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Review Article

Disparities in gynecologic cancer genetics evaluation

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HIGHLIGHTS

- Despite increases in the rate of testing for BRCA and Lynch syndrome, many high-risk women remain unidentified.
- Underserved populations who do not access genetics services are at risk of missing opportunities for cancer prevention.
- Socioeconomic factors, poor communication, concerns about misuse of genetic data contribute to poor use of genetic services.
- Research is needed to specifically identify barriers to receipt and use of cancer genetics services.

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ABSTRACT

An estimated 2–5% of endometrial cancers and 15–20% of high-grade, non-mucinous epithelial ovarian cancers have an underlying hereditary cause. Appropriate risk assessment, genetic counseling, and germline genetic testing for cancer predisposition genes in both gynecologic cancer patients and their at-risk relatives is essential for effective delivery of tailored cancer treatment and cancer prevention. However, significant disparities exist within medically underserved and minority populations in the United States regarding awareness of, access to, and use of genetic services. The objectives of this review are to summarize the literature on genetic counseling and genetic testing of gynecologic cancer patients, the cascade genetic testing of their families following the identification of a germline mutation associated with susceptibility to cancer, to highlight disparities between populations, and to present some potential remedies.

Contents

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1. Introduction

A diagnosis of invasive epithelial ovarian, fallopian tube, and primary peritoneal cancer (EOC) or endometrial cancer warrants the use of genetics services, including hereditary cancer risk assessment, genetic counseling, and germline genetic testing. Despite recommendations for genetics services in this patient population, substantial disparities exist in the awareness of, access to, and use of genetic services among medically underserved and minority populations.

A significant fraction (15–20%) of EOC has an underlying hereditary cause, especially those that have high-grade, non-mucinous histology [1,2]. For example, up to 25% of high-grade serous ovarian carcinomas are hereditary, primarily due to germline mutations in *BRCA1* and *BRCA2* (BRCA1/2) [1]. Identification of a germline mutation in BRCA1/2 can have significant implications for cancer treatment, including the use of pharmacologic inhibitors of the enzyme poly-ADP ribose polymerase (PARP). Additionally, studies have suggested that individuals with EOC and a germline BRCA1/2 mutation may have better responses to treatment, and better outcomes following treatment, as compared to those without germline mutations [2,3]. In addition to implications for EOC treatment, identification of a BRCA1/2 germline mutation can indicate increased lifetime risks for other types of cancer. Women with a BRCA1/2 mutation are estimated to have lifetime risks to develop breast cancer of approximately 40–80%, as compared to general U.S. population lifetime risk of approximately 12% [4]. Other cancer risks have been associated with germline BRCA1/2 mutations, including increased risks for pancreatic cancer, melanoma, male breast cancer, and prostate cancers [5]. Therefore, more frequent cancer screening and more aggressive risk-reduction strategies are warranted in populations with a BRCA1/2 mutation.

In addition to BRCA1/2, up to 10–15% of hereditary EOC may be due to germline mutations in the LS genes [6]. Identification of a germline mutation in a LS gene can have similar clinical implications (such as guiding decisions for cancer treatment, specifying cancer risks, and signaling cancer risks for family members), but differences exist by cancer types, lifetime risks, and risk-reduction strategies. Ovarian cancers associated with LS are more histologically variable, with mutations identified primarily among patients with endometrioid and clear cell carcinoma; with some cases of LS identified among individuals with high-grade serous, low-grade, and mucinous ovarian carcinomas [1]. Mutations in LS genes are also responsible for <5% of endometrial cancers [7]. Lifetime risks to develop endometrial cancer among women with LS are significantly increased, and the risks vary by gene (from lifetime risks as low as 15% associated with a *PMS2* mutation, to as high as 25–60% when an *MLH1* or *MSH2* mutation is present) [8]. Other gene-specific cancer risks have been associated with mutations in LS genes, including risks for prostate cancer (up to 30% lifetime risk), stomach cancer (up to 13% lifetime risk), hepatobiliary tract cancer (up to 4% lifetime risk), urinary tract cancer (up to 7% lifetime risk), small bowel cancer (up to 6% lifetime risk), and pancreatic cancer (up to 6% lifetime risk) [8]. From a treatment perspective, identification of a LS mutation typically indicates tumor mismatch repair deficiency and microsatellite instability (MSI) which have implications for immunotherapy treatment.

