screening guidelines, perceived barriers, and facilitators to its implementation in primary care practice and (2) identify implementation strategies to address barriers that providers raise that are most amenable to interventions.

Methods

Study design

Between November 2020 and May 2021, semistructured phone interviews were conducted involving 14 providers and 5 leaders recruited from Emory Healthcare primary care clinics and Phoebe Health Care. The structured interview questions were based on the Consolidated Framework for Implementation Research (CFIR) to assess barriers and facilitators at multiple levels (13). In this study, we define the **"high-risk screening pathway"** according to the USPSTF guidelines, which recommend that "primary care clinicians assess women with a personal or family history of breast, ovarian, tubal, or peritoneal cancer or who have an ancestry associated with *BRCA1/2* gene mutations with an appropriate brief familial risk assessment tool. Women who had a positive result on the risk assessment tool should receive genetic counseling and, if indicated after counseling, genetic testing" (1). The **"low-genetic risk screening pathway"** refers to the discussion of biennial mammography screening for average-risk women aged 50–74 years, which was supported by the 2016 USPSTF guidelines (14) and several international mammography screening guidelines (3). Average-risk women were defined as asymptomatic women who do not have preexisting breast cancer or a previously diagnosed high-risk breast lesion and who are not at a high risk for breast cancer because of a known underlying genetic mutation (such as a *BRCA1* or *BRCA2* gene mutation or other familial breast cancer syndrome) or a history of chest radiation at a young age. The institutional review board of Emory University approved this study (IRB00113501).

Recruitment

We enlisted key stakeholders, including primary care providers and organizational leadership staff, who were involved in the breast cancer risk assessment and screening. We targeted two primary care settings to represent health care organizations with different insurance structures that serve rural and urban catchment areas and diverse patient populations. Primary care clinics of Emory Healthcare are part of a large academic medical center, with a mix of multiple payers. Phoebe Putney is the major healthcare system in southwestern Georgia that serves a relatively large rural population covered by Medicaid. Gaining insights from these two different primary care settings is aimed at characterizing a comprehensive array of provider and system barriers and facilitators to inform intervention strategies with the potential scalability for implementation in diverse primary care practices across Georgia.

Recruitment strategies included (1) email outreach, (2) snowball sampling, and (3) recruitment at training sessions and

events such as Grand Rounds and the monthly Emory Primary Care Forum. If the providers were willing to participate in the Zoom interview, they were sent a consent form via email. At the beginning of the interview, the study team confirmed the participant's eligibility and reviewed the information included in the informed consent. The study team explained the purpose of the study and stated that participation was completely voluntary and that non-completion or withdrawal would not affect their employment status or academic standing at their institution. Participants were given the opportunity to ask questions, and if they agreed, verbal consent was obtained.

Data collection

The interview questions elicited descriptions of each participant's perceived role and experience with genetic-informed risk-stratified mammogram screening. Supplementary Table S1 shows how the constructs adapted from the CFIR are used to understand the implementation of the genetic-informed risk-stratified mammography screening guidelines. Participants were instructed to comment on a list of barriers and facilitators based on the CFIR, giving special attention to understanding which factors might be unique to their clinical setting and which are more universal, and therefore generalizable, to other healthcare systems. In addition, the interviewer (YG) asked participants to provide insights into approaches to address the identified barriers and facilitate the implementation process in primary care practice, with a particular focus on how readily the strategies can or cannot be integrated into the routine workflow.

Data analysis

Interview data were audio-recorded, transcribed, and imported to MAXQDA for analysis. We used structured methods, such as codebook development, double coding, and data interpretation/presentation. Each transcript was independently coded by two coders. Discrepancies between coders were discussed and resolved through consensus meetings to ensure reliability and consistency in the coding process. We conducted standard content analysis and thematic analysis (15) to identify distinct concepts and categories related to each interview question, such as why to accept or not the genetic-informed risk-stratified screening, barriers and facilitators to implementation, and recommended strategies for addressing barriers that are most amenable to an intervention to promote implementing guidelines in primary care practices. Extracted barriers and facilitators to screening guideline recommendations were grouped into three themes: patient-, provider-, and health care system–level factors.

Results

A total of 19 health professionals participated in semistructured qualitative interviews. Of these, 14 were primary care providers, and 5 were practice leaders (i.e., chiefs and practice directors). After de-identifying the qualitative data, interviews revealed that most participants were employed by Emory Healthcare ($n = 9$, 47.4%).

TABLE 1 Frequency of theme occurrence.

	Category		
	Total	High genetic risk[a]	Low genetic risk[b]
Barriers (%)			
Patient	7 (1.11)	2 (6.06)	5 (16.67)
Provider	30 (47.62)	17 (51.51)	13 (43.33)
Healthcare	26 (41.27)	14 (39.13)	12 (40.0)
Facilitators (%)			
Patient	18 (34.62)	5 (27.78)	13 (38.24)
Provider	22 (42.31)	5 (27.78)	17 (50.0)
Healthcare	12 (23.08)	8 (44.44)	4 (11.76)

The frequency of theme occurrence represents the number of times each theme was observed in the total sample ($N = 19$), with each theme contributing to more than one category. Percentage values are based on the sum of category-theme occurrences. [a]Implementation of screening guidelines for women at high genetic risk. [b]Implementation of screening guidelines for women at low genetic risk.

Table 1 illustrates the frequency of theme occurrence conveyed through the interview process. The most frequently reported barriers operated at the provider ($n = 30$, 47.6%) and healthcare system ($n = 26$, 41.3%) levels, regardless of risk-stratified mammography screening guidelines. Conversely, the provider ($n = 22$, 42.3%) and patient ($n = 18$, 34.6%) levels were most frequently cited as facilitators among both risk-stratified screening regimens.

Barriers and facilitators to high-risk screening pathway

Regarding the reported barriers and facilitators for women at *high genetic risk* (Figure 1), the most noted barriers among interviewees were *time constraints* ($n = 10$, 52.6%) and *logistics* (i.e., referral support; $n = 9$, 47.3%). In comparison, the most common facilitator was *feasibility* (i.e., user-friendly EHRs and referral streaming; $n = 8$, 42.1%).

Patient-level barriers and facilitators

The sole barrier that emerged at the patient level was *patient preference* ($n = 2$, 10.5%). Such resistance to risk-based screening results in diagnostic delays. Based on a practice leader's prior experience, they shared:

> Not every patient necessarily wants genetic screening for a few different reasons – "Do I potentially want to be pigeon-holed into this is what's wrong and now I know, and I have to do something, and I may not be able to get life insurance or certain types of insurance? So, there was definitely some things that I had to think about being at a young age and kind of what my future looks, I ended up wanting to know if I did or I didn't because I wanted to know whatever I have, I want to take care of it." (2)

Health professionals reported *cancer worry* ($n = 5$, 26.3%) as a facilitator. The patient's family history and degree of

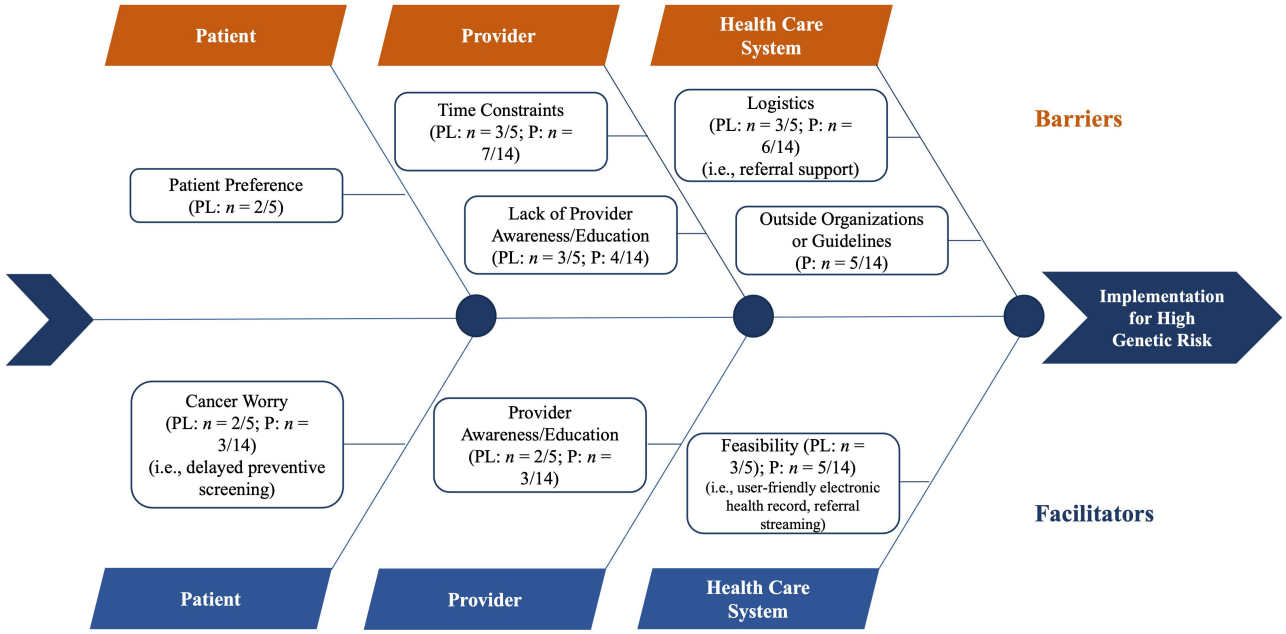

FIGURE 1
Meta-fishbone diagram of facilitators and barriers to implementing screening guidelines for women at high genetic risk as perceived by health professionals during in-depth interviews. PL, practice leaders; P, providers.

"cancer worry" were related to identifying cancer worry as a facilitator for considering increasing genetic counseling referrals for women who had a positive result on the risk assessment tool. Describing factors that would encourage patients to consider screening recommendations, one primary care provider stated:

> "Especially a lot of people may – as I mentioned – have a family history so they want to make sure that they are doing everything they should be and make sure that they are doing what is best for their health. (11)"

Provider-level barriers and facilitators

Barriers identified at the provider level encompass a *lack of provider awareness or education* and *time constraints*. Health professionals more often cited time constraints (n = 10, 52.6%) rather than a lack of provider awareness or education (n = 7, 36.8%) as a barrier to referring women for genetic counseling if they had a positive result on the risk assessment tool. Providers cited a need for additional time, mainly to fully capture all of a patient's medical history. If a patient presented with multiple complaints during an office visit, one provider stated:

> Our uptake in that [high-risk screening] procedure is relatively speaking, too low. It should be higher for the types of patients that we take care of. It just seems that those tasks that involve deeper, thoughtful time-consuming discussions may not take place as quickly as, "This is something that's recommended for you. You should get it, I'm going to order it." (8)

Given the time needed for a preventive care visit, providers suggested scheduling an additional office visit with the sole focus on high-risk screening. Recognizing the importance, a provider stated:

> Time would always be helpful and certainly perhaps maybe this visit – this topic [high-risk screening] could certainly be a whole visit in and of itself, very frankly, and especially if somebody is high risk, I would want to sit down and make sure I take the time to have a proper conversation with that patient instead of just a shorter version of what I may do for a recommending routine for breast cancer surveillance. (1)

In addition to time and workload pressures in primary care, providers expressed a lack of their peers' awareness or education as a barrier to successfully implementing high-risk screening guidelines. Describing what would happen if there were a higher volume of genetic counseling referrals, one provider shared:

> I think the main [barrier] is awareness of the tools and specifically when to refer someone. (13)
>
> When referencing a lack of provider awareness, a primary care provider stated:
>
> But truthfully, I do not know the best way to risk stratify these patients in terms of their low, medium, high risk. I would have a general understanding of, "Okay, if this patient did have a family history of breast cancer" it would raise my suspicion as more of a higher category. But then afterwards, I will say I'm not very knowledgeable on the recommended risk stratifying protocol afterwards. (1)

Participants perceived *provider awareness or education* (n = 5, 26.3%) as a facilitator for implementing the high-risk screening pathway. Participants mentioned that provider awareness and

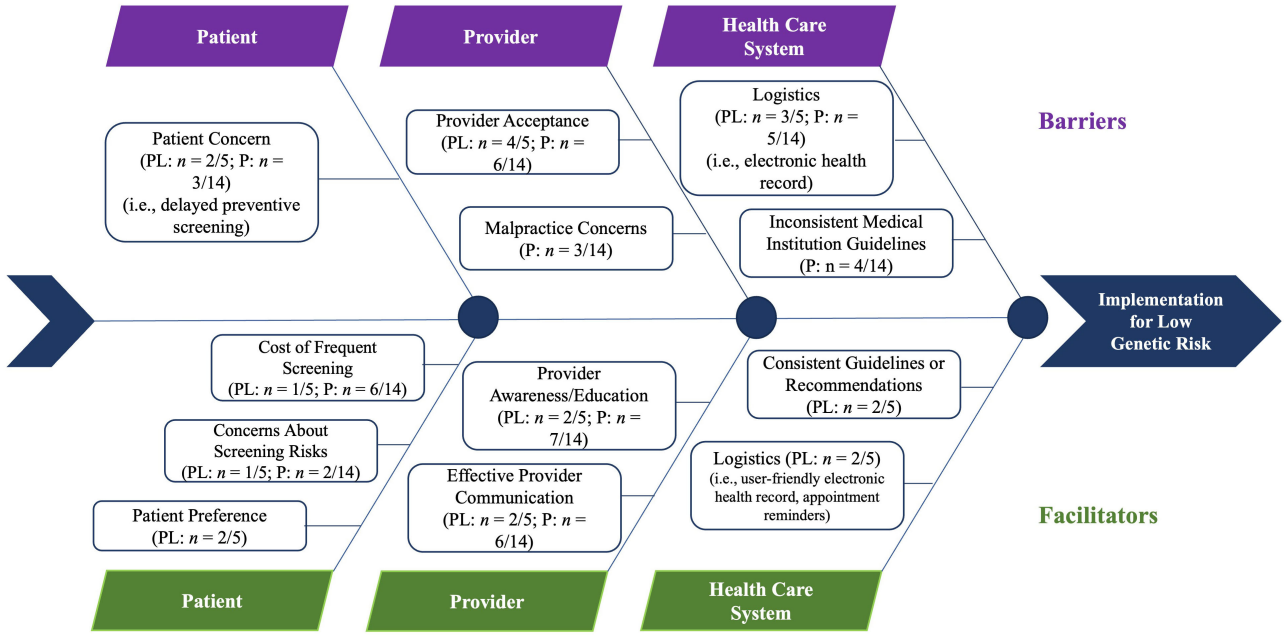

FIGURE 2
Meta-fishbone diagram of facilitators and barriers for implementing screening guidelines for women with *low genetic risk* as perceived by health professionals during in-depth interviews. PL, practice leaders; P, providers.

education promote the uptake of risk-based screening. A provider stated:

> So, two ways. One is I listen to a podcast. And so, I mean this is covered in several podcasts, but the JAMA podcast, the Journal of the American Medical Association, they interviewed – they do this for each of the USPSTF guidelines. . . . And then the second way is through continuing medical education. (18)

Healthcare system-level barriers and facilitators

Health professionals perceived *logistics* ($n = 9$, 47.4%) and *outside organizations or guidelines* ($n = 5$, 26.3%) as barriers to implementing the high-risk screening pathway. The lack of EHR support or disruption to workflow was related to identifying logistics as a barrier when considering increasing genetic counseling referrals for women who had a positive result on the risk assessment tool. When discussing family history analyses and EHR system integration, a practice leader stated:

> [I]t used to be – when we did paper records, we actually drew pedigrees and boxes and relations and stuff like that color in squares and circles and make notes and things like that. And now that we're working on a computer system, I haven't seen the ability to easily include those types of family pedigrees with relevant information. (8)

Furthermore, participants indicated a lack of institutional support in genetic-informed risk-stratified mammography referral. When discussing the decision to refer a patient to genetic counseling, a primary care provider said:

> I want to refer, but who do I refer them to? And, then you've got to stop, and you've got to dig, and if you're a practice that's working with a skeletal staff, who has the time to stop and figure all that stuff out? (15)

Similarly, another primary care provider stated:

> I think the main one is awareness of the tools and specifically when to refer someone. It requires me to step away from what I'm doing, go look at the screening tool, do the screening - how to do the referral. And I'll be honest, those aren't things that I have incorporated into my practice. (13)

Health professionals less frequently reported outside organizations or guidelines as a barrier when considering increasing referral of women with a positive result on the risk assessment tool for genetic counseling. The reputations of existing genetic counseling professional organizations or inadequate insurance coverage for services were related to identifying outside organizations or guidelines as a barrier.

The sole barrier that emerged at the healthcare system level was *feasibility* ($n = 8$, 42.1%). The capacity to build referral partnerships or ease of access to genetic counseling was related to identifying feasibility as a barrier.

Barriers and facilitators to low-risk screening pathway

Figure 2 illustrates the meta-fishbone diagram of reported barriers and facilitators for implementing screening guidelines for

women with *low genetic risk*. Across practice leaders and primary care providers, the most common barriers were *provider acceptance* ($n = 10$, 52.6%) and *logistics* (i.e., EHR; $n = 9$, 47.6%). Conversely, the most common facilitators were *provider awareness or education* ($n = 9$, 47.3%) and *cost* ($n = 7$, 36.6%).

