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REVIEW ARTICLE

Initiatives to Scale Up and Expand Reach of Cancer Genomic Services Outside of Specialty Clinical Settings: A Systematic Review

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Context: This systematic review aims to (1) characterize strategies used to identify individuals at increased risk for hereditary breast and ovarian cancer syndrome and Lynch syndrome outside of oncology and clinical genetic settings, (2) describe the extent to which these strategies have extended the reach of genetic services to underserved target populations, and (3) summarize indicators of the potential scalability of these strategies.

Evidence acquisition: Investigators searched PubMed, EMBASE, and PsycINFO for manuscripts published from October 2005 to August 2019. Eligible manuscripts were those published in English, those that described strategies to identify those at risk for hereditary breast and ovarian cancer syndrome or Lynch syndrome, those implemented outside of an oncology or genetic specialty clinic, and those that included measures of cancer genetic services uptake. This study assessed strategies used to increase the reach of genetic risk screening and counseling services. Each study was evaluated using the 16-item quality assessment tool, and results were reported according to the PRISMA guidelines.

Evidence synthesis: Of the 16 eligible studies, 11 were conducted in clinical settings and 5 in public health settings. Regardless of setting, most (63%, 10/16) used brief screening tools to identify people with a family history suggestive of hereditary breast and ovarian cancer syndrome or Lynch syndrome. When reported, genetic risk screening reach (range =11%-100%) and genetic counseling reach (range =11%-100%) varied widely across studies. Strategies implemented in public health settings appeared to be more successful (median counseling reach=65%) than those implemented in clinical settings (median counseling reach=26%). Most studies did not describe fundamental components relevant for broad scalability.

Conclusions: Efforts to expand cancer genomic services are limited outside of traditional oncology and genetic clinics. This is a missed opportunity because evidence thus far suggests that these efforts can be successful in expanding the reach of genetic services with the potential to reduce health inequities in access. This review highlights the need for accelerating research that applies evidencebased implementation strategies and frameworks along with process evaluation to understand barriers and facilitators to scalability of strategies with high reach.

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CONTEXT

ational and international guidelines (e.g., the U.S. Preventive Services Task Force, the Evaluation of Genomic Applications in Practice and Prevention Working Group)¹⁻³ and population health organizations (e.g., Healthy People 2020)⁴ all From the ¹Department of Behavioral, Social, and Health Education Sciences, Rollins School of Public Health, Emory University, Atlanta, Georgia; and ²Woodruff Health Sciences Center Library, Emory University, Atlanta, Georgia

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recommend that individuals at a heightened risk for hereditary cancers receive genetic counseling and, as appropriate, genetic testing. Implementing these guidelines is of critical importance because mutation carriers and their blood relatives have the potential to receive life-saving prevention and treatment options. ^{1,2} Much of these implementation efforts have focused on identifying carriers of genetic mutations associated with hereditary breast and ovarian cancer syndrome (HBOC) and Lynch syndrome (LS) because >1 million people in the U.S. are at increased risk for these conditions and related adverse health outcomes. ^{5,6}

Currently, efforts to identify carriers of genetic mutations are conducted predominantly in specialty cancer clinics (e.g., oncology, clinical genetic settings). However, the majority of the mutation carriers and their relatives remain unidentified. For example, in the U.S., genetic counseling referral and genetic testing rates are approximately 24%-52% of the population of patients with breast cancer and 15%-48% in the population of patients with ovarian cancer. ^{7–9} In addition, 28%–70% of patients with colon cancer who have LS remain unidentified because genetic screening has been limited to tumor testing for patients in specialty care settings who meet certain age or family history criteria. 10-13 It has been suggested that the expansion of genetic service reach will require that programs be extended beyond specialty care clinics. 14 This is especially critical for subgroups that are more difficult to reach. Those who live in rural settings, racial-ethnic minorities, and those with low education and income are unlikely to have access to genetic services. 15-17

The scope of efforts that are being implemented outside of specialty care clinics is largely unknown, and the investigation of optimal ways to implement and expand the reach of cancer genetic services is limited. 18,19 Implementation science frameworks (e.g., The Reach, Effectiveness, Adoption, Implementation, and Maintenance framework [RE-AIM]²⁰ and Proctor's implementation outcomes²¹) suggest processes and critical components to be considered in evaluating the likelihood that any intervention strategy will be scalable. These components include but are not limited to strategy complexity, setting characteristics, organizational supports, and cost.²² Guided by the above considerations, the authors conducted a systematic review to (1) describe strategies used to identify individuals at increased risk for HBOC and LS outside of oncology and clinical genetic settings, (2) describe the extent to which these strategies have extended the reach of genetic services to underserved target populations, and (3) summarize the components suggested by implementation frameworks to support the potential scalability of these strategies.