1.1. Current guidelines for genetics evaluation of patients with gynecologic cancer

The National Comprehensive Cancer Network (NCCN) and several professional organizations have produced guidelines to aid in the identification individuals suspected to have BRCA1/2 or LS mutations. In 2007, the NCCN guidelines recommended that all women diagnosed with EOC receive genetic risk evaluation, and consider germline BRCA1/2 genetic testing [9]. More recent versions of the NCCN guidelines acknowledge that BRCA1/2-related EOCs are typically epithelial with non-mucinous histology, whereas other histologic types of EOC may be associated with LS. In 2014, the Society of Gynecologic Oncology (SGO) produced a clinical practice statement recommending that all women diagnosed with EOC should receive genetic counseling and be offered genetic testing for BRCA1/2 [10]. More recent SGO statements have called for universal BRCA1/2 testing of patients with EOC and universal evaluation for LS among patients with endometrial cancer [11].

The guidelines for the evaluation of LS in women diagnosed with endometrial cancer are less direct. Current NCCN guidelines recommend evaluation for LS in women who are:

- Diagnosed with endometrial cancer under the age of 50, or
- Diagnosed with endometrial cancer and a synchronous or metachronous LS-related cancer, or
- Diagnosed with endometrial cancer with evidence of mismatch repair deficiency, or
- Diagnosed with endometrial cancer in the setting of a family history of LS-related cancers [12].

The NCCN's LS genetic testing strategy is similarly complex and includes first evaluating the endometrial tumor for mismatch repair deficiency either through immunohistochemistry (IHC) and/or microsatellite instability (MSI) analysis, or performing germline genetic testing of *MLH1*, *MSH2*/*EPCAM*, *MSH6*, and *PMS2*, or germline genetic testing using a multigene panel that includes LS genes as well as other relevant genes [12].

Best practice provision of genetics services in a well-resourced setting includes referral of patients with EOC and endometrial cancer for genetic counseling and a comprehensive risk assessment. Comprehensive risk assessment includes the collection of a three-generation cancer-specific family history (pedigree) and discussion of the benefits and limitations of current genetic testing options (which may include testing of a single gene mutation, hereditary cancer condition-specific testing such as evaluation of the LS genes, or multi-gene panel testing as indicated based on personal and family history of cancer). Tailored and personalized discussion of possible results of genetic testing and their implications for the patient and their family, provision of psychosocial support and anticipatory guidance, and disclosure of the results of genetic testing with a result-guided cancer risk assessment for the patient and their relatives should also be performed. Because African-American (AA), Latina, Asian, and Caucasian patient populations may have significantly different concerns regarding genetic testing and its implications, genetic counseling sessions should be customized and tailored to the health literacy, education, emotional, and cultural needs of patients [13,14]. Following the identification of a mutation, it is standard practice for the patient to receive a copy of his or her genetic testing results, along with a family letter designed to facilitate communication about the mutation and recommend cascade testing of relatives.

1.2. Current guidelines for genetics evaluation and cascade testing of first-degree relatives

Cascade testing is the process by which genetic counseling and site-specific genetic testing are completed among at-risk relatives of an index patient (or proband) in a sequential manner based on the

likelihood that they will test positive [15]. Mutations in BRCA1/2 and LS genes are inherited in an autosomal dominant fashion. A proband's first-degree relatives (biological children, full-siblings, and parents) have a 50% chance of inheriting the mutation and the associated elevated cancer risks. The current NCCN guidelines recommend that at-risk blood relatives of an individual diagnosed with a hereditary cancer predisposition gene mutation should be notified that a mutation has been identified in their family, and recommended to consider genetic counseling and genetic testing for the identified mutation [12,16]. Relatives found to have inherited the familial mutation are then encouraged to undergo NCCN guideline recommended intensive cancer screening, chemoprevention, and/or risk-reducing, prophylactic surgery.

1.3. Disparities in the receipt of genetics services among patients with gynecologic cancer

Although guidelines exist for assessment, genetic counseling, and genetic testing of patients diagnosed with EOC and endometrial cancer, patients are not receiving these services consistently or equitably.