Patient-level barriers and facilitators

Health professionals perceived *patient concern* ($n = 5$, 26.3%) as the sole barrier to implementing the low-risk screening pathway at the patient level. Health professionals suggested that women are more likely to undergo screening should somebody they know receive an abnormal mammogram. A primary care provider stated: "Because a friend was tested or was found to have at an earlier age than 40, and they just want to get ahead of it. And I don't have any problem with it, yeah" (18). To avoid undue worry caused by delaying screening, a practice leader stated: "I think it's become too of like everybody knows somebody who has had breast cancer. So, you see a friend, a colleague, a family member, go through it and it sparks your interest" (10).

For those women who routinely screen for breast cancer, a primary care provider said:

> "I think many women are uncomfortable waiting until 50 … they've done it every year, they've been told for years and years and years to do a breast self-exam every month, to get a mammogram every year. When they come in – and I'm often the first person to tell them, you don't need a mammogram until 50. (13)"

Under the patient level, facilitators that emerged include *concerns about screening risks, patient preference,* and *cost of frequent screening*. Health professionals frequently perceived the cost associated with frequent screening ($n = 7$, 36.8%) as a facilitator to considering delaying or reducing mammography screening before the age of 50 years. Describing the risks of the mammogram procedure and its associated out-of-pocket costs, one primary care provider stated:

> If you're not having issues, it's really an unnecessary test and an additional cost to you. We talk about the risks and harms of the procedure, that it may not detect all breast cancers. It also could detect benign lumps that then we have to do further workup and there are extra costs and procedures involved to make sure that it's benign. (14)

Health professionals less frequently reported factors surrounding patient preference ($n = 2$, 10.5%) as a facilitator to considering delaying or reducing mammography screening before age 50. One primary care provider said: "[T]he most important thing is probably patient preference for whether they want to engage in the service early or frequently" (19). Health professionals also alluded to the shared decision-making related to screening mammography. A primary care provider described this phenomenon:

> [I]f patients tell me, "I do not want to get a mammogram," I can't force them. So, it is definitely patient preference, and it's ultimately an informed decision between the patient and the provider, and the patient has to make the final decision on whether or not they're going to get it done. (14)

Provider-level barriers and facilitators

Barriers at the provider level include *provider acceptance* and *malpractice concerns*. Health professionals frequently perceived provider acceptance ($n = 10$, 52.6%) as a barrier to adopting the low-risk screening guidelines. The provider's comfort level with delaying or reducing mammography screening before the age of 50 years was related to identifying provider acceptance as a barrier to the USPSTF 2016 guideline implementation. A primary care provider mentioned:

> "When recommendations change to longer and less, it's sort of hard for us to get used to. Like when pap smears went from every year to every 3 years, you know? And there's still doctors that do them every year now. So, I think that moving from 40 to 50 would take us a while to feel comfortable with probably. (9)"

When asked about their major concerns regarding delaying screening, the provider stated, "Just missing something in that 10 years, you know?" (9).

Additionally, health professionals reported malpractice concerns ($n = 3$, 15.8%) as a barrier to implementation. The provider's awareness of the medical liability associated with failing to order mammography screening was related to identifying malpractice concerns when discussing barriers to delaying or reducing mammography screening before age 50. A primary care provider said:

> "I think everyone, like providers, are pretty aware that that's one of the high liability. Missing breast cancer is pretty high liability" (12). Similarly, in reference to the 2016 USPSTF's standard of care for breast cancer, another primary care provider said, "I think providers are concerned probably about not only missing patients that've been there, I think honestly always worried about malpractice and they don't want to be blamed if they didn't order a test" (11).

Facilitators that materialized under the provider level include *provider awareness or education* and *effective provider communication*. Health professionals frequently perceived provider awareness or education ($n = 9$, 47.4%) as a facilitator of adopting low-risk guidelines. A primary care provider mentioned:

> "[W]e stick to the habits that we've learned. So, for clinicians who are training now, if they're strongly taught 50, probably that will naturally start to delay because they just won't recommend it anymore. And, then, people like me, who have been trained a long time, we have to reeducate. (4)"

Continuing education opportunities provide an avenue for providers to stay up to date with the latest recommendations.

Furthermore, health professionals indicated the importance of effective provider communication (n = 8, 42.1%). The provider's ability to clearly communicate the benefits and harms of screening enhances adherence to risk-stratified screening regimens. One primary care provider said: "I think the most important factor is discussing with the patients their age, medical history, family history, and then having an educated conversation with them about the risks and benefits of preventive care, whether it is breast cancer screening, colon cancer screening, prostate cancer screening, among others. Furthermore, in most situations, when we have an educated discussion with them, they are happy to comply with the guidelines in the majority of cases" (5).

Healthcare system–level barriers and facilitators

Barriers identified at the health care system–level included *logistics* and *inconsistent medical institution guidelines*. Health professionals perceived logistics (n = 8, 42.1%) more frequently than inconsistent medical institution guidelines (n = 4, 21.1%) as a barrier to guideline implementation. Navigating the EHR system was related to identifying logistics when discussing barriers delaying or reducing mammography screening before age 50. During a discussion about healthcare system–level decision-making related to screening mammography, a practice leader shared:

> It's harder to do when we have to go into the chart to figure out whether something has been done and shared decision-making can be done extremely well, or it can be done in a way that is very cursory. And so, that's one of those difficult problems. An example would be that advanced care planning, which is now reimbursed for providers in primary care to receive funding for the work that they do there.

Similarly, another primary care provider indicated that the EHR presents difficulties in decision support with automated patient reminders for routine screening. When asked if they could override the EHR system reminder to screen for breast cancer, one primary care provider stated:

> Yeah, so you can override it, and usually in my case if I'm saying we're going to not get it this year just because of low risk, I mean, I usually document in the note too. I may write it out. But I just usually document as to, "We discussed the pros and cons of getting a mammogram at 40 and due to her low risk, patient" – and I usually will put, "Patient prefers to wait after a discussion of pros and cons." But yeah, there is a way to get that recommendation off the list if you're not going to do it. (5)

Health professionals less frequently reported factors surrounding inconsistent medical institution guidelines as a barrier to considering delaying or reducing mammography screening before age 50. One primary care provider said:

> So, if each institution has its own guidelines, it's very hard for us – or each organization has its own guidelines – so it's very difficult for an institution to adopt a firm guideline. "This is the age we're gonna start, this is the age we're gonna stop." I think overall – as we mentioned – it's really best for each patient to really have that conversation with her provider regarding this test and then determine a plan that's best for her. (1)

The facilitators that emerged at the health care system level include *logistics* and *consistent guidelines or recommendations*. Health professionals mentioned logistics (n = 2, 10.5%) as an implementation facilitator for the low-risk screening pathway. Improvements in the EHR system were related to identifying logistics as a facilitator of guideline implementation. Health professionals also perceived consistent guidelines or recommendations (n = 2, 10.5%) as a facilitator for adopting low-risk guidelines. When asked about their thoughts on delaying or reducing mammography screening before age 50, one practice leader responded:

> [I]f we're going down the line of saying that everyone is gonna go through genetic testing, and we can certainly stratify that point if you are low risk or high risk, then I think it might be more palatable to a physician to say, "Okay, I'm going to follow the United States Preventative Task Force Guidelines and starting at 50. And this is why you can start at 50, because we've tested you and you were at low risk." (7)

Discussion

The emphasis on genetic-informed risk-stratified breast cancer screening in primary care is the logical step in implementing precision medicine. However, current efforts to promote screening uptake have primarily targeted those at the highest risk of carrying a *BRCA1/2* mutation. McBride et al. (16) suggest that precision public health means carefully addressing the needs of high- *and* low-risk individuals, emphasizing that genomic-informed screening should be individualized for those with "negative" results as well as those at high risk. Our study showed that barriers and facilitators differ significantly between the high- and low-risk pathways, highlighting the need for tailored strategies to ensure successfully implementing a program for all.

For the high-risk pathway, primary care providers and practice leaders reported that knowledge barriers and a lack of clarity on referral pathways impeded using genetic counseling resources effectively. Facilitators of accurate, appropriate referrals for the high-risk pathway included a strong knowledge of genetics and established connections with genetic professionals, which is shown in other studies (17). These interrelationships demonstrate that provider-level and system-level resources influence referral decisions within the high-risk pathway.

EHR accessibility and streamlined referral processes emerged as critical facilitators in the high-risk pathway. These findings align with previous studies that identify EHR systems (e.g., integrating a risk assessment algorithm or platform into the EHR) as essential

for supporting genomic-informed decision-making in primary care (18, 19). However, quality improvements to the EHR often require healthcare system involvement and coordinated implementation efforts. Proper training in EHR functionality may enhance adopting risk-stratified screening guidelines for high-risk cases (20).

In contrast, the low-risk screening pathway presents distinct challenges. Most women who undergo family history screening did not have *BRCA1/2* mutations (21, 22), yet their risk of breast cancer is not zero. This context highlights the importance of clear communication, as implicit assumptions about negative results may lead patients to overlook ongoing risks. Conversely, women who overestimate their risk may distrust negative results and seek frequent mammograms, increasing their exposure to false positives (23). Few studies have applied theory-based communication approaches (e.g., dual-processing models and operant learning theory) to address barriers in low-risk pathways, and their effects remain limited (24). Further research is necessary to develop targeted communication strategies that effectively convey risk information and promote acceptance.

Institutional inconsistency in screening guidelines further complicates screening low-risk pathways (4). Our study found that varied guideline adoption among medical institutions contributes to barriers at the provider and system levels, particularly in screening practices for women younger than 50. Research has shown that inconsistent guidelines shape provider decision-making, potentially misaligning with USPSTF recommendations (4). To mitigate these issues, medical boards should rigorously evaluate national guidelines while institutions establish clear policies and supportive workflows.

Strengths and limitations

This study has several limitations, including the relatively small sample size of practice leaders and representatives from two southeastern healthcare systems and the subjective nature of the health professionals' responses, which reflect individual perceptions and knowledge. In addition, the findings are based solely on the perspectives of health professionals; future studies should investigate patients' perceived barriers and facilitators to risk-stratified breast cancer screening. However, these findings have implications for various healthcare settings, as we intentionally included two primary care sites with varied insurance structures, serving both rural and urban populations with a diverse patient base. Future research should examine whether these findings apply to other regions or healthcare systems with different policies, infrastructures, and resources. Our data collection and analysis, guided by fishbone diagrams and the comprehensive CFIR, enabled structured visualization of results at each level. Future research could enhance data analysis by integrating qualitative methods with natural language processing techniques, providing quantitative insights into theme importance and enabling cross-group comparisons (e.g., institutions and demographics) to identify subtle variations in perspectives (25, 26). A unique strength is the timing of data collection, completed before the recent changes to the USPSTF guidelines, allowing us to capture insights that can guide strategies for adapting to evolving and sometimes conflicting guideline recommendations in other healthcare settings, including the de-implementation of outdated practices.

Conclusion

Overall, our findings show that ongoing medical education for primary care providers and accessible clinical decision-making support for screening referrals serve as implementation facilitators for risk-stratified recommendations. By identifying the unique barriers and facilitators for high- and low-risk screening pathways, primary care clinics are better positioned to design and pilot targeted interventions that promote uptake and integration into clinical practice. Future risk-stratified screening programs should consider these insights, addressing the specific needs of high- and low-risk pathways simultaneously to optimize program effectiveness and sustainability.

Data availability statement

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

Ethics statement

The studies involving humans were approved by the Institutional Review Board of Emory University. The studies were conducted in accordance with the local legislation and institutional requirements. The Ethics Committee/institutional review board waived the requirement of written informed consent for participation from the participants or the participants' legal guardians/next of kin because that the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

Author contributions

YG: Formal analysis, Visualization, Writing – original draft, Writing – review & editing, Conceptualization, Data curation, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation. HB: Visualization, Formal analysis, Writing – original draft. CE: Validation, Visualization, Writing – review & editing, Conceptualization, Supervision. MC: Investigation, Resources, Validation, Visualization, Writing – review & editing. SA: Investigation, Resources, Validation, Visualization, Writing – review & editing. TJ: Conceptualization, Investigation, Resources, Supervision, Validation, Visualization, 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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The author(s) declare that no Gen AI was used in the creation of this manuscript.

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Regional population decline and health screening uptake in Korean adults: nationwide study using multilevel regression analysis

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Background: Health screening is crucial for detecting medical needs and presenting effective alternatives. As Korea undergoes rapid demographic shifts and widening regional gaps, screening is increasingly important to identify these needs. This study explores how changes in regional population size related to health screening uptake among Korean adults.

Methods: Data on 182,437 adults from the 2021 Korean Community Health Survey (KCHS) were used, with health screening divided into cancer and general medical screening. Regional population size, aging index and financial independence ratio from 2012 to 2022 KOSIS were linked to our data. Generalized linear mixed effects models were applied for hierarchical logistic regression analysis of the association between the regional population size and screening, controlling for regional- and individual-level variables.

Results: Decrease in regional population size were significantly associated with lower odds ratio (OR) of receiving health screening; OR 0.85 (95% CI 0.83–0.88), as well as cancer screening; OR 0.87 (95% CI 0.85–0.90). Similar results were observed in regions with stable in population size.

Conclusion: Our study findings indicate the significant associations between regional population size decline and screening. Population-based policies should consider regional attributes to ensure equitable access to screening services.

KEYWORDS

regional population change, health screening, cancer screening, medical accessibility, regional disparity

Background

Health screening has long been regarded as a primary preventative approach for incidence and progression of disease (1). In Korea, non-communicable diseases such as cancer have consistently ranked among the top causes of death for decades (2). As of 2022, the total number of prevalent cancer cases in South Korea has exceeded 2 million since 2018, indicating that approximately one in in 20 individuals has a history of cancer diagnosis (3, 4). Moreover, the five most common type of cancer are projected to account for 55.7% of the total cancer burden in Korea, a figure expected to rise as the population continues to age (5). To mitigate the burden of disease, health screening in Korea is offered through a variety of organized and opportunistic screening programs (6). National efforts to combat disease include the introduction of the

General Health Screening Program, which offers screening services at little to no cost to eligible individuals. Additionally, the Korean government launched the National Cancer Screening Program to address cancer-related mortality and its associated burdens (7, 8).

The healthcare costs are naturally expected to increase with aging, as risk of disease and geriatric conditions is increased exponentially (9, 10). Korea has crossed the threshold criteria of an aged society with a proportion of older adults of 17.5% in 2022, which could be attributed to an increase in life expectancy and a record-low in birth rates (11). In this context, timely screening becomes paramount due to the disappearance of regions caused by aging, decreasing fertility rates, and deepening regional gaps. These demographic shifts, such as population aging and declining fertility rates, have become primary drivers of changes in population dynamics and resultant population decline, leading to local extinction (12). In particular, it has been previously reported that many regions in Korea are currently experiencing rapid depopulation, with some on the verge of extinction, i.e., "shrinking cities" (13). This phenomenon is not confined solely to Korea; similar patterns have been observed in nearby Japan and China, as well as in certain regions across Europe and the US (14, 15).

Due to the government's concerns about regional extinction, various healthcare policies have been introduced and are being promoted to close the gap between regions. In 2022, the Korean government put forth a plan to tackle this issue by designating and providing financial support to a total of 90 regions known as "depopulation areas." Additionally, in terms of essential health services, policies are now being developed to address the medical imbalance between regions (16). Nonetheless, although existing literature suggests that the regional population decline may compromise the medical infrastructure and access to healthcare services, it is still unclear how health screening uptake due to depopulation may be impacted in the Korean setting (16, 17).

Moreover, a number of studies have reported on relevant individual-level factors to health screening, but impact of regional-level determinants such as population size change on screening is under-researched (18, 19). Growing evidence also points toward the importance of the incorporation of multilevel modeling strategies when identifying screening barriers (19). Therefore, our study's main objective was to shed light on the effects of regional population change on screening among adults in Korea using a multilevel modeling approach.

Methods

Participants

This study utilized data from the 2021 Korean Community Health Survey (KCHS), a nationwide health interview survey conducted by the Korean Centers for Disease Control and Prevention. The primary objectives of the KCHS are to establish and evaluate regional health plans, standardize the survey methodologies, and generate comparable regional health statistics (20, 21). This study included only participants aged 20 years and older and excluded those with missing data on variables on household income level, smoking status, region. A total of 46,566 individuals were excluded because they either considered the information sensitive or reported not knowing the answers. Consequently, a total of 182,437 individuals were included in the final analysis. Regional variables were obtained from the Korean Statistical Information Service (KOSIS) and were used to link each individual to their respective regional code.

Variables

The dependent variable of this study was health screening, which included both cancer screening and general medical checkups. Participants were categorized based on their response to the question: 'Did you undergo general checkups and a cancer screening to assess your health status, even in the absence of specific health problems?' Additionally, cancer screening were analyzed separately for a more detailed examination.