EVIDENCE ACQUISITION

Eligibility Criteria

For the purposes of this review, a strategy is defined as an intervention or systematic effort that is designed to identify individuals at increased risk of carrying a mutation for HBOC or LS. Manuscripts were eligible for this review if they included (1) strategies designed to identify individuals at risk for HBOC and LS (e.g., systematic implementation of family history assessment), (2) studies conducted outside of an oncology or genetic specialty clinic settings (e.g., conducted by a community organization), (3) studies that measured an outcome related to the uptake of cancer genetic services (e.g., complete genetic risk screening), and (4) studies published in English. The authors excluded studies in which cascade screening was the sole strategy used (e.g., mutation carrier engaged to identify family members) or studies involving quality improvement initiatives (e.g., establishing a new cancer genetic clinic). Studies not accessible in full text, conference and meeting abstracts, and nonresearch studies (e.g., commentaries, editorials, study protocols, literature reviews) were excluded.

Search Strategy

A total of 3 electronic databases (PubMed [National Library of Medicine], EMBASE [Elsevier], and PsycINFO [EBSCOhost]) were searched using the terms *genetic counseling, genetic testing, genetic screening, population surveillance registry, referral and consultation, screening,* or *mass screening* combined with terms related to HBOC and LS (Appendix Table 1, available online). The search was restricted to peer-reviewed journal articles published from October 2005 to August 2019. This timeframe was chosen because it follows the 2005 release of the U.S. Preventive Services Task Force's evidence-based HBOC screening recommendations when these genetic services outreach efforts were widely endorsed.²³

Study Selection

A systematic review was performed in accordance with PRISMA guidelines²⁴ and describes the process of study inclusion using a PRISMA flow diagram (Figure 1). The initial search executed on March 29, 2018 identified 18,455 publications, and 15,548 of these were unique titles. Investigators conducted an updated search on August 9, 2019 and identified 2,271 additional unique manuscripts published between March 2018 and August 2019. A total of 2 independent coders (YG and CMM) piloted the eligibility criteria and exhibited good agreement. A total of 4 members of the research team (YG, CGA, JZ, CMM) reviewed 17,819 titles/abstracts and excluded 17,732 manuscripts from full-text review. The 4 reviewers evaluated 87 full-text manuscripts for eligibility, and 16 studies met the inclusion criteria.

Data Extraction

The Population, Intervention, Comparator, Outcomes, Time-frame, and Study design framework²⁵ was used to guide the general characteristics of included studies to be extracted, including purpose, country, cancer type, study design, study setting, target population, and outcome measures. For intervention studies, the authors coded and reported strategy components that were evaluated to improve the uptake of genetic services; the usual care or control groups were not described.

Table 1. Indicators of the Potential Scalability of Strategies

Domain/code	Definition		
Strategy implementation			
Complexity	Components of the strategy, time/number of steps required to complete the strategy		
Setting	Geographic location, type of research setting		
Organizational implementers			
People deliver the strategy	Description of people who deliver the strategy, their expertise, and their roles		
Process factors			
Target population needs	Description of the target population, their needs, and resources		
User engagement	User engagement in the planning stage to gain feedback informing the strategy design		
Process evaluation	Process evaluation to get feedback on strategy implementation process		
Maintenance factors			
Resources	Training, education, or technical support dedicated for implementation		
Costs	Start-up cost, cost of strategy delivery, or cost of maintenance		

Informed by implementation science frameworks, ^{20,21} reach was characterized as the absolute number, proportion, and representativeness of individuals willing to participate in a given initiative. For the purposes of this review, to describe the extent to which the strategies have been successful in extending the reach of genetic services, 2 reach variables were operationalized: (1) genetic risk screening reach (the number of individuals who completed genetic risk screening divided by the number of individuals who could have been screened) and (2) genetic counseling service reach (the number of individuals who completed genetic counseling divided by the number of individuals found to be eligible for genetic counseling).

The risk screening reach variable is a required initial step for extending genetic services reach because individuals at high genetic risk must be identified first to be referred for genetic counseling. The genetic counseling service reach variable aligns with professional guidelines that genetic counseling be offered to all identified to be at heightened risk. Subsequent actions after genetic counseling (e.g., uptake of genetic testing) generally are not assessed in contexts outside of specialty clinical settings and are more fraught with complexity and nuance owing to factors such as personal preferences.

In addition, the authors reviewed details about how the strategy was implemented to gain insight into whether there was support for its potential scalability (Table 1). All studies were coded on whether they included any assessments that aligned with

implementation framework indicators of sustainability (1=presence, 0=absent).

A total of 3 members of the research team (YG, CGA, JZ) independently coded all eligible articles after coding 5 articles together for agreement. Any disagreement in the data collection process was resolved through discussion and consensus between the 2 reviewers and, if needed, with a third party (CMM).

Quality Assessment

This study used the 16-item quality assessment tool to assess the quality of each included study. ²⁶ Each study was rated on a scale of 0–3 for each criterion, with a higher score indicating greater methodologic rigor. Scores on the quality assessment tool can range from 0 to 42 (qualitative and quantitative studies) or 48 (mixed-methods studies). The overall rating, calculated as the total score divided by the total possible score, placed each study into categories of low- (<50%), medium- (50%–80%), or high-(>80%) quality evidence. ²⁶ The 3 reviewers coded 5 articles for agreement (YG, CGA, JZ), and 1 reviewer (YG) independently coded the remaining articles.