Among patients diagnosed with EOC, the rates of guideline-compliant referral to genetics services ranged from as low as 12% in patients diagnosed in 1999 to as high as 53% in 2012–2016 as shown in Table 1 [17,18]. Among ten studies specifically reviewing guideline-compliant referral and receipt of genetics services among patients with EOC in the U.S., only three studies specifically assessed the association between patient's race/ethnicity and referral rates [17–26]. Two studies found that AA and Hispanic race/ethnicity were associated with lower rates of referral [17,18].

Fewer studies have assessed guideline compliance or rates of tumor screening (IHC and/or MSI) completion, genetic counseling, or genetic testing among patients diagnosed with endometrial cancer in the U.S. Variability in current guideline recommendations for patients with endometrial cancer complicates the evaluation of guideline compliance. Clinical implementation of tumor screening is also variable from hospital to hospital, and can vary by which healthcare provider orders the testing, receives the results, interprets the findings, and triages patients to genetics services [27]. Rates of genetics evaluation among patients with endometrial cancer are as low as 13.4% to as high as 100%; the latter figure reported in the context of universal tumor testing in a research setting [28]. Most of the literature regarding universal testing of endometrial cancer tumors has evaluated outcomes of testing in a research environment, rather than the fidelity of universal testing

Table 1
Rates of genetics evaluation of patients with epithelial ovarian cancer stratified by race and ethnicity.

Publication	Population	Time period	Primary focus of publication	Rate	Race/ethnicity evaluation
Meyer et al. (2010) [17]	3765 "High risk" EOC patients at MD Anderson Cancer Center	1999–2007	Referral for GC/GT	1999: 12% (9/74) 2007: 48% (52/109)	82% of patients were white, 4% AA, and 10% Hispanic. AA patients were less likely to be referred than white patients (OR = 0.25, 95% CI: 0.09–0.70), $p = 0.009$
Powell et al. (2013) [19]	38 "High risk" EOC patients at Kaiser Permanente Northern California	Jan. 2008–June 2008	Referral for GC/GT Completion of GC	18.4% (7/38) 5.3% (2/38)	No difference in referral rates by patient race.
Petzel et al. (2014) [20]	495 EOC patients at University of Minnesota Women's Cancer Center	April 2007–April 2009	Referral for GC/GT	17–30%	Race/Ethnicity not reported in patient demographics.
Febbraro et al. (2015) [21]	290 EOC patients at Brown University Women's Oncology Center	2004–2010	Referral for GC/GT	14.5%	95% of patients were white. No difference in referral rates by patient race.
Wright et al. (2016) [22]	11, 966 EOC patients from U.S. MarketScan database	July 2009–June 2013	Completion of GT (BRCA1/2)	17.4%	Race/Ethnicity not reported in patient demographics.
Childers et al. (2017) [23]	206 EOC patients from U.S. National Health Interview Surveys	2005, 2010, 2015	Referral for GC/GT Completion of GT	13.1% 10.5%	Race/Ethnicity data collected but not analyzed in relation to referral or testing rates.
Uyar et al. (2018) [24]	207 EOC patients at a Medical College of Wisconsin Gynecologic Oncology	Jan. 2008–Nov. 2013 (baseline)	Referral for GC/GT Completion of GC Completion of GT	46% (96/207) 69.8% (67/96) 82.1% (55/67)	Race/Ethnicity not reported in patient demographics.
Swanson et al. (2018) [25]	75 EOC patients at Mayo Clinic Rochester	Jan. 2013–Dec. 2013 (baseline)	Referral for GC/GT Completion of GC Completion of GT	44.0% (33/75) 88% (29/33) 79% (23/29)	Race/Ethnicity not reported in patient demographics.
Gross et al. (2018) [26]	718 EOC and breast cancer patients from the Southern Community Cohort Study	March 2000 –June 2014	Completion of GT	8.7% (8/92) *includes breast and EOC patients	62% of patients were AA, and 33% white. Race/Ethnicity data collected but not analyzed in relation to testing rates.
Manrriques et al. (2018) [18]	236 EOC patients at UCSF Gynecologic Oncology	Aug. 2012 – Jan. 2016	Referral for GC/GT Completion of GC Completion of GT	53% (126/236) 68% (86/126) 92% (79/86)	60.2% of patients were white, 14% Latina, 13% Asian, and 4% AA. Rates of referral were lower for AA and Latina patients ($p = 0.035$). Rates of referral differed significantly by patient race, insurance type, and primary spoken language.