Population size changes in each region were calculated by dividing the 2022 population by the 2012 population, using data from KOSIS. These changes were treated as a continuous variable and then categorized into three groups: increase (greater than 0%), stable (0–10% reduction), or decrease (greater than 10% reduction). The 2022 data represented the most recent population statistics available, while 2012 marked a year of significant geographic changes, including the establishment of Sejong city as a self-governing province, making it a suitable reference point for a 10-year analysis. Additionally, as policies aimed at expanding health insurance coverage to improve patient access concluded in December 2009, this timeframe was appropriate for evaluating subsequent changes in public health conditions.

Region-related variables, including financial independence and the aging index, were obtained from the KOSIS and linked with each individual's regional codes of residence. These variables were measured using the combined regional codes, and median values for the low and high categories were calculated using the data from KOSIS. Regional financial independence ratio has shown that the capability level of an area to self-financing the government activities, development and provide the good service to people who paid off the taxes and levies as source of income whom needed by the region (22). Aging index is the age of a society, which is the ratio of those aged 65 and over against those aged 0–14 (23).

The individual-level characteristics controlled for in this study included age, sex, marital status, household income level, region, alcohol consumption status, smoking status, self-reported health status, and health literacy. Health literacy encompassed the ability to understand verbal health information, such as verbal explanation by clinicians, as well as the ability to comprehend written health information, such as that found on the internet or in brochure.

Statistical analysis

Chi-square tests were conducted to examine the general characteristics of the study population. Generalized linear mixed models (PROC GLIMMIX) were employed for hierarchical logistic regression analysis to investigate the association between regional population size and screening. A multilevel model is a special case of generalized linear mixed models that can be handled by the GLIMMIX procedure (24). These multilevel models were used to account for potential correlations within the same region (25). The initial model included individuals-level variables to access their

Abbreviations: CI, Confidence Interval; KCHS, Korean Community Health Survey; KOSIS, Korean Statistical Information Service; OR, Odds Ratio.

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TABLE 1 General characteristics of the study population.

Variables	Total		Health screening				*p*-value
			Yes		No		
	N	(%)	*N*	(%)	*N*	(%)	
Regional-level characteristics							
Regional population size							<0.0001
Decrease (≥ 10% reduction)	60,633	(33.2)	34,272	(56.5)	26,361	(43.5)	
Stable (0–10% reduction)	69,002	(37.8)	40,319	(58.4)	28,683	(41.6)	
Increase (> 0%)	52,802	(28.9)	30,869	(58.5)	21,933	(41.5)	
Aging index							<0.0001
Low	87,462	(47.9)	50,010	(57.2)	37,452	(42.8)	
High	94,975	(52.1)	55,450	(58.4)	39,525	(41.6)	
Financial independence ratio							<0.0001
Low	90,752	(49.7)	54,491	(60.0)	36,261	(40.0)	
High	91,685	(50.3)	50,969	(55.6)	40,716	(44.4)	
Individual-level characteristics							
Age (years)							<0.0001
19–39	39,302	(21.5)	9,698	(24.7)	29,604	(75.3)	
40–49	26,747	(14.7)	16,902	(63.2)	9,845	(36.8)	
50–59	33,316	(18.3)	23,028	(69.1)	10,288	(30.9)	
60–69	37,979	(20.8)	27,300	(71.9)	10,679	(28.1)	
≥ 70	45,093	(24.7)	28,532	(63.3)	16,561	(36.7)	
Sex							<0.0001
Male	81,446	(44.6)	44,462	(54.6)	36,984	(45.4)	
Female	100,991	(55.4)	60,998	(60.4)	39,993	(39.6)	
Marital status							<0.0001
Married	111,799	(61.3)	75,083	(67.2)	36,716	(32.8)	
Separated or divorced	38,769	(21.3)	23,257	(60.0)	15,512	(40.0)	
Unmarried	31,869	(17.5)	7,120	(22.3)	24,749	(77.7)	
Household income level							<0.0001
Low	29,693	(16.3)	16,474	(55.5)	13,219	(44.5)	
Middle	83,166	(45.6)	48,849	(58.7)	34,317	(41.3)	
High	69,578	(38.1)	40,137	(57.7)	29,441	(42.3)	
Region							<0.0001
Metropolitan	53,177	(29.1)	30,093	(56.6)	23,084	(43.4)	
City	38,887	(21.3)	20,325	(52.3)	18,562	(47.7)	
Rural	90,373	(49.5)	55,042	(60.9)	35,331	(39.1)	
Alcohol status							<0.0001
Never	42,635	(23.4)	25,964	(60.9)	16,671	(39.1)	
Ever	139,802	(76.6)	79,496	(56.9)	60,306	(43.1)	
Smoking status							<0.0001
Never	119,417	(65.5)	69,971	(58.6)	49,446	(41.4)	
Ever	63,020	(34.5)	35,489	(56.3)	27,531	(43.7)	
Self-reported health status							<0.0001
High	72,730	(39.9)	39,760	(54.7)	32,970	(45.3)	
Middle	77,280	(42.4)	46,585	(60.3)	30,695	(39.7)	

(Continued)

TABLE 1 (Continued)

Variables	Total		Health screening				*p*-value
			Yes		No		
	N	(%)	*N*	(%)	*N*	(%)	
Low	32,427	(17.8)	19,115	(58.9)	13,312	(41.1)	
Health literacy							<0.0001
Low	75,274	(41.3)	42,888	(57.0)	32,386	(43.0)	
High	107,163	(58.7)	62,572	(58.4)	44,591	(41.6)	
Total	182,437	(100.0)	105,460	(57.8)	76,977	(42.2)	

impact on screening. Model 2 focused on the influence of regional-level variables, with the region included as a random effect to explore its unique contributions. Finally, the last model (model 3) incorporated both individuals and regional-level variables. Intraclass correlations (ICC) were used to evaluate whether there was significant variation between groups compared to variation within those groups (26). ICC is calculated as the ratio of the variance between clusters to the total variance. Results are presented as odds ratio (OR) and confidence intervals (CI). Statistical significance was determined at p-value < 0.05. All data analyses used SAS 9.4 software.

Results

Table 1 describes the general characteristics of the study participants. Among 182,437 respondents, 105,460 individuals (or 57.8% of the total study sample) reported to have undergone health screening. In terms of regional-level characteristics, those who reported to have undergone health screening for regional population size were shown as follows: 56.5, 58.4 and 58.5% of participants in the 'decrease', 'stable' and 'increase' groups, respectively. For the aging index, those who reported to have undergone screening were 57.2% in the 'low' vs. 58.4% of individuals in the 'high' group. Additionally, 60.0% vs. 55.6% of participants in the 'low' and 'high' groups of the financial independence ratio reported to have undergone health screening.

The multilevel model analysis results for regional population size and health screening are shown in Table 2. We presented results on model 3 as its corresponding goodness-of-fit values indicated the best model fit. In model 3, compared to an increase in the regional population size: stable and decrease in regional population size reported lower odds of health screening: OR 0.95 (95% CI 0.92—0.98) and OR 0.85 (95% CI 0.82—0.88). Compared to a low financial independence ratio, a high ratio was associated with lower odds of health screening: OR 0.93 (95% CI 0.90—0.95).

Table 3 presents the results of multilevel analysis of regional population size and cancer screening. Model 3 (best fitting model) results for regional-level characteristics were as follows; for regional population size; stable: OR 0.96 (95% CI 0.94—0.99) and decrease in regional population size: OR 0.87 (95% CI 0.85—0.90) were associated with a lower odds ratio of cancer screening, compared to the increase group. Furthermore, a high financial independence ratio showed decreased odds OR 0.94 (95% CI 0.91—0.96) of cancer screening as compared to low financial independence.

Discussion

Our present study's results showed that a decrease in regional population size was significantly associated with the lowest likelihood of health screening. The findings also indicated a similar pattern for cancer screening in relation to regional population changes. Regional population decline, driven by aging, declining fertility rates, and migration, reduces access to medical care and challenges service quality, necessitating targeted interventions.

Recent changes in regional population size in 2022, compared to 2012 may be indicative of a variety of drivers including regional fluctuations in birth and mortality rates. Furthermore, a decrease in local population size due to youth out-migration is also an issue of great concern (27). Motivations behind inter-regional migration of young residents are numerous, including the pursuit of improved education, employment opportunities and overall quality of life in other (often more urbanized) regions (28). In 2022, 44.7% of Korea's total population resided in the capital city, Seoul, and its surrounding metropolitan areas (29). As such, overcrowding in urban areas and depopulation in rural areas may lead to an imbalance and eventual collapse in the medical infrastructure and access to healthcare services (30).

Changes in population size, such as shrinkage, and shifts in population structure, including aging, present significant challenges for many countries. Rural shrinkage, characterized by a sharply declining and increasingly aging population, is a widespread global phenomenon (31). Understanding how different countries manage these demographic shifts is crucial, as many are experiencing similar post-growth trajectories. For instance, in Taiwan, the share of the population aged 65 and over was just 8.4% in 2000 but had nearly double to 16.0% by 2020 (32). In 2021, the proportion of the population aged 65 and older was 28.9% in Japan, 16.6% in South Korea, and 14.2% in China (31). Given that many countries have already entered or are on the brink of population decline, comprehensive investigations into its impact are of considerable significance (33).

As a consequence of an interplay of these factors, most depopulated areas are predominantly inhabited by older adults (30). Aging populations face numerous challenges, including a higher burden of chronic disease and limitations in daily activities, which, in turn, increase the demand for expanded screening services (34, 35). Ensuring adequate screening resources for this vulnerable population is particularly crucial for time-sensitive conditions such as cancer (36). Given these considerations, the inclusion of the aging index was expected to provide valuable insight in our study; however, no

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TABLE 2 Results of regional population size and health screening.

Variables	Health screening											
		Model 1				Model 2				Model 3[a]		
		OR (95% CI)				OR (95% CI)				OR (95% CI)		
Fixed effects intercept (S.E)		0.39*(0.05)				0.94*(0.09)				1.09*(0.08)		
Regional-level characteristics												
Regional population size												
Decrease (≥ 10% reduction)	0.88	(0.85)	–	(0.90)					0.85	(0.82)	–	(0.88)
Stable (0–10% reduction)	0.96	(0.94)	–	(0.99)					0.95	(0.92)	–	(0.98)
Increase (> 0%)	1.00								1.00			
Aging index												
Low	1.00								1.00			
High	1.09	(0.94)	–	(1.27)					0.93	(0.84)	–	(1.04)
Financial independence ratio												
Low	1.00								1.00			
High	0.87	(0.84)	–	(0.89)					0.93	(0.90)	–	(0.95)
Individual-level characteristics												
Age (years)												
19–39					0.28	(0.27)	–	(0.29)	0.28	(0.27)	–	(0.29)
40–49					1.00				1.00			
50–59					1.30	(1.25)	–	(1.35)	1.30	(1.26)	–	(1.35)
60–69					1.64	(1.58)	–	(1.70)	1.64	(1.58)	–	(1.70)
≥ 70					1.40	(1.34)	–	(1.45)	1.40	(1.35)	–	(1.45)
Sex												
Male					0.80	(0.78)	–	(0.83)	0.80	(0.78)	–	(0.83)
Female					1.00				1.00			
Marital status												
Married					1.00				1.00			
Separated or divorced					0.70	(0.68)	–	(0.72)	0.70	(0.68)	–	(0.72)
Unmarried					0.36	(0.35)	–	(0.37)	0.36	(0.35)	–	(0.37)
Household income level												
Low					0.61	(0.59)	–	(0.64)	0.61	(0.59)	–	(0.64)
Middle					0.83	(0.81)	–	(0.85)	0.83	(0.81)	–	(0.85)
High					1.00				1.00			
Region												
Metropolitan					1.00				1.00			
City					0.83	(0.68)	–	(1.01)	0.81	(0.69)	–	(0.96)
Rural					1.08	(0.89)	–	(1.30)	1.06	(0.91)	–	(1.24)
Alcohol status												
Never					1.00				1.00			
Ever					1.15	(1.12)	–	(1.18)	1.15	(1.12)	–	(1.18)

(Continued)

TABLE 2 (Continued)

Variables	Health screening											
		Model 1				Model 2				Model 3[a]		
		OR (95% CI)				OR (95% CI)				OR (95% CI)		
Smoking status												
Never					1.00				1.00			
Ever					0.89	(0.87)	-	(0.92)	0.89	(0.86)	-	(0.92)
Self-reported health status												
High					1.00				1.00			
Middle					1.03	(1.01)	–	(1.05)	1.03	(1.01)	–	(1.06)
Low					0.89	(0.86)	–	(0.92)	0.90	(0.87)	–	(0.92)
Health Literacy												
Low					0.78	(0.76)	–	(0.80)	0.78	(0.76)	–	(0.80)
High					1.00				1.00			
Error variance												
Level-2 intercept (S.E)		0.01*(0.02)				0.007*(0.015)				0.004*(0.01)		
Model fit												
-2LL		247046.7				216690.7				216555.9		
Pearson Chi-Square/ DF		1.00				1.00				1.00		

*$p < 0.05$; ICC (Intraclass correlation coefficient): 0.0500 (<0.0001).
[a]Best fitting model.

statistically significant associations were observed with any type of screening. Previous study shown that older adults are more likely to undergo health checkups, with cancer screening participation rates peaking among individuals aged 60–69 years (37, 38).

In 2022, the Korean government designated approximately 90 regions as 'depopulation area' and established one trillion won annual fund to address local extinction risk (16). To address regional health challenges, the government continues to develop strategies across various sectors, including healthcare. This study calculated the regional extinction index by analyzing local population changes to capture both population inflow and outflow. This index serves as a representative measure of population change (39). Unlike previous studies that primarily focused on economically active populations, our approach provides a more comprehensive understanding of overall population dynamics (40). Give that population decline is a significant national concern, it is essential to examine regional population circulation structures, including both inflow and outflow, to inform effective policy responses (16).

From a population perspective, regional-level financial independence reflects the ability of local governments to maintain financial independence. The degree of financial independence of local governments is closely linked to the demographic factors such as an aging population and low birth rates (41). In our study, a high financial independence ratio was found to be inversely associated with health screening attendance. This finding contrasts with the results of Park et al., who, using the 2017 KCHS data, examined the relationship between individual and regional factors and health screening participation. In contrast to our study, they reported no significant associations between financial independence and health screening participation (42). Although the financial independence ratio may not fully represent the overall financial condition of a local government, it remains a key indicator of its fiscal health (41). Therefore, a low financial independence ratio, coupled with unstable demographic trends, could serve as valuable evidence to inform active management and policy interventions aimed at bolstering healthcare infrastructure.

As the population decreases, tax revenue naturally diminishes, which can adversely affect the financial independence ratio. Even with a reduced population, municipalities are required to maintain the same infrastructure network. However, the shrinking tax base may result in higher tax rates or insufficient revenue, ultimately leading to a deterioration in the quality of public services. Furthermore, reductions in gross product and consumption may occur, potentially leading to cuts in essential infrastructure, including health services (43). These demographic shifts are expected to have broad societal implications, including a contraction of labor markets, employment medical examination increased tax burdens to sustain pension systems, and economic stagnations (44). Therefore, proactive government intervention is essential to ensure continued access to infrastructure for residents in areas experiencing population decline.

At the individual-level, health literacy emerged as a significant risk factor for screening participation in our study, irrespective of the type of screening. Limited health literacy is a barrier that may negatively impact screening by affecting the extent to which health information is assimilated, thereby de-empathizing the importance of seeking screening services (45). Given that inadequate health literacy appears to impact Korean older adults more often than their younger counterparts, we believe that focusing on enhancing health literacy could yield additional advantages when customizing relevant health

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TABLE 3 Results of regional population size and cancer screening.