Data Analysis

The authors analyzed the data extracted from the included studies using simple frequency counts and a narrative approach to illustrate similarities and differences across strategies.²⁷ They described general characteristics of included studies, participants, setting, and outcomes. Percentages were reported that reflected the extent of reach and counts of studies that included any implementation framework indicators of sustainability.

EVIDENCE SYNTHESIS

Study Design

Of the 16 included studies, 11 were single-arm designs (Appendix Table 1, available online), 10 were cross-sectional designs, $^{28-37}$ and 1 was a pre—post design. 38 A total of 2 studies were RCTs that compared different reach strategies, 39,40 2 were non-RCTs, 41,42 and 1 employed a mixed-methods design. 43 A total of 10 studies focused on identifying individuals at risk for HBOC, 28,29,32,34,36,37,39,40,42 and 3 focused on LS. 30,35,38 Another 3 studies evaluated reach strategies for several hereditary cancers simultaneously. 31,33,43 The majority of the studies (n=12) were conducted in the U.S. $^{28,30,32-40,43}$; 4 were conducted in European countries, including Italy, 29 Latvia, 31 and the Netherlands; 42 and 1 was conducted in Israel. 41

Implementation Setting

Most strategies were implemented in clinical settings (n=11, 69%), $^{28,29,32,33,35-38,41-43}$ such as primary care practices (n=4), 32,33,42,43 community mammography screening practices (n=4), 28,29,36,37 community gastroenterology practices (n=2), 35,38 and multiple clinics (n=1). Additional strategies were implemented within public health settings $(n=5, 31\%)^{30,31,34,39,40}$:

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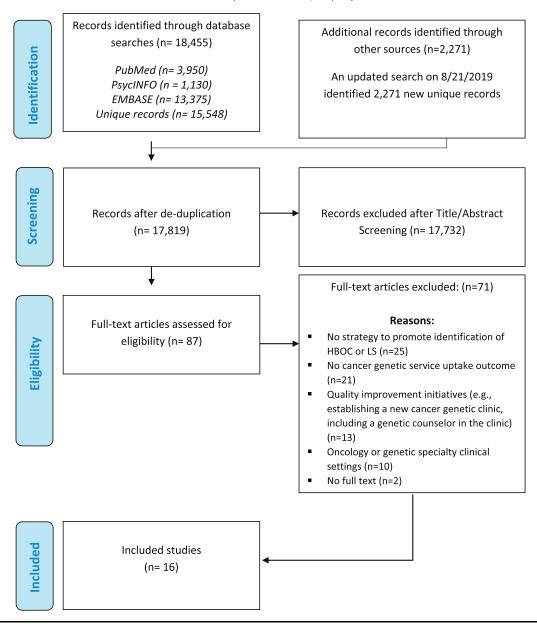


Figure 1. PRISMA flowchart of the process of study selection. HBOC, hereditary breast and ovarian cancer syndrome; LS, Lynch syndrome.

collaborating with population-based cancer registries (n=2), 30,34 national or local healthcare call centers (n=2), 39,40 or another unspecified community setting (n=1). 31

Target Population

Among the studies conducted in the clinical settings, 9 (56%) included patients only, ^{28,29,32,33,35–38,41} and 2 (13%) solely targeted primary care physicians. ^{42,43} In public health settings, 4 studies (25%) focused on the general public, ^{31,39–41} and 2 studies (13%) focused

on patients identified from population-based cancer registries. 30,34

Studies employed a variety of approaches. Participants were proactively recruited through postal invitations, telephone calls, and targeted advertisements 34,38,42,43 or opportunistically invited when they accessed a call-in service $^{39-41}$ or at clinic appointments. $^{28,29,32,33,35-37,41}$ Studies commonly reported inclusion and exclusion criteria (n=15, 94%) $^{28-33,35-43}$ and characteristics of participants (n=13, 81%). $^{28,30,32-41,43}$ However, the representativeness of participants was often not computable because few studies compared the characteristics

of those who participated with the characteristics of those who declined or were not engaged (n=6, 38%), 30,32,33,37,40,43

In 4 studies, researchers partnered with local community healthcare practices to expand the reach of genetic risk assessment to minority and low-income populations. For instance, Wernke et al. 36 administered family history-based screening among Black women with low SES who were underinsured and receiving care in a safety net hospital. Participants in the study of McGuinness and colleagues³⁷ were predominantly Hispanic (77%) and were recruited from a low-income, multiethnic population in New York. Anderson et al.32 also focused on minority women (74% Black, 26% Hispanic) seen at 2 federally qualified health centers' clinics in Chicago. Pasick and colleagues⁴⁰ partnered with a statewide cancer screening call center that served low-income populations in San Francisco Bay Area counties to reach participants from diverse ethnic backgrounds (30% White, 9% Black, 16% Asian, 40% Hispanic, 5% Other race).

Study Outcomes

Most studies were designed to evaluate the uptake of genetic risk assessment $^{28,30-32,34,36-38,43}$ or genetic counseling as the primary outcomes. Few studies (n=3) included the primary outcome of completing genetic testing 33,35,41 (Figure 2).