Abbreviations: EOC, epithelial ovarian cancer; GC, genetic counseling; GT, genetic testing; AA, African-American/Black.

Table 2
Rates of genetics evaluation of patients with endometrial cancer stratified by race and ethnicity.

Publication	Population	Time period	Primary focus of publication	Rates	Race/ethnicity evaluation
Universal tumor testing					
Batte et al. (2014) [29]	614 total EC patients at MD Anderson Cancer Center (408 + 206)	All prior to & including 2011 - Aug 2013	LS-suggestive tumor testing result	10.3% (63/614)	Race/Ethnicity not reported in patient demographics.
			Completion of GC	50.8% (32/63)	
			Completion of GT	78.1% (25/63)	
Dillon et al. (2017) [30]	233 EC patients at Dartmouth-Hitchcock Medical Center	May 2015-Dec 2016	LS-suggestive tumor testing result	4.7% (11/233)	Race/Ethnicity not reported in patient demographics.
			Referral for GC/GT	90.9% (10/11)	
			Completion of GT	80.0% (8/10)	
Adar et al. (2018) [28]	484 EC patients at Massachusetts General Hospital and North Shore Medical Center	2013–2015	LS-suggestive tumor testing result	6.6% (32/484)	84% of patients were white. Race/Ethnicity data collected but not analyzed in relation to testing rates.
			Referral for GC/GT	100% (32/32)	
			Completion of GC	53.1% (17/32)	
			Completion of GT	94.1% (16/17)	
Mixed evaluation guidelines					
Moline et al. (2013) [31]	245 EC patients at Cleveland Clinic. (3 cohorts based on date of diagnosis corresponding guideline)	June 2009-Dec. 2012	LS-suggestive tumor testing result	18.0% (44/245)*	Race/Ethnicity not reported in patient demographics.
			Referral for GC/GT	95.5% (42/44)*	
			Completion of GC	81.0% (34/42)*	
			Completion of GT	82.4% (28/34)*	
Frolova et al. (2015) [32]	637 EC patients at Barnes Jewish Hospital. (2 cohorts based on pre/post-universal tumor testing initiated Dec. 2012)	Jan. 2011-Dec. 2013	Completed IHC tumor testing	58.9% (375/637)*	Race/Ethnicity not reported in patient demographics.
			LS-suggestive tumor testing result	11.2% (42/375)*	
			Referral for GC/GT	>100% (44/42)*	
			Completion of GC	79.5% (35/44)*	
			Completion of GT	74.3% (26/35)*	
Lee et al. (2018) [33]	583 EC patients at 2 NYU Oncology Care Centers. (1 cohort, 4 ways to meet "High risk" criteria)	Nov 2012-Dec 2016	"High risk" criteria met	31.6% (184/583)*	50.9% of patients were white. "High risk" criteria were met most frequently among Asian women and least among AA women. Rates of genetic testing were <45% in each race/ethnicity
			Referral for GC/GT	57.6% (106/184)*	
			Completion of GC/GT	61.3% (65/106)*	
Other process/evaluation guidelines					
Backes et al. (2011) [34]	384 EC patients at Ohio State University Medical Center	2007–2009	"High risk" criteria met	12.2% (47/384)	Race/Ethnicity not reported in patient demographics.
			Referral for GC/GT	57.4% (27/47)	
			Completion of GC	48.1% (13/27)	
			Completion of GT	61.5% (8/13)	
Febbraro et al. (2015) [21]	216 EC patients at Brown University Women's Oncology Center	2004–2010	Referral for GC/GT	13.4%	92.3% of patients were white. No difference in referral rates by patient race.

Key: * = cumulative totals across cohorts.
Abbreviations: EC, endometrial cancer; IHC, immunohistochemistry; LS, Lynch syndrome; GC, genetic counseling; GT, genetic testing; AA, African-American or black.

implementation in a clinical environment. Of eight studies reviewed in Table 2 that specifically addressed rates and outcomes of tumor testing, genetic counseling, and genetic testing among endometrial cancer patients in the U.S. [21,28–34] three occurred in controlled, research-based environments [28–30]; three evaluated the effects of shifting screening guidelines [31–33]; and two evaluated general genetics evaluation processes [21,34]. Only one of these studies attempted to evaluate the association between patient race/ethnicity and receipt of genetics services, and the results of the analysis found tumor testing rates were low (<45%) across all racial/ethnic groups [33].