Variables	Cancer screening											
	Model 1				Model 2				Model 3[a]			
	OR (95% CI)				OR (95% CI)				OR (95% CI)			
Fixed effects												
Intercept (S.E)		0.44*(0.05)				1.03*(0.09)				1.16*(0.08)		
Regional-level characteristics												
Regional population size												
Decrease (≥ 10% reduction)	0.89	(0.87)	–	(0.92)					0.87	(0.85)	–	(0.90)
Stable (0–10% reduction)	0.97	(0.94)	–	(1.00)					0.96	(0.94)	–	(0.99)
Increase (> 0%)	1.00								1.00			
Aging index												
Low	1.00								1.00			
High	1.10	(0.94)	–	(1.28)					0.93	(0.83)	–	(1.05)
Financial independence ratio												
Low	1.00								1.00			
High	0.87	(0.85)	–	(0.90)					0.94	(0.91)	–	(0.96)
Individual-level characteristics												
Age (years)												
19–39					0.29	(0.28)	–	(0.30)	0.29	(0.28)	–	(0.30)
40–49					1.00				1.00			
50–59					1.28	(1.24)	–	(1.33)	1.28	(1.24)	–	(1.33)
60–69					1.62	(1.56)	–	(1.68)	1.62	(1.57)	–	(1.69)
≥ 70					1.35	(1.30)	–	(1.41)	1.35	(1.30)	–	(1.41)
Sex												
Male					0.75	(0.73)	–	(0.78)	0.75	(0.73)	–	(0.78)
Female					1.00				1.00			
Marital status												
Married					1.00				1.00			
Separated or divorced					0.69	(0.67)	–	(0.71)	0.69	(0.67)	–	(0.71)
Unmarried					0.34	(0.33)	–	(0.35)	0.34	(0.33)	–	(0.35)
Household income level												
Low					0.63	(0.61)	–	(0.65)	0.63	(0.61)	–	(0.66)
Middle					0.85	(0.82)	–	(0.87)	0.85	(0.82)	–	(0.87)
High					1.00				1.00			
Region												
Metropolitan					1.00				1.00			
City					0.84	(0.68)	–	(1.03)	0.82	(0.69)	–	(0.98)
Rural					1.08	(0.89)	–	(1.32)	1.07	(0.91)	–	(1.27)
Alcohol status												
Never					1.00				1.00			
Ever					1.15	(1.12)	–	(1.18)	1.15	(1.12)	–	(1.18)
Smoking status												
Never					1.00				1.00			

(Continued)

TABLE 3 (Continued)

Variables	Cancer screening											
	Model 1				Model 2				Model 3[a]			
	OR (95% CI)				OR (95% CI)				OR (95% CI)			
Ever					0.91	(0.88)	–	(0.94)	0.91	(0.88)	–	(0.94)
Self-reported health status												
High					1.00				1.00			
Middle					1.04	(1.01)	–	(1.06)	1.04	(1.01)	–	(1.06)
Low					0.90	(0.87)	–	(0.93)	0.90	(0.87)	–	(0.93)
Health literacy												
Low					0.78	(0.76)	–	(0.79)	0.78	(0.76)	–	(0.79)
High					1.00				1.00			
Error variance												
Level-2 intercept (S.E)		0.011*(0.03)				0.007*(0.02)				0.005*(0.01)		
Model fit												
-2LL		245070.4				214561.6				214467.1		
Pearson Chi-Square/ DF		1.00				1.00				1.00		

*$p < 0.05$; ICC (Intraclass correlation coefficient): 0.0500 (<0.0001). [a]Best fitting model.

policies (46). In addition to expanding local infrastructure, improving health literacy and implementing public education and awareness campaigns are essential strategies for promoting preventive health behaviors, including participation in health screening programs among local populations.

Limitations were present in our study. First, due to the cross-sectional nature of the data, causal relationships could not be established. Therefore, we cannot determine a causal relationship between regional population decline and health screening. Furthermore, despite efforts by the surveying agency to minimize bias, the data used in this study were primarily self-reported, making them susceptible to potential recall bias. Third, although we adjusted for various regional- and individual-level covariates that could influence the results, we cannot entirely rule out residual confounding, as some unmeasured or unconsidered factors may still exist. Lastly, this study may not fully capture individual-level variations within regions. While regional-level characteristics provide valuable insights into broad trends, individuals variation within these regions may not be fully accounted for.

Nonetheless, there were also some notable strengths. To the best of our knowledge, our study is one of the very first population-based studies to examine the influence of regional population change on health screening using a multilevel modeling approach. We included measures that reflect a region's population structure and economic status such as the aging index and the financial independence ratio, which are readily available by the KOSIS. The current study also has the advantage of incorporating a large, nationally representative sample of Korean adults.

Conclusion

Decrease in regional population size was found to show the lowest significant odds with all types of screening. Regional-level intervention programs targeted at growing screening rates may prove effective, on the condition that unique characteristics of the regions including population demographics and size are taken in account.

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/s.

Ethics statement

The studies involving humans were approved by this study was reviewed and approved by the Institutional Review Board of the National Cancer Center (IRB no. NCC2024_0086). 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

WJ: Conceptualization, Formal analysis, Writing – original draft. WK: Writing – review & editing. K-TH: 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.

Generative AI statement

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

Publisher's note

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Difference-making factors for successful implementation of a multicomponent colorectal cancer screening program in rural clinics (SMARTER CRC)

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Introduction: Rural disparities in colorectal cancer (CRC) screening persist despite the availability of effective, evidence-based interventions. In this study, we aimed to understand what characteristics lead to success when implementing a multicomponent CRC screening intervention in rural primary care clinics in a pragmatic clinical trial (SMARTER CRC).

Methods: We applied coincidence analysis to identify solution pathways that led to successful implementation during the first year of SMARTER CRC in intervention clinics. We assessed clinic success as high/low rates of fecal immunochemical testing (FIT) and overall CRC screening. Factors included in the analysis were collected through qualitative interviews, practice facilitation notes, and project datasets.

Results: A total of 14 intervention clinics were included in our analysis. Post-intervention, overall clinic-level screening rates for CRC ranged from 12.6 to 22.0%, while FIT completion rates among patients who were mailed a kit ranged from 12.3 to 41.7%. Values for three factors perfectly distinguished between clinics with higher and lower CRC screening rates: clinics sending a pre-FIT introduction letter on their own, clinics having prior (or current) experience with CRC screening campaigns, and clinics changing the type of FIT they used. For FIT screening rates, two factors perfectly distinguished between clinics with higher and lower rates: clinics sending introduction letters on their own and clinic staff attending four or more health plan/clinic meetings.

Discussion: Higher FIT and CRC screening rates were associated with clinics that were able to mail an introductory letter, had experience in CRC screening campaigns, did not change their FIT, and attended the health plan/clinic meetings. These clinic-level factors appear to be difference-makers to the successful implementation of a CRC screening program in rural settings.

KEYWORDS

colorectal cancer, colorectal cancer screening, fit testing, implementation science, coincidence analysis (CNA)

Introduction

Colorectal cancer (CRC) is the fourth most common type of cancer and the second leading cause of cancer deaths in the United States, representing approximately 8% of new cancer diagnosis and over 50,000 deaths in 2023 (1). Screening for CRC is highly effective in detecting cancer in early stages, achieving a 90% 5-year survival rate when found at the localized stage; however, between 2016 and 2020, approximately only one in three cancers were identified at this stage (2). More than half of CRC deaths can be prevented by screening and early detection, yet barriers persist at the patient, provider, and health system levels, with unique challenges in rural and frontier communities (3–6). Rural residents experience higher mortality from CRC than their urban counterparts due to persistent rural disparities in cancer screening and prevention (7). It is well-documented that these health disparities are often attributed to limited access to healthcare, inadequate health insurance, and higher poverty rates for rural Americans than their urban counterparts (8).

The implementation of mailed fecal immunochemical testing (FIT) and patient navigation programs can increase the uptake of CRC screening in clinical practices (9, 10). Prior research reports the effectiveness of CRC screening programs, including FIT screening and patient navigation in large health systems (10–13). While there has been an increase in the use of FIT as a first-line mechanism for CRC screening, substantial variation remains in implementation strategies and program adaptations when this evidence-based intervention is integrated into practice (14–19). Clinic and health plan partnered programs can increase the uptake of screening and follow-up through patient navigation; however, a better plan is needed to understand the key implementation factors for success (20, 21). Limited research has explored the factors associated with the successful implementation of multi-level programs to increase CRC screening in rural primary care settings (22).

This study examines features affecting the effectiveness of a multicomponent program of mailed FIT outreach and patient navigation to boost CRC screening in rural primary care. The SMARTER CRC study tested the implementation of a mailed FIT and patient navigation program in rural and frontier clinics using a multi-level clinic and health plan partnered approach (23). Implementation was supported by study practice facilitators trained in the intervention (24). We used data from the SMARTER CRC study to understand which clinic- or community-level characteristics explained implementation success. We aimed to understand combinations of implementation-related activities and clinic conditions that consistently distinguished intervention clinic sites with higher overall CRC screening rates compared to those with lower ones, as well as FIT return rates from mailed outreach. These findings can be used more broadly in the planning, adaptation, and implementation of mailed FIT programs in rural settings.

Methods

Study setting

SMARTER CRC is a pragmatic implementation trial partnering with Medicaid health plans and rural primary care clinics in Oregon to support the implementation of a mailed FIT outreach and patient navigation program (23). This study was conducted as part of the National Cancer Institute-funded Accelerating Colorectal Cancer Screening and Follow-up through Implementation Science (ACCSIS) Program. The overall aim of ACCSIS is to conduct multi-site, coordinated, transdisciplinary research to evaluate and improve CRC screening processes using implementation science. This study was approved by the Oregon Health & Science University Institutional Review Board (STUDY00020681); individual consent was not required from clinical patients receiving the intervention as it was determined to be a pragmatic extension of clinical practice. Qualitative interview participants verbally consented to the interviews.

Details of the SMARTER CRC design and outcomes have been described in a previous study (23, 30). In brief, intervention clinics were randomly selected to implement the mailed FIT outreach and patient navigation program during the first year of the trial, while the remaining clinics continued with usual care. Medicaid health plans affiliated with intervention clinics generated the lists of patients due for CRC screening and provided them to the clinics. Clinic staff reviewed the list and removed any patients who were ineligible for screening or had not yet established care. The revised lists were sent to a mailed vendor who mailed patients' FITs and clinics and/or health plans sent FIT reminders. At each clinic, medical assistants or other patient support staff received training for patient navigation. Patient navigators (usually medical assistants or outreach staff) then provided navigation support through phone calls to patients with abnormal FIT results to complete a colonoscopy. Intervention clinics received practice facilitation as an implementation strategy. Practice facilitators are individuals trained to support clinical practices in capacity building and evidence-based intervention implementation (25, 26). Practice facilitators supported the navigators throughout the project; however, the implementation varied across clinics. For example, some clinics mailed introductory letters on their own, some opted to attend monthly meetings with clinics and health plans, and others opted to change their FIT types.

Within 28 randomized clinics, eligible patients were identified, and the intervention was implemented over 1 year, ranging from May 2021 to June 2022 (23). In this analysis, only data from the Year 1 ($N = 14$) intervention clinics are included.

Study outcomes

Coincidence Analysis (CNA) is a configurational comparative method that enables the analysis of clinical, community, intervention, and implementation components that lead to implementation success (27).

CNA focused on two research questions from the Year 1 outcomes (main outcomes):

1) Which combinations of implementation-related activities and clinic conditions consistently distinguished sites with higher CRC screening rates from those with lower CRC screening rates?
2) Which combinations of implementation-related activities and clinical conditions consistently distinguished sites with higher FIT return rates from those with lower FIT return rates?

Outcomes for the CNA include overall CRC screening rates (high/low) and FIT return rates (high/low). CRC screening rates are

calculated from the overall eligible population, while the FIT return rates are calculated from the population who were mailed kits.

Intervention and measures

Data were generated from clinic intake surveys, practice facilitation field notes, qualitative interviews, claims data, and data logged by the clinics in the REDCap research data capture tool during program implementation (28, 29). First, data were collected through a Baseline Intake Survey that was distributed to the clinics by the research team. This survey collected information concerning clinic activities, including prior CRC screening programs, FIT, CRC screening rates, and staffing. Data were also collected through practice facilitation notes and activities. The practice facilitators documented scheduled and *ad hoc* interactions, level of engagement, progression of study activities, concerns about the ability to progress, facilitator-needed supports to help clinical practices, and adaptations through contemporaneous contact logs entered in structured forms in REDCap.

Qualitative interviews were conducted with at least one staff member at each clinic (e.g., practice managers, clinical informatics/EHR specialists, quality improvement specialists, medical assistants, providers) at baseline and included information on the clinic and health plan relationship, clinic characteristics, and details about the clinical experience. The interviews were recorded, professionally transcribed, and validated against source audio for accuracy and stored in ATLAS.ti for management. Questions related to specific study activities and site characteristics were identified within the clinic baseline interviews, and clinic answers were categorized into yes/no or high/medium/low variables for the analysis. Quantitative data included data collected from the Medicaid health plans (i.e., claims data) and data collected from clinics and stored in project datasets (REDCap).

Data were collected from the above sources into a single dataset to determine which implementation-related activities for the 14 intervention sites together might explain the outcomes (Table 1). The original dataset had 58 potential explanatory variables, with two different outcomes of interest: overall CRC screening rates (any modality) and FIT return rates.

Analysis

The R package "cna" was used to analyze the dataset. RStudio, R, and Microsoft Excel were also used to support the analysis. The site-level overall CRC screening rates were calculated by the number of patients completing any CRC screening out of the intention-to-treat (ITT) population (30). The overall CRC screening values after 1 year for the 14 sites ranged from 12.6 to 22%, with a median value of 19.1% and a full 1.5-point difference between the two closest outcome values on either side of the meridian value (18.4% vs. 19.9%). For the analysis, sites with overall CRC values above the median were categorized as sites with higher rates and assigned an outcome value of 1; sites with overall CRC values below the median were categorized as sites with lower rates and assigned an outcome value of 0.

The site-level FIT return rates were calculated as the number of patients who returned a FIT divided by the number of patients that were mailed a FIT. The FIT outcome values ranged from 12.3 to 41.7%. Given the relative tight clustering of values between 18.9 and 21.4% for six sites, followed by a full 2-point gap until the next highest value of 23.7%, the analysis categorized FIT values of ≥23% as sites with higher FIT rates and assigned an outcome value of 1 and FIT values of <23% were categorized as sites with lower FIT rates and assigned an outcome value of 0.

To prepare the dataset for analysis with CNA, continuous variables were recoded as categorical factors, and missing values were temporarily assigned a dummy value to keep them from dropping out of the analysis.

To achieve data reduction, an exploratory data analysis was conducted on the entire dataset to inform the selection of a smaller subset of candidate factors for use in subsequent model development. Specifically, the "minimally sufficient conditions" (i.e., "msc") function from the R package "cna" was used to search across all 61 cases and all process and context factors (with process factors assessed by three rates across all five time points) to identify redundancy-free configurations of specific conditions with specifically strong connections to the outcome of interest (19, 31–39). This exhaustive process considered every possible one-, two-, and three-condition configuration present in the dataset, assessed each configuration against a prespecified consistency threshold, and retained configurations that meet the consistency threshold.

During this exploratory data analysis, the "msc" function was run multiple times at different consistency levels (95, 90, 85, 80, and 75%) to compare output at different thresholds (32, 33). The study team reviewed the output to identify a small number of "best of class" configurations that met all of the following criteria: (1) the highest coverage score within configurations of identical length (i.e., the "complexity level"); (2) having a significant difference between top-scoring coverage configuration and its next-nearest neighbor within the same complexity level; (3) substantive plausibility; (4) and relevance to our research question.

We then iterated the model using the subset of factors represented by these best-of-class configurations. Using this bottom-up approach, the original dataset was inductively analyzed in its entirety, drawing upon substantive knowledge when interpreting the mathematical output generated by the msc routine, and ultimately identified a subset of candidate factors for model development during the next step of the CNA.

During model development, the goal was to develop overall models that met all of the following criteria: scores of >80% for both consistency and coverage; inclusion of the same factors (taking on different values) to explain both the presence and the absence of the outcome; alignment with theory and prior knowledge; inclusion of at least one program-related factor; relevance to our research question; and absence of model ambiguity.

Results

Of the 14 clinics in the first year of SMARTER CRC, CRC screening rates among the identified eligible population ranged from 12.6 to 22.0%, and FIT return rates among patients who were mailed a FIT ranged from 12.3 to 41.7% (Table 2). The number of eligible patients ranged from 32 to 1,154, and the number of patients who were mailed a FIT ranged from 14 to 579 across these clinical sites.

TABLE 1 Implementation factors and clinic conditions included in CNA model.

Source	Description
Quantitative data	
Clinic characteristics	Federal designation, network structure, EHR, lab
Community data	Income to poverty level, % of adults with less than high school education, poverty status, total population, % of non-Hispanic whites, % of female-headed households, % households receiving public assistance, % of men who are unemployed
Rurality	Oregon rural health designation, Rural–Urban Commuting Area Codes (RUCA)
Clinic survey characteristics	CRC champion, prompt calls, FIT characteristics (i.e., where FITs processed, FIT test), reminders (i.e., messages to patients, reminder texts, reminder calls), navigation, scrub, clinician attitudes on CRC screening, clinic supports, clinic priorities, leadership characteristics
Health plan characteristics	Health plans, mailing characteristics, text reminders
Qualitative data	
Clinic health plan relationship	Research staff perception of relationship of clinic to health plans, clinic perception of health plan-clinic relationship, clinic perception of level of health plan support received
Clinic characteristics	Staffing issues prior to implementation, attitude toward FIT, prior disruptions (new EHR or increases in pop serving), attitude to Mailed FIT, Training on CRC screening (ongoing training of MAs, staff, providers, etc. on workflow or choices)
Clinic experience	Involvement in awareness campaigns, prior FIT Mailing, other current CRC campaigns past or current
Practice facilitation acquired data	
Project characteristics	Health plan supplied FIT vs. clinic supplied FIT, clinic choice to scrub the patient list, clinic choice to send an introduction letter, introduction letter sent by health plan, implementation of clinic-level prompt calls, implementation of health plan-delivered prompt calls, implementation of clinic-delivered reminder calls, implementation of health plan-delivered reminder calls
Engagement	Monthly health plan-clinic meeting attendance, patient navigation training attendance, level of engagement in study activities (beginning, mid-point, and end of Year 1)
Disruptions	Disruption in main point of contact
Adaptations	Clinic-level adaptation where there was a mention of significant adaptation in REDCap

TABLE 2 Clinical characteristics and outcomes.