Of studies reporting the number or proportion of individuals who completed cancer genetic services, 15 reported completion of genetic risk assessment for HBOC or LS (63%), ^{28,30-43} 6 reported referral to genetic

counseling or testing (38%), 28,36,38,40,42,43 13 reported completion of genetic counseling (81%), $^{28-30,33-36,38-43}$ and 10 reported completion of genetic testing (63%). $^{29-31,33,35,38,41-43}$

Reach

Genetic risk screening reach (i.e., the number of individuals who completed genetic risk screening among individuals who could have been screened) was available in 13 studies (81%). 30-40,42,43 It is noteworthy that the denominator for target populations varied widely across studies (mean=4,798; median=1,212), ranging from 30 (patients with a diagnosis of ovarian cancer)⁴² to 24,210 (general population).³¹ Genetic risk screening reach in clinical settings varied widely, ranging from 11% to 100% (median=57%). The 2 studies with 100% screening reach were conducted in clinical settings. Helsper et al.⁴² used medical records to identify all patients with an ovarian cancer diagnosis (N=30) in a primary care practice. Gunaratnam and colleagues³⁸ implemented risk assessment among all patients (N=6,031) referred during the study period to open access colonoscopy at a community-based practice.

There was less variability in the reach of public health strategies, ranging from 31% to 77% (median=57%). Genetic risk screening reach was highest (77%, 18,642/24,210) in a study that implemented family history screening among all adult residents in 4 towns in Latvia.³¹

Genetic counseling service reach (i.e., the number of individuals who completed genetic counseling among individuals found to be eligible for genetic counseling)

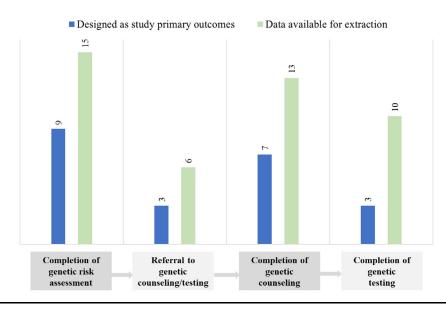


Figure 2. The number of studies that reported cancer genetic service uptake outcomes.

was reported in 10 studies (63%); 8 of these studies reported counseling uptake on the basis of clinical validation, $^{28,33,36,38,40-43}$ and 2 studies used participants' self-report. 30,34 Strategies implemented in public health settings (median=65%, range =11%-66%) had generally higher reach than those implemented in clinical settings (median=26%, range =1%-100%).

Programs that achieved high service reach included the program of Pasick's et al.,⁴⁰ in which HBOC screening assessment was conducted among callers to a community-based cancer screening call center; free genetic counseling and testing were provided. This program achieved a 68% (30/44) counseling service reach. Niendorf and colleagues³⁴ targeted individuals diagnosed with cancer enrolled in a population-based cancer registry to consider cancer genetic services (service reach=65%, 500/769). One clinical study⁴¹ achieved a 100% (1,771/1,771) service reach by implementing population-based streamlined *BRCA* genetic counseling and testing for Ashkenazi Jewish participants in multiple clinics (e.g., ambulatory clinics, mammogram screening clinics).

Indicators of the Potential Scalability of Strategies

Strategy implementation. Strategies used were heterogeneous across studies and typically included multiple components (Appendix Table 1, available online). The most commonly reported component was the use of family history—based risk assessment tools as part of the genetic risk screening process (*n*=10, 63%). ^{28,29,31,32,34 –37,39,40} In particular, 6 studies (38%) implemented family history screening tools in person, in primary care practice, or in community clinics. ^{28,29,32,35–37} A total of 3 more studies (19%) conducted telephone family risk assessment through local healthcare call centers ^{39,40} or by reaching out to those identified through a state's cancer registry. ³⁴ A total of 1 study implemented a family history questionnaire at the population level in 4 Latvian towns. ³¹

Other elements included developing educational materials about hereditary cancers, genetic risk assessment, genetic counseling and testing (n=6, 38%), 30,34,35,39,42,43 establishing new infrastructure supports (e.g., telemedicine, electronic medical record system; n=6, 38%), 32,33,35,38,42,43 and providing free inhouse genetic counseling or testing services (n=3, 19%). 28,30,40 None of the studies specified details about demands of the screening supports (e.g., time to complete the family history screening or the educational supplements) that would be important for assessing scalability.

Organizational implementers. A total of 10 studies (63%) used existing personnel of the institution (e.g., clinicians, staff) to administer the strategy^{28–31,33–35,38–40}; 6 of these studies involved nongenetic professionals who conducted genetic risk assessment (e.g., endoscopists, registry staff with no medical training; 37%), $^{31,34,35,38-40}$ and 4 relied on a genetic counselor^{28,30,33} or medical geneticist²⁹ to provide genetic counseling services. Less than half of the studies (n=6, 37%) mostly relied on research staff outside the institution to implement the strategy. $^{32,36,37,41-43}$

Process factors. The majority of the studies described the needs and resources of the target population (n=10, 63%). $^{28,30,33,35-37,39,40,42,43}$ A couple of studies described tailoring their strategy to target populations (e.g., translating the tool to different languages). 28,40 Reported approaches to engage the intended target population included focus groups, usability testing, and surveys. However, user engagement in designing the strategy was infrequent (n=5, 31%). 28,30,39,40,43 Most studies did not assess the quality of the implementation process. However, 2 studies conducted evaluations through surveys and interviews with staff clinicians to assess their attitudes and opinions regarding the implementation process. 35,43

Maintenance factors. Providing training or technical support for implementation was not commonly reported (n=5, 31%). Such informational support was mainly for individuals without genetic training (e.g., registry and clinic staff). None of the included studies reported numerical values for intervention development cost or implementation cost indicators (i.e., capacity building, maintenance, formal cost analysis).

Quality Assessment

On the basis of the quality assessment tool criteria, 2 of the 16 studies were rated as high quality (13%), 39,43 9 were rated as medium quality (56%), 30-38,40-42 and 5 (31%) were rated as low quality 28,29,36,37,42 (Appendix Table 2, available online; Figure 1). The 2 high-quality studies included an RCT and a mixed-methods design. 39,43

DISCUSSION

Description of Strategies Implemented Outside of Specialty Clinical Settings

Evidence-based guidelines were established more than a decade ago to address how to broaden screening to identify individuals with HBOC or LS. However, little empirical work (0.1%, 16 of 17,819 publications) has been conducted to implement these guidelines outside of

Table 2. Summary of the Strategy Reach (N=16)

	Genetic risk screening reach (n=13)			Genetic counseling service reach (n=10)		
Reference	Number of individuals who completed genetic risk screening (numerator)	Number of individuals who could have been screened (denominator)	Screening reach, %	Number of individuals who completed genetic counseling (numerator)	Number of individuals found to be eligible for genetic counseling (denominator)	Counseling reach, %
Clinical settings						
General practice						
Scheuner (2014) ⁴³	1,275	2,321	55	104	166	63
Anderson (2015) ³²	237	448	53	NA	NA	NA
Bradbury (2016) ³³	82	100	82	61	100	61
Helsper (2018) ⁴²	30	30	100	5	19	26
Community screening mammography practice						
Lee (2005) ²⁸	7,316	NA	NA	74	280	26
Seymour (2008) ²⁹	NA	NA	NA	NA	707	NA
Wernke (2019) ³⁶	126	1,169	11	4	35	11
McGuinness (2019) ³⁷	3,055	18,502	17	NA	NA	NA
Community gastroenterology practice						
Gunaratnam (2016) ³⁸	6,031	6,031	100	7	848	1
Luba (2018) ³⁵	3,134	5,287	59	177	NA	NA
Multiple clinics (e.g., mammography center, ambulatory clinics)						
Lieberman (2017) ⁴¹	1,771	NA	NA	1,771	1,771	100
Public health settings						
Healthcare call center						
Miller (2005) ³⁹	279	492	57	NA	NA	NA
Pasick (2016) ⁴⁰	709	1,212	58	30	44	68
Population-based cancer registry						
Lowery (2010) ³⁰	181	575	31	20	181	11
Niendorf (2016) ³⁴	869	1,992	44	500	769	65
Unclear community setting						
Vanags (2010)31	18,642	24,210	77	NA	NA	NA

NA, not available.

cancer specialty settings (e.g., urban cancer centers). The most common strategy used was family history—based risk assessment, which looks promising with respect to screening and service reach in resource-limited settings. A total of 10 of 16 studies implemented brief screening tools to identify people with a family history suggestive of HBOC or LS. This approach was typically combined with other institutional-level strategies such as establishing supportive infrastructure, personnel education and training, and financial support. Strategy reach and potential for scalability may be most promising in settings with an existing population that offers ongoing cancer-related services (e.g., registries, healthcare call centers).

Reach of Cancer Genetic Services to Underserved Populations

With respect to increasing access among subgroups such as minorities and those living in rural settings, family history—based screening in these groups specifically showed some success in both clinical and public health settings. Family history screening for HBOC provided in settings that serve a large proportion of minorities have shown high reach potential for risk screening and genetic counseling.^{32,40} Although the research base is limited, these findings, taken together, support continued efforts to explore context-specific approaches for implementing family history—based screening to reach underserved populations and reduce disparities in access to cancer genetic services.

Indicators of the Potential Scalability of Strategies

It is noteworthy, however, that only 6 of the 16 studies reported the racial/ethnic status of the target population: 2 study populations consisted primarily of Whites, ^{33,39} whereas 4 studies focused on low-SES areas or minority ethnic groups. ^{32,36,37,40} Clearer characterization of the target population intended for expanded reach will be critically important going forward to inform strategy development and evaluation.

Strategies implemented in public health settings appeared to be most consistently successful in reaching the target population compared with those implemented in clinical settings. Studies reporting the greatest service reach embedded risk assessment into existing infrastructures that had an established and delineated target population. For example, Pasick et al.⁴⁰ implemented risk assessments for HBOC among callers to a community-based healthcare call center and provided free genetic counseling and testing. Niendorf and colleagues³⁴ targeted individuals diagnosed with cancer enrolled in a population-based cancer registry to consider cancer genetic services. Given the relatively small number of

studies, it is difficult to draw any firm conclusions. Yet, clearly, there is a need to continue to explore linking genetic risk identification and service access through public health infrastructures.