Clinic	Number of eligible patients	CRC screening rate*	Mailed FIT	FIT screening rate**	CRC screening rate at randomization	Health plan (1, 2, 3)	RUCA† code
Clinic 13	91	22.0%	44	29.5%	52%	2	7
Clinic 5	32	21.9%	14	21.4%	60%	2	4
Clinic 10	183	21.7%	114	24.3%	55%	2	4
Clinic 12	83	21.7%	24	41.7%	Unknown	2	4
Clinic 8	159	21.4%	113	23.9%	39%	2	7
Clinic 9	45	20.0%	35	20.0%	40%	1	5
Clinic 11	256	19.9%	216	18.5%	50%	1	7
Clinic 3	49	18.4%	30	13.3%	52%	1	5
Clinic 14	47	17.0%	31	19.4%	31%	1	4
Clinic 4	39	15.4%	29	13.8%	41%	1	5
Clinic 7	145	15.2%	96	18.8%	50%	2	10
Clinic 6	106	15.1%	73	12.3%	32%	1	4
Clinic 1	1,154	13.3%	579	16.4%	18%	3	4
Clinic 2	224	12.6%	91	18.9%	33%	1	4

Green color shows high outcome; orange color shows low outcome. *% of all eligible patients; **% of patients mailed FIT.
†Rural–Urban Commuting Area Codes, 1 is metropolitan, 10 is rural.

The analysis results presented in Table 3 focused on the research question: *Which combinations of implementation-related activities and clinical conditions consistently distinguished sites with higher CRC screening rates from those with lower CRC screening rates?* The final models for CRC screening featured just three factors: clinics that were mailed pre-FIT introduction letters on their own; clinics that had past or current CRC screening campaigns; and clinics that did not change their FIT type. The positive model (CRC screening

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TABLE 3 CNA analysis for CRC screening outcomes.

Clinic	CRC screening rate		Did the clinic mail out introduction letters?	Other CRC campaigns, past or current	Clinic adaptation, FIT type
	CRC screening rate ≥ 19.1%*		Solution path 1	Solution path 2	
Clinic 5	21.9%		1	0	0
Clinic 12	21.7%		1	0	0
Clinic 8	21.4%		1	0	0
Clinic 13	22.0%		1	1	0
Clinic 10	21.7%		1	1	0
Clinic 9	20.0%		0	1	0
Clinic 11	19.9%		0	1	0
	Overall model scores	Consistency	100% (7/7)		
		Coverage	100% (7/7)		
	CRC screening rate < 19.1%*		Solution path 1	Solution path 2	
Clinic 3	18.4%		0	Missing	1
Clinic 4	15.4%		0	Missing	1
Clinic 7	15.2%		0	1	1
Clinic 14	17.0%		0	0	1
Clinic 6	15.1%		0	0	0
Clinic 1	13.3%		0	0	0
Clinic 2	12.6%		0	0	0
	Overall model scores	Consistency	100% (7/7)		
		Coverage	100% (7/7)		

*The median value of overall CRC outcome values is 19.1%. Green color shows high outcome; dark orange color shows low outcome. Solution path shading (violet and orange) is used to highlight solutions.

rate ≥ 19.1% = 1) featured two solution paths (i.e., two different paths to higher overall CRC screening rates). Solution Path 1 included clinics that chose to send out an introduction letter on their own, and Solution Path 2 included a combination of two conditions: clinic experience with past or current CRC campaigns ("other CRC campaign") together with no clinic-level adaptation of FIT type (they did not change their FIT mid-project). The negative model for clinics with lower CRC screening values consisted of two solution pathways featuring the same three factors, but with different values. Solution Path 1 for the negative model involved the bundle of clinics not sending out the introduction letter on their own, together with no experience with other CRC campaigns. Solution Path 2 for the negative model involved clinics changing their FIT type. The model for the presence of the CRC screening outcome and the model for the absence of the outcome had perfect scores for consistency (7/7, 100%) and coverage (7/7, 100%). Consistency refers to how often clinics identified by the model had the higher screening rate present, while coverage accounts for the percentage of clinics with higher screening rates explained by the model. The same three factors perfectly distinguished between the clinics with higher and lower CRC screening rates.

The final models for higher vs. lower FIT return rates consisted of only two factors: whether or not clinics decided to send out introduction letters on their own and whether or not clinic staff attended four or more health plan/clinic meetings (Table 4). The positive model (FIT screening rate ≥ 23%) comprised a single solution pathway: the joint presence of sending out introduction letters on their own together with clinic staff attending four or more health plan/clinic meetings. The absence of either of these two factors was sufficient for lower FIT return rates. The positive model achieved perfect scores for both consistency (4/4, 100%) and coverage (4/4, 100%), as did the negative model, which also demonstrated both consistency (10/10, 100%) and coverage (10/10, 100%). There was modest model ambiguity in the results, in that a second, different factor was also identified as a candidate for both the positive and negative models for FIT return rates: whether the clinic reported navigating at least one patient with an abnormal FIT result. For the positive model, navigating at least one patient for an abnormal FIT result and deciding to send out introduction letters on their own independently accounted for all four clinics with higher FIT return rates, whereas the absence of either factor was sufficient for lower FIT screening rates. This alternative positive model had perfect scores for both consistency (4/4, 100%) and coverage (4/4, 100%), as did this alternative negative model for both consistency (10/10, 100%) and coverage (10/10, 100%). We ultimately selected "clinic staff attending four or more health plan/clinic meetings" as the second factor in our preferred models based on theoretical and practical grounds (which we address further in the "Discussion" section).

Discussion

Higher FIT return and CRC screening rates were associated with clinics that were able to mail an introductory letter, had experience in

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TABLE 4 CNA analysis for FIT screening outcome.

Fit screening rate ≥ 23%*			Solution path 1	
Clinic	FIT screening rate		Did the clinic mail out introduction letters?	Did the clinic attend 4 + project meetings?
Clinic 12	41.7%		1	1
Clinic 13	29.5%		1	1
Clinic 10	24.3%		1	1
Clinic 8	23.9%		1	1
	Overall model scores	Consistency	100% (4/4)	
		Coverage	100% (4/4)	
Fit screening rate < 23%			Solution path 1	Solution path 2
Clinic 5	21.4%		1	0
Clinic 9	20.0%		0	0
Clinic 2	18.9%		0	0
Clinic 6	12.3%		0	0
Clinic 14	19.4%		0	1
Clinic 7	18.8%		0	1
Clinic 11	18.5%		0	1
Clinic 1	16.4%		0	1
Clinic 4	13.8%		0	1
Clinic 3	13.3%		0	1
	Overall model scores	Consistency	100% (10/10)	
		Coverage	100% (10/10)	

*The median value of FIT Screening Rate values is 23%. Green color shows high outcome; dark orange color shows low outcome. Solution path shading (orange) is used to highlight solutions.

CRC screening campaigns, did not need to change their FIT types, and attended the health plan-clinic meetings. Because SMARTER CRC was a pragmatic trial, each health plan approached program implementation differently, depending on their organizational context. While many clinical and implementation characteristics were assessed, the analysis identified success based on implementation choices and prior implementation experience. These approaches could be successfully employed across many settings and populations. Consistent engagement and participation in the project are crucial for implementation success.

Prior studies conducted by members of this team used CNA to understand implementation characteristics that improved the performance of mailed FIT programs. For example, one study found that involving support staff improved FIT completion rates in community clinics, as evidenced by higher screening rates following the implementation of a centralized mailed FIT program in clinics that had increased back-or front-office staff, had staff help patients resolve barriers to CRC screening, or handed out FITs while educating patients (14). Another study found that centralized implementation teams with dedicated staffing time and the mailing of an introductory letter led to the implementation success of increased FIT mailings (31). A final study using CNA found that health systems that used multiple adaptations to a screening program had higher screening rates, but no single adaptation clearly led to higher screening rates (19).

Regarding any CRC screening, our findings in this project suggest that the implementation strategies most closely associated with success included clinics choosing to send the introduction letter on their own, those participating in a past or current other CRC screening campaign, and maintaining clinics' FIT type. Regarding FIT return rates, our findings suggest that the implementation strategies most predictive of success were clinics choosing to send their own introduction letter and attending four or more health plan-clinic meetings. Health plan 2 utilized a third-party full-service vendor with a specific FIT type and non-customizable materials. Health plans 1 and 3 were more customizable, allowing each clinic to choose which FIT to use and to customize materials to include clinic and health plan branding. For health plan 1, the clinic could choose to use the health plan FIT with central processing. Health plans 1 and 3 offered clinics to process FITs using their typical process.

Notably, clinical practices choosing to send the introduction letter on their own were a key difference maker for both CRC screening and FIT return outcomes. Furthermore, this intervention component has been predictive of screening success in prior studies (31). However, not all clinics were given the option of sending their own letter. One health plan partnered with a third-party vendor with vendor-branded materials, and clinics were given the option to send their own clinic-branded letter; many of these clinics chose to also send their own clinic-branded letter, leading to the patient receiving two notification letters. For the others, the health plans and clinics collaborated to produce co-branded materials that were mailed by the health plan. This intervention component may also be a clinical indicator of fidelity to the project and the recommended processes.

In this study, clinics collaborated with their Medicaid health plans to implement program components, and not all implementation elements were decided at the clinic level. This program included the mailing of a customized introductory letter that emphasized the importance of CRC screening and this easy, at-home testing option. The ability to execute the program was largely identified as high for

clinics that had prior experience with CRC screening campaigns. When the introductory letter was sent from the clinic, the messaging was customized to the patient population and branded with clinic materials, potentially creating a greater sense of trust among the patient recipients. Successful clinics did not need to adapt the FIT they were using. Finally, monthly health plan-clinic meetings, led by the research team, served as a platform to share information about the program broadly and ask health plans and clinics to share their progress, successes, and lessons learned. The clinics that attended the meetings regularly experienced a greater success rate on their screening program, potentially indicating a clinic-level indicator of fidelity.

It should be noted that Rural–Urban Commuting Area Codes (RUCA) for rural designation failed to emerge as difference-makers in implementation success, although RUCA explained one case in the CNA. RUCA codes categorize geographical areas (zip) by population size (40). The RUCA codes indicated clinics were located in the micropolitan, rural and frontier areas. Clinics in rural and frontier areas are small enough to have easily changeable screening rates but have struggled with making practice changes and changing patient behavior. The complexity of rural and frontier clinics will need to be further studied to better understand implementation successes and challenges.

As mentioned in the "Results" section, some model ambiguity emerged due to a second, different factor identified as a candidate in both the positive and negative models for FIT return rates: whether the clinic reported navigating at least one patient for an abnormal FIT result. We ultimately selected the models featuring "clinic staff attending four or more health plan-clinic meetings" instead of this alternative second factor, as it demonstrated their investment in the intervention and could potentially reflect a broader implementation of CRC screening in their clinics. The clinics were willing to take the time to attend the meetings. The meetings themselves provided substantial advice regarding how to best implement the intervention components and offered an opportunity to workshop problems that arose during the roll-out of activities. Regardless, the dedication to conducting navigation may be an indicator of fidelity to the program as well as the navigator had to follow research processes to log navigation activities.

Implications

With persistent disparities in CRC screening, these results point to the importance of engaging clinical practices and health plans in screening outreach campaigns to reduce the urban–rural practice gap. Our results indicate that clinical practices need a starting point to implement programs based on evidence-based strategies. Developing new screening programs, or evaluating prior screening programs and current testing processes, could be an intervention strategy for increasing implementation success.

It is important to create opportunities for collaboration between clinics and health plans (i.e., collaborative cross-sector meetings) to support program implementation. A key factor for success was the regular engagement with participating clinical practices, most notably during the monthly health plan and clinic meetings. This regular meeting cadence enables clinical practices to maintain momentum in their efforts and holds them accountable, as they are required to report on their current progress and any challenges they are experiencing. We found that this was a key component for clinical practices to maintain fidelity to the program.

Limitations

This study is not without its limitations. First, given that the intervention occurred in rural and frontier primary care settings, the population sample size was inherently small. The threshold for clinical practices to engage in the study required at least 30 patients who met CRC screening eligibility criteria. It was not expected that all eligible patients would screen; therefore, the results were expected to encompass a small sample. Second, the intervention occurred during the height of the COVID-19 pandemic. Although a mailed screening outreach program has its benefits during a time when in-person interactions are discouraged, a majority of the primary care workforce was pulled to respond to the pandemic, limiting some staff capacity to fully engage in the programmatic activities (41).

Future studies

It will be important for future research to continue exploring the complexity and nuances of the rural primary care environment, which includes collaborating with clinical practices that have not engaged in CRC screening programs to build the knowledge base of clinic-led CRC screening program implementation.

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 Oregon Health & Science University Institutional Review Board. The studies were conducted in accordance with the local legislation and institutional requirements. The ethics committee/institutional review board waived the requirement of written informed consent for participation from the participants or the participants' legal guardians/next of kin because the OHSU IRB granted a waiver of informed consent as the study involves minimal risks. Qualitative interview participants verbally consented to the interviews.

Author contributions

AP: Conceptualization, Data curation, Investigation, Methodology, Supervision, Visualization, Writing – original draft, Writing – review & editing, Project administration, Resources. BB: Conceptualization, Methodology, Writing – original draft, Writing – review & editing, Data curation, Project administration. MD: Conceptualization, Funding acquisition, Methodology, Writing – review & editing. EJM: Conceptualization, Data curation, Formal analysis, Methodology, Writing – original draft, Writing – review & editing. JC: Conceptualization, Project administration, Supervision, Writing – review & editing. EK: Conceptualization, Data curation, Validation, Writing – review & editing. JS: Data curation, Methodology, Validation, Writing – review & editing. RD: Data curation, Methodology, Writing – review & editing. AE: Data

curation, Project administration, Visualization, Writing – review & editing. AH-O'N: Data curation, Methodology, Writing – review & editing. EM: Data curation, Methodology, Project administration, Writing – review & editing. GC: Conceptualization, Funding acquisition, Investigation, Methodology, Writing – review & editing.

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Building the foundations for an organized population-based cervical cancer screening program with primary HPV self-sampling in Catalonia, Spain: findings from a pilot implementation study

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Introduction: As part of the transition from opportunistic cytology-based screening to an organized, population-based HPV screening program, Catalonia, Spain, launched an implementation pilot in 2021.

Methods: The pilot combined home-based HPV self-sampling with pharmacy-based distribution, coordinated by a screening office using an SMS-based invitation and reminder system, alongside structured follow-up of HPV-positive cases by midwives.

Results: From July 2021 to December 2023, 6,355 women seeking cervical cancer screening were invited to participate in HPV self-sampling via SMS, with high participation (80.9%). Among HPV-positive women (11.8%), compliance with triage cytology was high (98.7%), as with colposcopy referrals when indicated (97.2%). CIN2+ detection rates (3.6% overall, 13.1% in HPV-16 positive) aligned with international studies, reinforcing the value of genotype-specific risk stratification and risk-adapted follow-up pathways in our setting. This organized approach facilitated timely case management and demonstrated the feasibility, acceptability, and effectiveness of the model.

Discussion: While conducted in an opportunistic screening context with a relatively short follow-up time, these findings support HPV self-sampling as an effective primary screening strategy, including women who regularly attend cervical cancer screening, and provide key insights for its scalability within a population-based program, which began its pilot phase in 2024 and is set for full implementation in 2025.

KEYWORDS

Uterine cervical neoplasms, early detection of cancer, mass screening, human papillomavirus viruses

Introduction

Human papillomavirus (HPV) self-sampling is increasingly recognized as a primary screening method in well-established cervical cancer screening programs worldwide. A growing number of countries include self-sampling within their official screening guidelines or are evaluating its use in pilot projects (1). In 2022, the European Commission updated its screening recommendations, advocating for the use of only clinically validated HPV assays as the preferred method for women aged 30 to 65, with screening intervals of at least 5 years (2). The updated recommendations also emphasize the provision of self-sampling kits for cervical cancer screening, particularly targeting women who do not participate regularly in screening programs. Aligned with this approach, the EU aims to ensure that by 2025, 90% of the eligible population is offered screening for breast, cervical, and colorectal cancers (3).

During the past decade, HPV self-sampling has emerged as a promising strategy to improve screening participation, particularly among non-attenders, including women from rural areas and racial, ethnic, sexual, and gender minorities (4, 5). By improving accessibility in hard-to-reach populations, self-sampling increases the capacity to reach individuals at higher risk of cervical cancer (6). Research shows that both regular and non-attenders experience less shame, anxiety, and discomfort with self-sampling compared to clinician-based screening, making it a well-accepted alternative (4, 7). HPV self-sampling may help overcome structural barriers to screening participation, such as social class, gender, education, income, and ethnicity, thereby promoting more equitable screening (8, 9). Combined with its comparable clinical accuracy to clinician-collected samples using HPV assays with PCR amplification (10–12), these advantages reinforce self-sampling's potential to facilitate participation within organized screening programs. However, most supporting evidence for self-sampling use in cervical cancer screening comes from studies in hard-to-reach populations, leaving a significant gap in data on its use in routine screening populations (10, 13, 14).