Descriptions of most studies did not include foundational components relevant to scalability. With regard Proctor's implementation outcomes, 21 only 5 studies^{28,30,39,40,43} reported using collaborative processes such as engaging the target population to guide their strategy design, and few conducted process evaluations for acceptability. No study reported adaptations, maintenance plans, or monetary costs related to building new infrastructure or the workforce necessary to deliver the strategy within the clinical and public health settings. This lack of consideration of scalability potential is not specific to genetic services and continues to be a wellrecognized gap in the field. Moving forward, assessment components to determine whether a strategy is scalable across multiple subgroups, settings, or time are needed.22,44

To the authors' knowledge, this is the first review to systematically characterize efforts to broaden cancer genomic service reach outside of specialty clinical settings. Previous reviews on genomic medicine implementation have focused on screening in highly specialized clinical settings¹⁸ or using a cascade testing approach where the mutation carrier was already identified in a family.¹⁹

Limitations

Although the reported results carry important implications for implementation research in precision public health, there were limitations to this systematic review. It only included studies published in English and in peer-reviewed literature. Many initiatives do not progress to published literature, especially programs operated by state public health departments, and therefore, publication bias is likely to be present.

The results are based only on what was reported in the article, and the research team did not correspond with authors to assess additional details of study design. There were generally few details provided regarding the strategy implementation experience, which limited the ability to identify clear patterns that distinguished studies with high or low reach. The lack of reporting should not be viewed as a quality issue of the study design but rather highlights the need for future research to incorporate implementation science to understand barriers and facilitators and implementation strategies for genomic interventions that could inform the scale up of effective strategies to diverse populations and settings.

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CONCLUSIONS

The pressing challenge for addressing heritable cancer syndromes is to expand the reach of screening and genetic services beyond traditional cancer specialty centers. These findings suggest that these efforts are still nascent. Extending the reach of genetic services is an ambitious goal that can only be achieved through collaborations across multiple disciplines. Future efforts need to be partnered with appropriate access to risk-reducing screening and treatment services for mutation carriers. In addition, emerging clinical practice is emphasizing the use of multigene panels. This approach will undoubtedly introduce new challenges around the amount and complexity of outreach strategies.

That said, the findings suggest that implementing family history—based screening as a part of existing infrastructures that are already reaching well-delineated target populations has the potential to expand the reach of genetic services related to hereditary cancers, especially for ethnic minorities and those living in low-resource settings. These results highlight the need for accelerating research that applies evidence-based implementation strategies and frameworks along with process evaluation to understand barriers and facilitators to the scalability of strategies with high reach.

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SUPPLEMENTAL MATERIAL

Supplemental materials associated with this article can be found in the online version at https://doi.org/10.1016/j.amepre.2020.08.029.

REFERENCES

- Evaluation of Genomic Applications in Practice and Prevention (EGAPP) Working Group. Recommendations from the EGAPP working group: genetic testing strategies in newly diagnosed individuals with colorectal cancer aimed at reducing morbidity and mortality from Lynch syndrome in relatives. *Genet Med.* 2009;11(1):35–41. https://doi.org/10.1097/GIM.0b013e31818fa2ff.
- Nelson HD, Pappas M, Cantor A, Haney E, Holmes R. Risk assessment, genetic counseling, and genetic testing for BRCA-related cancer in women: updated evidence report and systematic review for the U.S. Preventive Services Task Force. *JAMA*. 2019;322(7):666–685. https://doi.org/10.1001/jama.2019.8430.
- Modell SM, Greendale K, Citrin T, Kardia SL. Expert and advocacy group consensus findings on the horizon of public health genetic testing. *Healthcare (Basel)*. 2016;4(1):14. https://doi.org/10.3390/ healthcare4010014.
- 4. Healthy People 2020: genomics. Office of Disease Prevention and Health Promotion. https://www.healthypeople.gov/2020/topics-objectives/topic/genomics/objectives. Updated August 10. Accessed September 22, 2020.
- 5. Petrucelli N, Daly MB, Pal T, et al. BRCA1- and BRCA2-associated hereditary breast and ovarian cancer. In: Adam MP, Ardinger HH, Pagon RA, eds. GeneReviews® [Internet]. Seattle, WA: University of Washington, Seattle, 2016. https://www.ncbi.nlm.nih.gov/books/NBK1247/. Accessed September 22, 2020.
- Kohlmann W, Gruber SB, et al. Lynch syndrome. In: Adam MP, Ardinger HH, Pagon RA, eds. GeneReviews® [Internet]. Seattle, WA: University of Washington, Seattle, 2018. https://www.ncbi.nlm.nih. gov/books/NBK1211/. Accessed September 22, 2020.
- Drescher CW, Beatty JD, Resta R, et al. The effect of referral for genetic counseling on genetic testing and surgical prevention in women at high risk for ovarian cancer: results from a randomized controlled trial. *Cancer*. 2016;122(22):3509–3518. https://doi.org/ 10.1002/cncr.30190.
- Powell CB, Littell R, Hoodfar E, Sinclair F, Pressman A. Does the diagnosis of breast or ovarian cancer trigger referral to genetic counseling?
 Int J Gynecol Cancer. 2013;23(3):431–436. https://doi.org/10.1097/IGC.0b013e318280f2b4.
- 9. Wright JD, Chen L, Tergas AI, et al. Underuse of BRCA testing in patients with breast and ovarian cancer. *Am J Obstet Gynecol.* 2016;214(6):761–763. https://doi.org/10.1016/j.ajog.2016.02.011.
- Hampel H, Frankel WL, Martin E, et al. Feasibility of screening for Lynch syndrome among patients with colorectal cancer. *J Clin Oncol*. 2008;26(35):5783–5788. https://doi.org/10.1200/JCO.2008.17.5950.
- 11. Morrison J, Bronner M, Leach BH, Downs-Kelly E, Goldblum JR, Liu X. Lynch syndrome screening in newly diagnosed colorectal cancer in general pathology practice: from the revised Bethesda guidelines to a universal approach. *Scand J Gastroenterol*. 2011;46(11):1340–1348. https://doi.org/10.3109/00365521.2011.610003.
- Tranø G, Sjursen W, Wasmuth HH, Hofsli E, Vatten LJ. Performance of clinical guidelines compared with molecular tumour screening methods in identifying possible Lynch syndrome among colorectal cancer patients: a Norwegian population-based study. *Br J Cancer*. 2010;102(3):482–488. https://doi.org/10.1038/sj.bjc.6605509.
- 13. van Lier MG, Leenen CH, Wagner A, et al. Yield of routine molecular analyses in colorectal cancer patients ≤70 years to detect underlying Lynch syndrome. *J Pathol.* 2012;226(5):764–774. https://doi.org/10.1002/path.3963.
- Khoury MJ, Bowen MS, Clyne M, et al. From public health genomics to precision public health: a 20-year journey. *Genet Med.* 2018;20 (6):574–582. https://doi.org/10.1038/gim.2017.211.
- 15. Dheensa S, Lucassen A, Fenwick A. Limitations and pitfalls of using family letters to communicate genetic risk: a qualitative study with patients and healthcare professionals. *J Genet Couns.* 2018;27(3):689–701. https://doi.org/10.1007/s10897-017-0164-x.

- Pozzar RA, Berry DL. Patient-centered research priorities in ovarian cancer: a systematic review of potential determinants of guideline care. Gynecol Oncol. 2017;147(3):714–722. https://doi.org/10.1016/j. ygyno.2017.10.004.
- Williams CD, Bullard AJ, O'Leary M, Thomas R, 4th Redding TS, Goldstein K. Racial/ethnic disparities in BRCA counseling and testing: a narrative review. J Racial Ethn Health Disparities. 2019;6(3):570–583. https://doi.org/10.1007/s40615-018-00556-7.
- Roberts MC, Kennedy AE, Chambers DA, Khoury MJ. The current state of implementation science in genomic medicine: opportunities for improvement. *Genet Med.* 2017;19(8):858–863. https://doi.org/ 10.1038/gim.2016.210.
- Roberts MC, Dotson WD, DeVore CS, et al. Delivery of cascade screening for hereditary conditions: a scoping review of the literature. *Health Aff (Millwood)*. 2018;37(5):801–808. https://doi.org/10.1377/ hlthaff.2017.1630.
- Glasgow RE, Vogt TM, Boles SM. Evaluating the public health impact of health promotion interventions: the RE-AIM framework. Am J Public Health. 1999;89(9):1322–1327. https://doi.org/10.2105/ajph.89. 9.1322.
- Proctor E, Silmere H, Raghavan R, et al. Outcomes for implementation research: conceptual distinctions, measurement challenges, and research agenda. Adm Policy Ment Health. 2011;38(2):65–76. https://doi.org/10.1007/s10488-010-0319-7.
- Milat AJ, King L, Bauman AE, Redman S. The concept of scalability: increasing the scale and potential adoption of health promotion interventions into policy and practice. *Health Promot Int.* 2013;28(3):285–298. https://doi.org/10.1093/heapro/dar097.
- U.S. Preventive Services Task Force. Genetic risk assessment and BRCA mutation testing for breast and ovarian cancer susceptibility: recommendation statement. Ann Intern Med. 2005;143(5):355–361. https://doi.org/10.7326/0003-4819-143-5-200509060-00011.
- Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med. 2009;6(7):e1000097. https://doi.org/10.1371/journal.pmed.1000097.
- Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *Ann Intern Med.* 2009;151(4):W65–W94. https://doi.org/10.7326/0003-4819-151-4-200908180-00136.
- Sirriyeh R, Lawton R, Gardner P, Armitage G. Reviewing studies with diverse designs: the development and evaluation of a new tool. *J Eval Clin Pract*. 2012;18(4):746–752. https://doi.org/10.1111/j.1365-2753.2011.01662.x.
- Greenhalgh T, Robert G, Macfarlane F, Bate P, Kyriakidou O, Peacock R. Storylines of research in diffusion of innovation: a meta-narrative approach to systematic review. Soc Sci Med. 2005;61(2):417–430. https://doi.org/10.1016/j.socscimed.2004.12.001.
- Lee R, Beattie M, Crawford B, et al. Recruitment, genetic counseling, and BRCA testing for underserved women at a public hospital. *Genet Test*. 2005;9(4):306–312. https://doi.org/10.1089/gte.2005.9.306.
- Seymour IJ, Casadei S, Zampiga V, et al. Results of a population-based screening for hereditary breast cancer in a region of North-Central Italy: contribution of BRCA1/2 germ-line mutations. *Breast Cancer Res Treat*. 2008;112(2):343–349. https://doi.org/10.1007/s10549-007-9846-7.
- Lowery JT, Axell L, Vu K, Rycroft R. A novel approach to increase awareness about hereditary colon cancer using a state cancer registry. *Genet Med.* 2010;12(11):721–725. https://doi.org/10.1097/GIM.0b013 e3181f1366a.