In 2021, the Catalan Health Department launched an implementation pilot to evaluate HPV self-sampling as primary sample collection method within its opportunistic screening program. A previous clinical trial conducted among women attending public cervical cancer screening services in the region demonstrated high acceptability of home-based HPV self-sampling, with 75.5% of women returning the self-sampling kit when offered by their healthcare provider (15). Building on these findings, and in response to the COVID-19 pandemic, which severely disrupted cancer screening programs, there was a recognized need to rethink screening strategies and adopt alternative approaches to maintain coverage while reducing reliance on in-person healthcare visits (16–18). This implementation pilot aimed to provide critical insights to assess feasibility, acceptability, and sustainability, as well as operational requirements before upscale of a new organized HPV-based screening program.

Transitioning from opportunistic to organized, population-based cervical cancer screening presents significant challenges. Experience from several European countries shows that this shift requires restructuring service delivery, enhanced coordination, and the establishment of robust quality assurance mechanisms. In this context, piloting is essential to validate screening circuits and assess key operational components, such as governance, quality assurance, information systems, and monitoring, all needed to align with international best practices for organized screening programs (19). This study contributes to that evidence by summarizing the findings from the implementation pilot conducted from 2021 to 2023 in Catalonia. This opportunistic pilot supported further piloting of the population-based approach with individual invitations in 2024, followed by scale-up in 2025 to nearby areas, with full implementation across the entire Catalan region planned by 2029.

Materials and methods

Setting

In Spain, healthcare competencies are fully decentralized, with regional governments overseeing healthcare services. In Catalonia, the Catalan Health Department holds sole authority over decisions on cancer screening. Within this framework, the implementation pilot started in 2021 in some municipalities of the southern metropolitan area of Barcelona.

The pilot was first launched in El Prat de Llobregat municipality in July 2021, targeting 16,898 eligible women aged 30 to 65 years. In June 2022, the program was expanded to the Baix Llobregat-Litoral area, covering the municipalities of Begues, Botigues de Sitges, Castelldefels, Gavà, Sant Climent de Llobregat, and Viladecans, with a total eligible population of 53,340 women aged 30–65 years. These two areas correspond to two ASSIRs (Sexual and Reproductive Health Care Units), which are gynecologic primary care centers integrated within primary and specialized healthcare services.

ASSIRs provide comprehensive sexual and reproductive health services, including cervical cancer prevention and related gynecological care. Each ASSIR is staffed by midwives, obstetrician-gynecologists, nurses, psychologists, and administrative staff, ensuring a multidisciplinary approach to patient care.

Before the transition to a population-based cervical cancer screening, ASSIRs have served as the main access point for women within the opportunistic cervical cancer screening model in Catalonia. Every woman has a designated reference ASSIR and can freely schedule an appointment for cervical cancer screening. During the visit, a midwife collects a cervical sample for testing, and if the result is positive, the woman is referred to a gynecologist for further evaluation and management. The entire process follows standardized protocols, ensuring consistency and quality (20).

Abbreviations: ASSIR, Sexual and Reproductive Health Care Units; AGC, Atypical glandular cells; AIS, Adenocarcinoma in situ; ASC-H, Atypical squamous cells, cannot exclude high-grade squamous intraepithelial lesion; ASC-US, Atypical squamous cells of undetermined significance; HPV, Human papillomavirus; hrHPV, high-risk HPV; HSIL, High-grade squamous intraepithelial lesion; HSIL/CIN2+, High-grade squamous intraepithelial lesion/cervical intraepithelial neoplasia grade 2 or higher; HSIL/CIN3+, High-grade squamous intraepithelial lesion/cervical intraepithelial neoplasia grade 3 or higher; HSIL/CIN2-3, High-grade squamous intraepithelial lesion/cervical intraepithelial neoplasia grade 2 or 3; IQR, interquartile range; LSIL, Low-grade squamous intraepithelial lesion; LSIL/CIN1, Low-grade squamous intraepithelial lesion/cervical intraepithelial neoplasia grade 1; NILM, Negative for intraepithelial lesion or malignancy; NNF, Number needed to follow-up; NNS, Number needed to screen; PPV, Positive predictive value; SMS, Short message service.

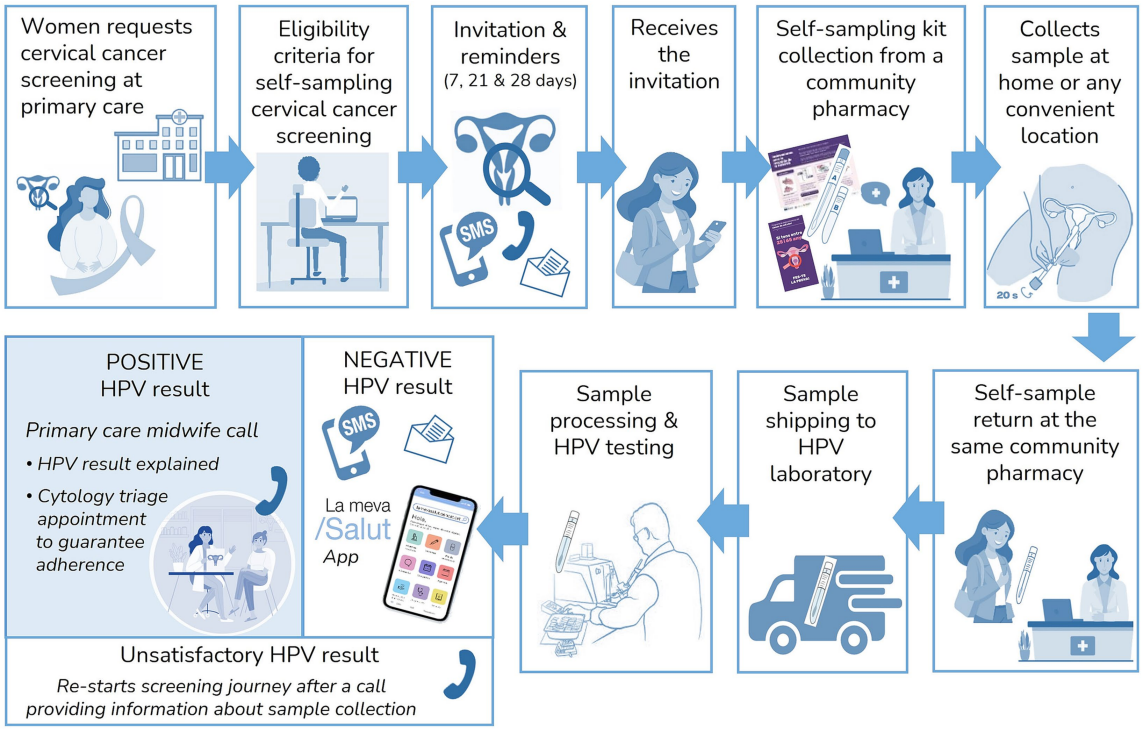

FIGURE 1
Screening process within the implementation pilot.

Participants

The inclusion criteria for participation in the cervical cancer screening program with self-sampling in Catalonia include being aged 30 to 65, or older than 65 with a history of treatment for high-grade squamous intraepithelial lesion/cervical intraepithelial neoplasia grade 2 or higher (HSIL/CIN2+) within the past 25 years. The exclusion criteria include: residing outside the designated territories for the self-sampling implementation pilot (as described in the *Setting* section, in *Methods*); absence of a cervix due to a cause unrelated to HPV (e.g., hysterectomy for benign or malignant disease unrelated to HPV, trachelectomy, congenital cervical aplasia, or being a transgender women); presence of gynecological symptoms (such as abnormal bleeding, dyspareunia, or pelvic pain); being under ongoing follow-up for cervical pathology; having had a recent screening (cytology within the past 3 years or HPV testing within the past 5 years); being pregnant (second or third trimester) or postpartum; and having a physical or mental disability that prevents sample collection.

Screening process

The screening process and adaptations made for the implementation pilot are shown in Figure 1.

Women who request cervical cancer screening at their primary care centers or gynecologic primary care centers are referred to the cervical cancer screening program to assess their eligibility for HPV self-sampling. Eligible women receive an invitation to participate in the screening program via telephone call followed by a short message service (SMS) or directly via SMS. If a telephone number is not available in the National Health System database, they are invited by letter. The SMS and letter include brief information about the screening program, the HPV test, and home-based self-sampling, along with a link[1] directing women to the official Health Department website,[2] where detailed information on the screening process is available. Following the initial invitation, additional reminders are sent using the same invitation method (SMS or letter) on days 7 and 21. A follow-up phone call was made on day 28 during the pilot, given that women participating in the implementation pilot demanded screening voluntarily (opportunistic program), to reinforce the importance of screening, educate women on the novel sample collection method, resolve doubts and gather the reasons for their non-participation. Reminders were only sent to women who had not participated at each stage. Those who declined self-sampling were offered an appointment for a clinician-collected HPV test in primary centers.

Pharmacies serve as distribution points for self-sampling devices. Each participant collects a kit containing the self-sampling device (FLOQSwabs®, Copan, Italy), a printed instruction sheet outlining the sample collection process,[3] and an informational brochure on cervical cancer prevention.[4] Upon kit collection, the pharmacist provides a brief explanation of how to use the self-sampling device and addresses any participant questions. When returning the sample, the pharmacists visually assess its quality, ensuring it is free of visible blood, properly

1 https://canalsalut.gencat.cat/pccu1
2 https://canalsalut.gencat.cat/pilot-automostra
3 https://scientiasalut.gencat.cat/handle/11351/10477.2
4 https://scientiasalut.gencat.cat/handle/11351/10788

sealed, and undamaged, and collected within the past 7 days (20). For sample transport and analysis, the existing shipping logistics used in the colorectal cancer screening program are utilized. Samples are dispatched daily to the laboratory for analysis (as described in the *Sample processing and HPV testing* section, in *Methods*). Samples should be processed within a two-week period from arrival at the laboratory and at a maximum time of 4 weeks after the return date of the sample to the pharmacy, as established in the screening protocol (20). HPV results are delivered to the cervical cancer screening office for participant notification and case management.

Negative HPV results are communicated via SMS or letter (depending on the original invitation method used), directing women to access their results through the official Health Department App,[5] where a detailed screening report specifies their results and the recommended interval for the next screening test (5 years). Unsatisfactory samples due to insufficient material are reported to women via telephone call, re-inviting them to collect a new self-sampling kit, following the same procedure as the initial invitation. If a second unsatisfactory result is obtained, women are referred for a clinician-collected sample. Women with positive HPV results are scheduled for a telephone consultation with a midwife within one to two working days. During this consultation, the midwife informs the participant of the results, clarifies doubts, and schedules further tests, such as triage cytology. The cervical cancer screening office ensures follow-up throughout the entire episode to guarantee appropriate management according to established clinical algorithms and time frames. In cases where women are lost to follow-up or a required procedure is not completed, the screening office contacts the responsible clinicians, and an educational e-mail is sent with guidance on the screening algorithms to facilitate adherence to protocols. Details of screening results management, follow-up and diagnostic procedures are outlined in Figure 2. The definitions used in the screening process are outlined in Table 1.

The entire screening process is managed by the cervical cancer screening office at the Catalan Institute of Oncology, which oversees eligibility assessment, invitation and reminders, results management, quality assurance, and program evaluation. All screening data is registered in a unified screening registry within the Catalan Health Information system.

Sample processing and HPV testing

All screening samples are analyzed at the laboratory of Bellvitge University Hospital. Upon arrival, dry swabs were resuspended in 5 mL of PreservCyt™ Solution (Hologic®, Marlborough, Massachusetts, USA). HPV detection is performed using the Cobas®4,800 PCR assay (Roche Diagnostics, Basel, Switzerland), which identifies HPV16, HPV18 and a pooled group of 12 other high-risk HPV (hrHPV) genotypes (31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68). To ensure sample adequacy and minimize false-negative results, the presence of human DNA is verified by detecting the beta-globin gene; samples that do not meet this criterion are classified as unsatisfactory.

5 La Meva Salut, https://lamevasalut.gencat.cat/

Data sources

Multiple data sources are used for the cervical cancer screening registry, to assess eligibility and evaluate follow-up. The target population was identified using data from the central registry of publicly insured individuals in Catalonia. Further information was obtained from the shared Medical History of Catalonia, which integrated health information from all the public healthcare centers in the region. All information from different data sources is compiled in the cervical cancer screening registry. Given that multiple municipalities with varying socioeconomic levels participated in the implementation pilot, the MEDEA index was used as a proxy for socioeconomic deprivation as it is the most used index to assess deprivation's impact on health in our region (21–24). The MEDEA index reports deprivation for urban and rural areas, separately, establishing 4 levels of deprivation in urban settings (1U, 2U, 3U, and 4U, which correspond to least, moderately, highly and most deprived urban areas) and 2 levels in rural areas (1R and 2R, corresponding to semirural and semiurban, respectively) (23, 24). The MEDEA index is calculated using the following socio-economic information: unemployment rates, manual workers, illiterate adults and school leavers before age 16. Further details on the MEDEA index can be found elsewhere (21, 23, 24).

Statistical analysis

Descriptive statistics were used to summarize participation and acceptance rates, as well as screening results. Categorical variables were presented as absolute frequencies and proportions. Continuous variables were categorized. Time periods were reported as medians with interquartile ranges (IQRs) due to their non-normal distribution. Differences between groups were assessed using the Chi-Square test for categorical variables and the Fisher's Exact test when there are very low expected frequencies in the cells (<5), and the Mann–Whitney U test for non-normally distributed continuous variables. The Kolmogorov–Smirnov statistic test was performed to compare time to accept and time to participate between territories. Statistical significance was set at $p\text{-value} < 0.05$. All statistical analyses were conducted using R software (R version 4.4.1; R Core Team) through the RStudio integrated development environment (version 2024.04.2 Build 764; Posit Software, PBC) (25).

Reporting guidelines

This study follows the RECORD guidelines (26) for the transparent reporting of observational studies using routinely collected health data. The completed RECORD is provided in Supplementary Table 1.

Ethical approval and data protection

This study was conducted in the context of approval by the Research Ethics Committee of the Hospital Universitari de Bellvitge for activities derived from cervical cancer screening (PR271/11). It was carried out in compliance with Regulation (EU) 2016/679 of the European Parliament and of the Council, of April 27, 2016, on the protection of individuals regarding the processing of personal data. Although formal written consent was waived, participants were

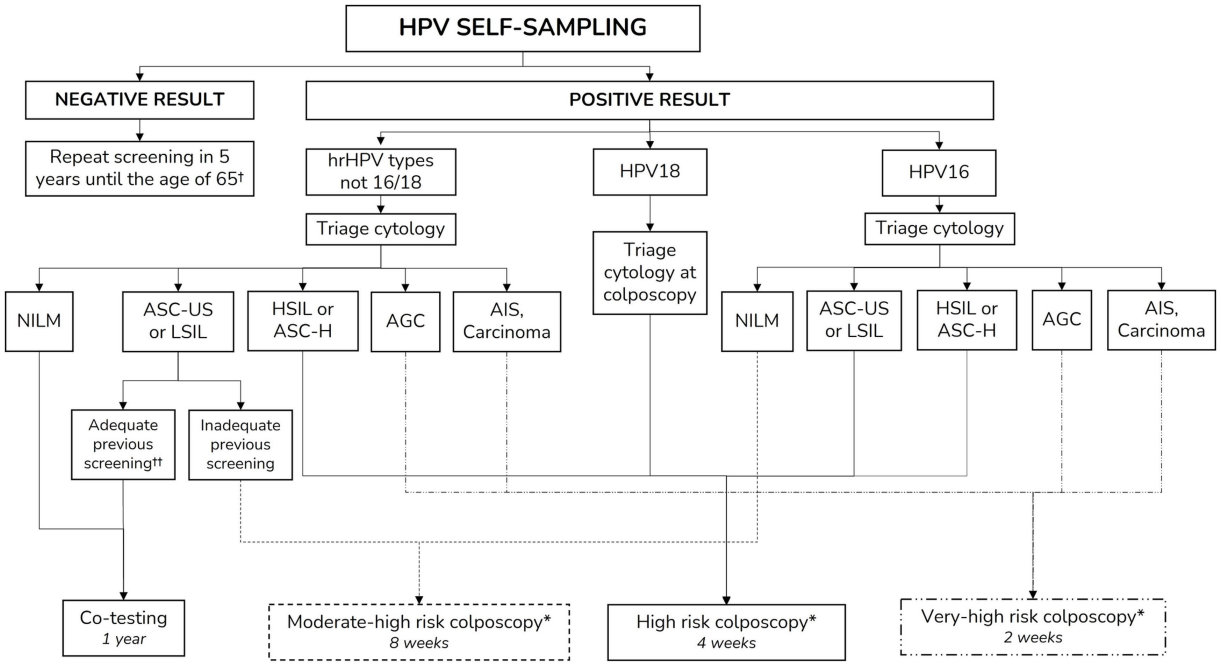

FIGURE 2
Clinical management based on HPV self-sampling test and triage cytology results. AGC, atypical glandular cells; AIS, adenocarcinoma *in situ*; ASC-H, atypical squamous cells, cannot exclude high-grade squamous intraepithelial lesion; ASC-US, atypical squamous cells of undetermined significance; HPV, Human papillomavirus; hrHPV, High-risk HPV; HSIL, High-grade squamous intraepithelial lesion; LSIL, Low-grade squamous intraepithelial lesion; NILM, Negative for intraepithelial lesion or malignancy. †Or after 25 years of follow-up despite the age in case of HSIL/CIN2+ lesion treatment (19). ††Adequate previous screening is defined if previous negative screening with cytology within the last 3 years or with HPV testing within the previous 5 years (19). *Colposcopy risk differentiation is based on the immediate risk of high-grade squamous intraepithelial lesion/cervical intraepithelial neoplasia grade 3 or higher (HSIL/CIN3+) as defined in the Catalan cervical cancer screening protocol (19).