- Vanags A, Strumfa I, Gardovskis A, et al. Population screening for hereditary and familial cancer syndromes in Valka district of Latvia. Hered Cancer Clin Pract. 2010;8(1):8. https://doi.org/10.1186/1897-4287-8-8.
- Anderson EE, Tejeda S, Childers K, Stolley MR, Warnecke RB, Hoskins KF. Breast cancer risk assessment among low-income women of color in primary care: a pilot study. *J Oncol Pract.* 2015;11(4):e460–e467. https://doi.org/10.1200/JOP.2014.003558.
- Bradbury A, Patrick-Miller L, Harris D, et al. Utilizing remote realtime videoconferencing to expand access to cancer genetic services in community practices: a multicenter feasibility study. *J Med Internet* Res. 2016;18(2):e23. https://doi.org/10.2196/jmir.4564.
- Niendorf KB, Geller MA, Vogel RI, et al. A model for patient-direct screening and referral for familial cancer risk. Fam Cancer. 2016;15 (4):707–716. https://doi.org/10.1007/s10689-016-9912-6.
- Luba DG, DiSario JA, Rock C, et al. Community practice implementation of a self-administered version of PREMM_{1,2,6} to assess risk for Lynch syndrome. *Clin Gastroenterol Hepatol.* 2018;16(1):49–58. https://doi.org/10.1016/j.cgh.2017.06.038.
- 36. Wernke K, Bellcross C, Gabram S, Ali N, Stanislaw C. Impact of implementing B-RSTTM to screen for hereditary breast and ovarian cancer on risk perception and genetic counseling uptake among women in an academic safety net hospital. Clin Breast Cancer. 2019;19(4):e547–e555. https://doi.org/10.1016/j.clbc.2019.02.014.
- McGuinness JE, Trivedi MS, Silverman T, et al. Uptake of genetic testing for germline BRCA1/2 pathogenic variants in a predominantly Hispanic population. *Cancer Genet.* 2019;235–236:72–76. https://doi.org/10.1016/j.cancergen.2019.04.063.
- Gunaratnam NT, Akce M, Al Natour R, et al. Screening for cancer genetic syndromes with a simple risk-assessment tool in a community-based open-access colonoscopy practice. Am J Gastroenterol. 2016;111(5):589–593. https://doi.org/10.1038/ajg.2016.84.
- Miller SM, Fleisher L, Roussi P, et al. Facilitating informed decision making about breast cancer risk and genetic counseling among women calling the NCI's Cancer Information Service. J Health Commun. 2005;10(suppl 1):119–136. https://doi.org/10.1080/07366290500 265335.
- Pasick RJ, Joseph G, Stewart S, et al. Effective referral of low-income women at risk for hereditary breast and ovarian cancer to genetic counseling: a randomized delayed intervention control trial. Am J Public Health. 2016;106(10):1842–1848. https://doi.org/10.2105/ AJPH.2016.303312.
- Lieberman S, Tomer A, Ben-Chetrit A, et al. Population screening for BRCA1/BRCA2 founder mutations in Ashkenazi Jews: proactive recruitment compared with self-referral [published correction appears in *Genet Med.* 2020;22(3):672]. *Genet Med.* 2017;19(7):754–762. https://doi.org/10.1038/gim.2016.182.
- Helsper CW, Van Vliet LM, Velthuizen ME, et al. Identifying patients with a history of ovarian cancer for referral for genetic counselling: non-randomised comparison of two case-finding strategies in primary care. *Br J Gen Pract*. 2018;68(676):e750–e756. https://doi.org/10.3399/ bjgp18X699533.
- Scheuner MT, Hamilton AB, Peredo J, et al. A cancer genetics toolkit improves access to genetic services through documentation and use of the family history by primary-care clinicians. *Genet Med.* 2014;16 (1):60–69. https://doi.org/10.1038/gim.2013.75.
- Chambers DA, Feero WG, Khoury MJ. Convergence of implementation science, precision medicine, and the learning health care system: a new model for biomedical research. *JAMA*. 2016;315(18):1941–1942. https://doi.org/10.1001/jama.2016.3867.