TABLE 1 Definitions of screening participation categories.

Eligible women	Women who *meet the inclusion criteria* for participation in HPV self-sampling cervical cancer screening.
Invited women	Eligible women who *are invited* (SMS or letter) to participate in HPV self-sampling cervical cancer screening.
Women who collects self-sampling at a pharmacy	Invited women who *collect* the HPV self-sampling kit from the pharmacy, accepting the invitation to participate in HPV self-sampling screening.
Self-sampling screening participants	Invited women who *collect* the HPV self-sampling kit from the pharmacy and *return* the sample to the pharmacy.
Self-sampling rejection	Invited women who *do not collect* the HPV self-sampling kit from the pharmacy.
Non-participating women with acceptance	Invited women who *collect* the HPV self-sampling kit from the pharmacy but *do not return* their sample.

informed via SMS and invitation letters about the nature and purpose of the program, including the use of their screening data and samples for research. Consent was considered implied upon their agreement to participate, in accordance with ethical best practices.

Results

Study population and participation

From July 2021 to December 2023, 6,802 women requested cervical cancer screening in their primary gynecologic care centers (ASSIR). Of these, 6,355 (93.4%) met the eligibility criteria and were subsequently invited to participate in self-sampling. Among them, 5,467 women (86.0%) accepted the invitation and collected a self-sampling kit from pharmacies. A total of 5,140 women (94.0% of those who collected the self-sampling kit and 80.9% among the total invited) returned their self-collected samples, completing the self-sampling screening process. Women who declined self-sampling were offered the option of clinician-collected sampling, and 380 women (6%) opted for an in-person visit for sample collection by a healthcare professional. Figure 3 shows the participant flowchart, from eligibility assessment to pilot participation.

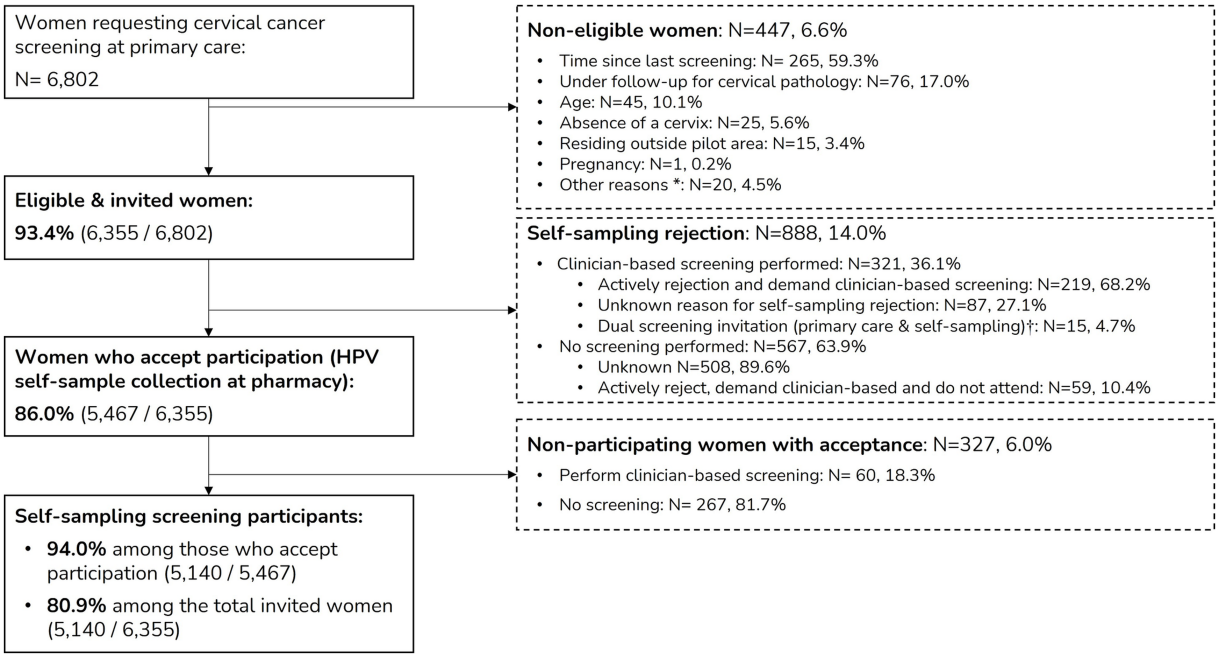

FIGURE 3
Participation flowchart. Definitions of screening participation categories can be found in Table 1. *Includes three HIV-positive women referred to primary care for clinician-collected sample due to other ongoing follow-ups, 14 women with physical disabilities and three women unable to read or understand self-sampling instructions. †At the start of the pilot, due to technical issues, 15 women were mistakenly invited to self-sampling screening while simultaneously scheduled for a gynecologic primary care visit. As a result, these women had their screening samples collected during the scheduled visit, thus not participating in HPV self-sampling screening despite receiving an invitation.

Self-sampling participation

The sociodemographic characteristics of invited women and self-sampling screening participants are summarized in Table 2.

The median age of eligible women asking for screening was 46 years (interquartile range [IQR]: 39–54 years). Self-sampling participation was significantly higher among older age groups compared to younger ones ranging from 72% among women aged 30–34 years to 86.3% among those aged 60–65 years. Self-sampling participation varied significantly according to the MEDEA index of socioeconomic deprivation. Women living in the most deprived urban areas (4U) showed the highest participation (84.2%), while the lowest (73.3%) was observed among women living in the least deprived areas (1U) areas (Table 2). Additionally, the same participation gradient by age was observed across highly and most deprived urban areas (3U and 4U), with younger women showing lower participation rates compared to older women (Supplementary Table 2). Women who had previously participated in the cervical cancer screening program were more likely to participate in self-sampling compared to those whose screening history is unknown (82.3% vs. 74.4%) (*data not shown*).

Time from invitation, self-sampling kit collection and sample return

Figure 4 illustrates the cumulative percentage of participation over time, showing the number of days from invitation to HPV self-sampling kit collection at the pharmacy as well as the time from kit collection to return. The median time from receiving the SMS invitation to collecting the self-sampling device at the pharmacy was 10 days (IQR: 4–20 days). The median time between collection and sample return was 3 days (IQR: 1–8 days).

Participation reminders

Immediately after receiving the invitation SMS, 37.9% of women participated in the pilot. The first reminder, sent 7 days after the invitation, raised participation to 65.6%. After the second reminder, at 21 days, it further increased to 76.6%, reaching a peak of 80.9% following the third reminder (28 days). On average, the number of reminders per participant woman was 2.9, including reminders to participate as well as those to return the sample after collection.

Turnaround times for sample processing and testing

The median time between sample return registration at the pharmacy and its arrival at the laboratory was 3 days (IQR: 2–5 days), varying slightly depending on the pharmacy and the pharmaceutical distributor. By day 7 after sample return, 89.2% of samples had already arrived at the laboratory, and by day 14, over 98.0% had been received. The median time from the sample's arrival at the laboratory to result availability was 3 days (IQR: 1–5 days). Nearly all test results (99.7%) were available within 3 weeks of sample arrival, aligning with protocol requirements, only the results of 17 samples were reported beyond

TABLE 2 Sociodemographic characteristics of invited and participation status.

	Invited women		Self-sampling participants		Participation (%)[2]	*p*-value[3]
	N	%[1]	*N*	%[1]		
Total	6,355	100.0	5,140	100.0	80.9	
Age groups						<0.001
30–34 years	779	12.3	561	10.9	72.0	
35–39 years	910	14.3	714	13.9	78.5	
40–44 years	1,143	18.0	911	17.7	79.7	
45–49 years	1,249	19.7	1,031	20.1	82.5	
50–54 years	939	14.8	774	15.1	82.4	
55–59 years	694	10.9	596	11.6	85.9	
60–65 years	641	10.1	553	10.8	86.3	
Medea Index[4]						<0.001
Semirural areas (1R)	108	1.7	84	1.6	77.8	
Least deprived urban areas (1U)	416	6.5	305	5.9	73.3	
Moderately deprived urban areas (2U)	–	–	–	–	–	
Highly deprived urban areas (3U)	3,731	58.7	2,982	58.0	79.9	
Most deprived urban areas (4U)	2,100	33.0	1,769	34.4	84.2	
ASSIR Region						<0.001
El Prat de Llobregat	2,749	43.3	2,324	45.2	84.5	
Baix Llobregat-Litoral	3,606	56.7	2,816	54.8	78.1	

[1]Percentages correspond to column percentages.
[2]Percentages calculated comparing participants among the total invited; corresponds to row percentage.
[3]*p*-value resulting from the comparison between participants and non-participants.
[4]MEDEA Index for the participating municipalities included. No 2R or 2U areas were participating in the implementation pilot. *p*-value was calculated only comparing urban settings (1U, 3U, 4U).

21 days. Globally between sample return to the pharmacy and the availability of test results, the median time was 8 days (IQR: 6–12 days), and by day 21, 97.0% of women had already received their screening results.

Repeated self-sampling collection and testing

A total of 59 women had to collect two self-sampling devices due loss of the sample during screening process ($N = 25$, 42.4%), insufficient sample ($N = 19$, 32.2%), suboptimal sample conditions ($N = 2$, 3.4%), unknown reasons/not reported ($N = 13$, 22.0%). Among these women, 53 received a valid test result after the second sample collection, two had an invalid/poor-quality result twice and were referred to a midwife for sample-collection, and four women had not yet returned their second screening sample to the pharmacy at the time of data analysis.

HPV screening results

Among the 5,140 self-samples processed, 608 tested positive for HPV, resulting in an overall positivity of 11.8% (Figure 5). The most frequent result was hr-HPV other than HPV16/HPV18, accounting for 79.3% ($N = 482$) of positive results (Figure 5). Positivity decreased with age, with the highest positivity rate (21.7%) observed in the 30–34 age group. The same HPV positivity gradient by age was observed across highly and most deprived urban areas (3U and 4U), with younger women showing higher positivity than older women (Supplementary Table 3). HPV screening results stratified by age and other sociodemographic characteristics are described in Table 3.

Triage cytology results

All HPV-positive women were referred to gynecologic primary care centres for triage cytology, with samples collected by a healthcare professional. This follow-up was completed in 98.7% of positive cases ($N = 600$) up to the end of April 2024 (4 months after pilot participation was completed).

Triage cytology results by HPV genotype are presented in Figure 5 and in Supplementary Table 4. The most frequent cytological abnormalities were ASC-US and LSIL, each occurring in approximately 15% of the HPV-positive cases

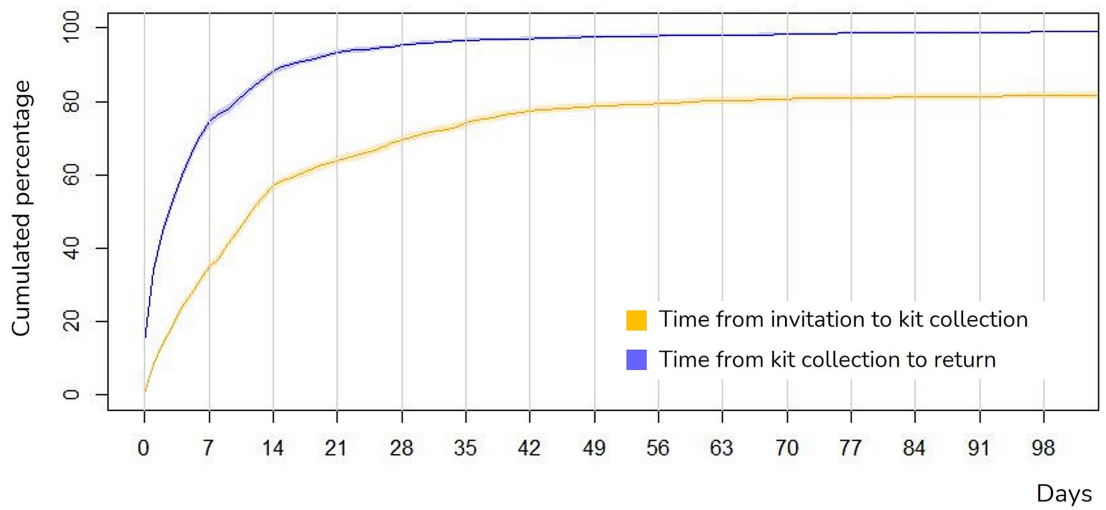

FIGURE 4
Time from invitation, self-sampling kit collection and return. Figure truncated at 100 days of follow-up, with 97.5% of women having accepted and 98.9% of women having returned the self-sample. Reminders were sent on days +7, +21, and +28.

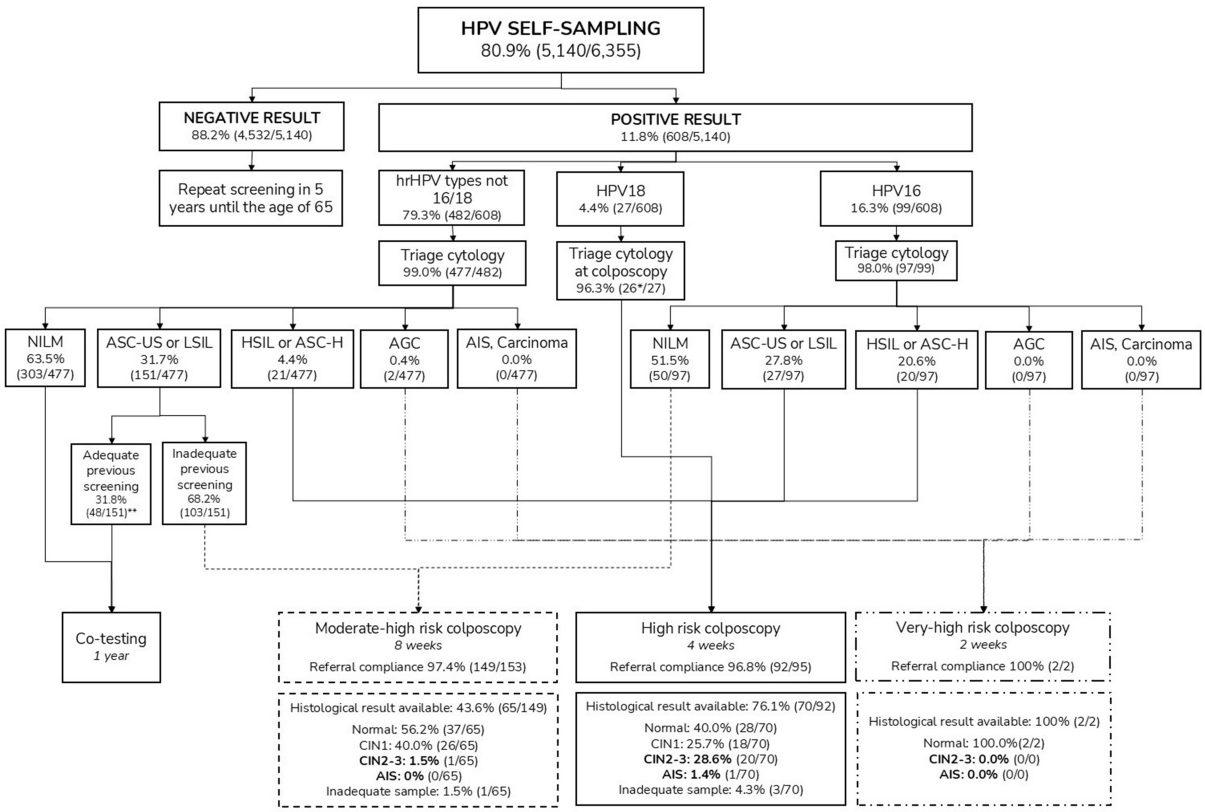

FIGURE 5
Clinical results after HPV self-sampling. AGC, atypical glandular cells; AIS, adenocarcinoma *in situ*; ASC-H, atypical squamous cells, cannot exclude high-grade squamous intraepithelial lesion; ASC-US, atypical squamous cells of undetermined significance; HPV, Human papillomavirus; hrHPV, High-risk HPV; HSIL, High-grade squamous intraepithelial lesion; LSIL, Low-grade squamous intraepithelial lesion; NILM, Negative for intraepithelial lesion or malignancy. *One woman underwent colposcopy, but triage cytology was not performed. **Ten women were referred for colposcopy and biopsy, not following the protocol recommendations (co-testing after 1 year).

(Supplementary Table 4). When cytological results were grouped into low-grade (ASCUS and LSIL) and high-grade lesions (HSIL, ASC-H and AGC-NOS), statistically significant differences were observed across age groups, with low-grade lesions being more frequent in younger women (*p-value = 0.008; data not shown*).

TABLE 3 Screening results by sociodemographic characteristics.

	Total screened	Positivity		*p*-value[2]	hrHPV positive no HPV16/18		HPV16 positive		HPV18 positive	
	N	*N*	%[1]		*N*	%[1,3]	*N*	%[1,3]	*N*	%[1,3]
Total	5,140	608	11.8		482	79.3	99	16.3	27	4.4
Median age		43	[36–50]	<0.001	43	[36–50]	43	[36–50]	43	[36–47]
Age groups				<0.001						
30–34 years	561	122	21.7		98	80.3	20	16.4	4	3.3
35–39 years	714	115	16.1		91	79.1	16	13.9	8	7.0
40–44 years	911	113	12.4		85	75.2	23	20.4	5	4.4
45–49 years	1,031	111	10.8		90	81.1	15	13.5	6	5.4
50–54 years	774	66	8.5		56	84.8	9	13.6	1	1.5
55–59 years	596	48	8.1		36	75.0	10	20.8	2	4.2
60–65 years	553	33	6.0		26	78.8	6	18.2	1	3.0
Medea Index[4]				0.18						
Semirural areas (1R)	84	12	14.3		8	66.7	4	33.3	0	0.0
Least deprived urban areas (1U)	305	46	15.1		41	89.1	5	10.9	0	0.0
Moderately deprived urban areas (2U)	–	–	–		–	–	–	–	–	–
Highly deprived urban areas (3U)	2,982	348	11.7		273	78.4	58	16.7	17	4.9
Most deprived urban areas (4U)	1,769	202	11.4		160	79.2	32	15.8	10	5.0
ASSIR region				0.01						
El Prat de Llobregat	2,324	246	10.6		200	81.3	36	14.6	10	4.1
Baix Llobregat-Litoral	2,816	362	12.9		282	77.9	63	17.4	17	4.7

[1]Percentages correspond to row percentages. For continuous variables, IQR is used.
[2]*p*-value resulting from the comparison between HPV positives and HPV negatives.
[3]Percentage calculated among those HPV positives.
[4]MEDEA Index for the participating municipalities included. No 2R or 2U areas were participating in the implementation pilot. *p*-value was calculated only comparing urban settings (1U, 3U, 4U).

HPV16 was associated with the highest proportion of cytological abnormalities, with 49.5% of women showing a positive triage cytology result. It also had the highest proportion (20%) of high-grade lesions (HSIL, ASC-H, AGC-NOS) compared to HPV18 (7.4%) and other hr-HPV infections (6.8%) (Supplementary Table 4).

Colposcopy referrals, biopsies and conization results

Among the 600 available triage cytology results, 41.7% of women ($N = 250$) required colposcopy referral as per protocol. Of these, 61.2% were classified as moderate-high risk ($N = 153$), 38.0% as high risk ($N = 95$), and 0.8% ($N = 2$) as very-high risk colposcopies. Within 7 months after the expected date of performance according to protocol, a total of 243 colposcopies were performed, resulting in a colposcopy referral protocol compliance of 97.2%.

Following the initial colposcopy ($N = 243$), a total of 137 biopsies (56.4%) were performed after a period of 7 months (Figure 5). Overall, the most common histological result was normal (48.9%, $N = 67$), followed by LSIL/CIN1 (32.1%, $N = 44$), HSIL/CIN2-3 (15.3%, $N = 21$) and AIS (0.7%, $N = 1$). Four samples were suboptimal for pathological diagnosis. Additionally, 10 colposcopies and biopsies were performed outside protocol recommendations, which advised co-testing after 1 year. All procedures ruled out a pathological result (Figure 5).

The positive predictive value (PPV) of referral for colposcopy was 8.4%. The overall detection rate of CIN2+ among HPV-positive women was 3.6% (22/608), while among those with HPV16, the detection rate was notably higher at 13.1% (13/99).

Among those 22 women with histological confirmation of HSIL/CIN2+ at biopsy, 21 women (95.4%) subsequently underwent

conization and one woman opted for clinical surveillance due to childbearing wish. Conization confirmed one case of AIS (4.8%), as well as 16 HSIL/CIN2-3 lesions (76.2%). In one case the conization yielded an LSIL/CIN1 lesion and in two cases the result was negative for intraepithelial lesions or malignancy. In one case, the result is not available as it was performed in the private sector.

HPV self-sampling screening and follow-up efficiency

When considering the total screened population ($N = 5,140$), the number needed to screen (NNS) to detect one CIN2+ case was 234. This means that 234 women needed to be screened to detect one case of CIN2+, highlighting the overall effectiveness of the screening strategy.

The overall detection rate of CIN2+ among HPV-positive women was 3.6% (22/608), resulting in a number needed to follow-up (NNF) of 28, indicating that 28 HPV-positive women required follow-up to detect one case of CIN2+. If considering the HPV16 women, the NNF decreases to 8, being thus 8 HPV16 women requiring follow-up to detect one case of CIN2+, while the NNF for other hr-HPV cases rises to 54.

Discussion

This implementation pilot supports home-based HPV self-sampling as an effective primary screening strategy for women regularly attending cervical cancer screening. Findings show high self-sampling participation (80.9%) and engagement across all age groups. The active involvement of primary care providers, midwives, and community pharmacies, combined with an SMS-based invitation and reminder system coordinated by a dedicated screening office, played a crucial role in maximizing participation and ensuring follow-up. A high return rate for self-collected samples (94.0%) was achieved, along with strong compliance with triage cytology (98.7%) and colposcopy referrals (97.2%), ensuring timely management of HPV-positive cases and the prompt treatment of high-grade cervical lesions. The study also reinforces the clinical value of HPV genotype-specific risk stratification in our screening setting, confirming the different positive predictive values associated with combinations of results and how this stratification helps to prioritize and optimize clinical pathways.

Although we were working with a population highly engaged in cervical cancer screening, community pharmacies and primary care midwives played essential roles in outreach, participation, and follow-up. Our findings support both the feasibility of this model in our setting and its potential adaptability and applicability to other healthcare systems. In contrast to our approach, established screening programs such as Australia's—where self-sampling requires a provider's order and is performed in clinical setting—have reported a preference for self-sampling of 40.4% and a six-month colposcopy adherence rate of 81.3% (27). Similarly, the English model, which focuses on non-attenders and relies on in-person consultations, has reported a self-sampling uptake of 55.9% (28). These differences highlight the advantages of our strategy, with pharmacies facilitating participation by addressing barriers to self-sampling and midwives ensuring follow-up after screening positive results, achieving comparable outcomes without requiring direct provider involvement in the primary testing phase (29). The success of pharmacy-based distribution aligns with studies showing a preference for pharmacy-based kit collection (15), where extended hours, proximity, and a trusted environment helped overcome logistical and psychological barriers. Pharmacist counseling increased confidence in self-sampling and self-efficacy, contributing to a high return rate (94.0%), surpassing mail-to-all strategies, where unreturned kits remain a challenge (30, 31). Additionally, this approach reduced the environmental impact associated with mailed self-sampling programs, another strategy piloted in England (28, 32). Pharmacy-based distribution model success may vary according to setting and the attributions of the pharmacy. Our findings suggest that pharmacist engagement and their role as community health agents (33) are key determinants of the success of this model, and reinforcing the need for trainings programs, such as those designed in our program (34). Our pilot also incorporated complementary studies on the impact of various communication strategies, refining invitations and reminders to optimize engagement (35, 36). Results from these studies informed adjustments that improved participation, with SMS reminders significantly increasing participation (35, 36). This underscores the potential for mobile health solutions and telemedicine follow-up in maximizing preventive healthcare efforts (37).

Participation in self-sampling increased significantly by age, with older women being more likely to participate than their younger counterparts. This finding is particularly noteworthy as older women have historically demonstrated lower participation rates in cytology-based screening (38, 39). However, a recent study in Catalonia found that self-sampling was highly preferred among older age groups (15), suggesting that this strategy may help overcome age-related barriers to screening, which in our specific context may be explained by the accessibility and convenience of visiting pharmacies given the long-standing pharmacy-based colorectal cancer screening program which targets women over 50 years (40, 41). Conversely, higher cervical screening participation among younger women has traditionally been linked to more frequent gynecological visits for family planning purposes (42), which may explain their stronger preference for clinician-collected samples and the lower self-sampling uptake observed in our study. This lower uptake among younger women may also be influenced by cultural and demographic factors. For example, in Spain, approximately 35% of women aged 30–44 are migrants (43), a population group that often faces multiple barriers to preventive healthcare, including language, administrative, and socioeconomic challenges. A similar age-related pattern has been observed in Australia's self-sampling screening program, where uptake increases with age and peaks among women aged 70–74, with 47% of women opting for self-sampling (27). In contrast, the Dutch cervical cancer screening program has reported higher self-sampling acceptability among younger women (6). This trend has been attributed to the Dutch model's use of mailed self-sampling kits to eligible women, which reduces logistical barriers and better accommodates younger women's competing priorities, such as work and childcare responsibilities (6). Further research is needed to better understand these intersecting factors and to design tailored strategies that address age and context-specific barriers to self-sampling.

Our findings indicate high acceptance of home-based self-sampling among regular attendees, supporting its integration into organized programs while maintaining clinician-based options to

maximize coverage. One modality does not have to detract from the other. Ultimately, it is participation, rather than screening modality, that determines program success. Ensuring accessibility and providing choice between self-sampling and clinician-based collection can optimize engagement, expand coverage, and strengthen cervical cancer prevention efforts. Notably, self-sampling acceptance by socioeconomic status in urban areas (Medea Index) exceeded 73% across all groups, with the highest participation (84.2%) in the most deprived area. This aligns with global studies that advocate for the adoption of self-sampling among hard-to-reach populations as a valuable screening tool (10, 13, 14). Our findings also suggest that pharmacy-based self-sampling distribution effectively reaches lower socioeconomic groups in our setting.

Our clinical findings align with previous research, confirming higher HPV positivity among younger women and the strong association of HPV16 with high-grade cytological abnormalities and HSIL/CIN2+ detection. The overall hrHPV positivity rate (11.8%) is consistent with national studies (~12%) (44), and similar to other European countries (45–47).

A major challenge in HPV self-sampling implementation, as highlighted by the IARC guidelines, is ensuring adequate triage and follow-up compliance, as loss to follow-up can significantly reduce program effectiveness (9). Our approach achieved remarkably high adherence to cytological triage (98.7%) and compliance with colposcopy referral (97.2%), demonstrating the effectiveness of a structured implementation strategy that integrates self-sampling within primary care workflows. Midwives played a key role in ensuring triage attendance by directly communicating results by phone, while the screening coordination office ensured protocol compliance through continuous monitoring and coordination with gynecologic primary care and referral hospitals. The protocol-established turnaround times (20) were successfully met, facilitating timely follow-up for HPV-positive women and validating the approach for the future population-based program. CIN2+ detection rates (3.6% overall, 13.1% in HPV16 infections) were comparable to international studies, reinforcing the value of genotype-specific risk stratification and risk-adapted follow-up pathways (48–50).

These findings have several potential policy implications, particularly in the context of the ongoing reforms in cervical cancer screening programs across Spain. The evidence generated by this study supports the transition towards a fully organized, population-based screening program in the region, aligned with Spanish regulations that require the entire eligible population to be actively invited to cervical cancer screening by 2029 (51). The high screening uptake observed among women over the age of 55 and from lower socioeconomic backgrounds suggests that self-sampling HPV screening can overcome structural barriers and facilitate the inclusion of underscreened groups in Spain (38). Expanding the program further could potentially help reduce cervical cancer incidence in the region, as international evidence shows that long-standing population-based screening programs—such as those in the Nordic countries—have led to significant declines in cervical cancer incidence (52). The demonstrated feasibility and high adherence rates indicate that integrating HPV self-sampling with pharmacy-based distribution of screening kits, as well as midwife-led follow-up offers a scalable model to enhance participation and reduce loss to follow-up. Therefore, investing in the training and engagement of community pharmacies and primary care midwives in program as key stakeholders is crucial for successful program delivery.

However, barriers such as differences in population engagement between opportunistic and fully population-based settings must be acknowledged. Thus, a limitation of this study is that its findings may not be fully generalizable to population-based screening programs, as it was conducted in an opportunistic screening setting where women actively sought screening. Consequently, in such context, self-sampling acceptability and follow-up compliance among those with HPV detected may be overestimated compared to organized, population-based programs that invite all eligible women. In the general population, awareness of the importance of screening and appropriate adherence to follow-up may be lower, potentially leading to reduced engagement in follow-up care. Conversely, population-based programs have a broader reach and may achieve higher detection rates of high-grade lesions, along with a greater positive predictive value for colposcopy referrals. This could enhance the overall program effectiveness and potentially result in outcomes that differ from those observed in our study (53). From an equity perspective, analyses of European screening programs have shown that the type of screening program (opportunistic versus population-based) accounts for 13.6% of the observed inequalities in screening participation (54). These findings suggest that a population-based approach could further reduce disparities compared to those observed in this study.

Furthermore, participation rates in population-based programs tend to be lower due to challenges in reaching all eligible women, including those who are underscreened or hard to reach. Therefore, targeted outreach and culturally sensitive communication strategies will be essential to replicate these participation rates in a broader population. Similarly, although SMS-based reminder system and pharmacy-based distribution offer alternative pathways that may address some of the barriers to screening, they may require adaptation to other contexts. In this sense, future research should explore barriers to self-sampling uptake, including reasons for refusal among women who collected but did not use the self-sampling device and those who declined participation altogether. Understanding these factors and nuances will be crucial for maximizing acceptability, participation, coverage and equity in a population-based approach.

Additionally, data availability gaps identified during the pilot indicated areas for further improvement. For example, data on past screenings was incomplete and thus could not be incorporated in the present analysis, despite its relevance as a key risk determinant. Moreover, the dataset lacked sociodemographic information needed to identify ethnic, migrant, or minority groups, which are important for detecting potential inequalities in screening participation. Enhancing data completeness and accuracy will be essential for improving future evaluations of the program. Moreover, the short follow-up period limits the assessment of long-term screening outcomes, including the detection of HSIL/CIN2+ cases in women under one-year follow-up with co-testing, as well as the long-term program impact.

Future directions

Future research should move beyond merely identifying barriers to screening participation by thoroughly investigating the underlying

factors driving these differences. Ongoing qualitative studies within this population are currently being conducted. Moreover, successful implementation depends not only on the program's effectiveness but also on its long-term sustainability, including economic viability. To this end, a short-term budget impact analysis from a national health system perspective, based on data from this pilot is currently underway. These economic evaluations, along with the findings presented in this article, will provide policymakers with critical evidence to guide informed decisions regarding program scale-up and resource allocation. Given the importance of evaluating participation among migrant and minority groups in screening programs, future research should prioritize the systematic collection of variables that identify individuals from these populations. This is essential for assessing equity in screening participation and ensuring that underserved groups are effectively reached. Furthermore, future work should continuously investigate short-, mid-and long-term screening outcomes, cost-effectiveness, and patient-reported experiences to refine screening protocols and optimize implementation strategies, ensuring the program's effectiveness and sustainability over time.

Conclusion

This pilot study has been instrumental in validating circuits, workflows, and protocols, laying the foundation for the transition to a population-based cervical cancer screening program using home-based self-sampling in Catalonia. With a population-based pilot phase launched in 2024 and full-scale implementation set for 2025, these findings provide a strong basis for scaling up the program in our region and may serve as a reference model for other regions considering similar transitions. The combination of coordinated invitation and reminder strategies via SMS, pharmacy-based kit distribution, and dedicated follow-up through gynecologic primary care ensured an efficient, high-adherence screening model, facilitating timely management of HPV-positive cases while promoting equitable access. Beyond its regional impact, this study adds to the growing body of evidence supporting self-sampling integration into national cervical cancer prevention strategies. It offers valuable insights to policymakers and public health leaders seeking to expand self-sampling as a scalable and sustainable strategy for improving access, participation, and early detection of cervical cancer.

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 Research Ethics Committee of the Hospital Universitari de Bellvitge (PR271/11). The studies were conducted in accordance with the local legislation and institutional requirements. The ethics committee/institutional review board waived the requirement of written informed consent for participation from the participants or the participants' legal guardians/ next of kin because lack of direct contact to participants and impossible to collect the consent directly.

Author contributions

PP-T: Conceptualization, Formal analysis, Investigation, Methodology, Project administration, Supervision, Visualization, Writing – original draft, Writing – review & editing. ER: Writing – original draft, Writing – review & editing, Data curation, Formal analysis, Investigation, Methodology, Visualization. VR-S: Writing – original draft, Writing – review & editing, Investigation, Visualization. FM: Writing – original draft, Writing – review & editing, Data curation, Formal analysis, Investigation, Methodology, Visualization. RF: Writing – original draft, Writing – review & editing. MC: Investigation, Writing – original draft, Writing – review & editing. CR: Writing – original draft, Writing – review & editing. RI: Writing – original draft, Writing – review & editing. LP: Writing – original draft, Writing – review & editing, Investigation. LT: Writing – original draft, Writing – review & editing. DC: Writing – original draft, Writing – review & editing. DF: Writing – original draft, Writing – review & editing. JE: Writing – original draft, Writing – review & editing. LB: Writing – original draft, Writing – review & editing, Conceptualization, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Visualization.

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Conflict of interest

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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/fmed.2025.1580665/full#supplementary-material

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