1.4. Disparities in genetic evaluation and cascade testing of first-degree relatives

Probands disclose and share their genetic testing results with over 80% of their first-degree relatives, but rates of subsequent genetic testing among those relatives remain low, with only 15–51% of relatives completing cascade testing [35,36]. Following the identification of a BRCA1/2 mutation, results are more likely to be communicated to first-degree and female relatives, but less often to more distant relatives [37]. Unsurprisingly, females and first-degree relatives were more likely to pursue genetic testing [35,37].

Among families diagnosed with LS, a systematic review reported that uptake of genetic testing among first-degree relatives was 52%, with female gender, higher level of education, and age <50 years all predictive of uptake [38]. In terms of disclosure to more distant relatives, one study reported that positive test results for a LS mutation were disclosed to 64% of second-degree relatives [39]. Again, females and first-degree relatives were more likely to follow up with a clinician [39].

The majority of studies regarding cascade testing have been performed among predominantly Caucasian women of middle to high socioeconomic status, most often recruited from tertiary care centers [35,37]. One survey study of racially and socioeconomically diverse patient populations reported that probands with a BRCA1/2 mutation seen at a public hospital had lower rates of cascade testing among their blood relatives (29%) than probands seen at a tertiary care center (77%), and also suggested that relatives of non-white patients were less likely to undergo cascade testing [40]. However, this study did not report the overall number of at-risk relatives, so the rates of family communication and cascade testing are unknown. A subsequent structured interview study of 73 patients from the same public hospital and tertiary care center who tested positive for a BRCA1/2 mutation reported proband disclosure of test results to 73% of at-risk relatives, and a self-reported testing uptake rate of 31% among those relatives [36]. The study determined that the proband's race was a significant predictor of both result disclosure and cascade testing uptake among relatives, with AA and Asian/Pacific Islander probands significantly less likely to disclose results, and relatives of AA probands less likely to have been tested [36].

1.5. Current barriers to genetic testing among patients with gynecologic cancer

Barriers to genetic risk assessment, genetic counseling, and genetic testing of patients with gynecologic cancer exist throughout the U.S. population, but racial and ethnic minority populations may encounter unique barriers. A study conducted by Glenn et al. [41] from 2004 to 2006 revealed that a leading reason why AA, Asian, and Hispanic women did not undergo BRCA1/2 testing was lack of awareness of the availability of this service. By contrast, a greater medical knowledge base is positively associated with increased motivation to undergo genetic counseling and testing, and this also is associated with patient-initiated inquiry for services [42]. Furthermore, racial/ethnic disparities in testing are driven, at least in part, by differences in physician's recommendations for genetics evaluation. Both oncologists and surgeons treating patients with breast cancer are less likely to recommend BRCA1/2 testing to AA women than to white women, even after adjusting for the predicted risk of a mutation [43].

Following a recommendation or referral for genetics evaluation services, barriers to patient receipt of genetics services include lack of awareness of the purpose or goal of having genetic services, poor communication or limited knowledge of family medical history, inaccurate risk perception (regarding cancer risks and risks of inheriting a hereditary cancer predisposition), time required to travel to and attend genetics and other medical appointments, and other socioeconomic factors [44,45]. Additionally, distrust of the medical system as well as concerns about how genetic information may be used have been demonstrated to contribute to disparities in testing for breast cancer patients, with one study reporting strong correlation between medical mistrust and lower genetic testing engagement [46–48]. In addition, the current demand for risk assessment and counseling by certified genetic counselors exceeds the U.S. workforce supply. Clinical genetic counseling services are also unequally distributed across the U.S., with services primarily located in major cities and academic medical centers, which may exacerbate patient barriers related to poor geographic access, especially for individuals living in rural communities [49]. In the past, the cost of genetic testing was a significant barrier to individuals who have received recommendations to undergo testing. Although genetic testing costs have since decreased, after a mutation is identified, there are significant concerns about financial support and insurance coverage for individuals with BRCA1/2 or LS mutations to obtain the recommended cancer screening, preventive services, and risk-reducing surgeries [50]. Patients may also have concerns about data privacy, insurance, and employment discrimination, which may be particularly relevant in populations who obtain health insurance or employment through informal means or through small businesses and agencies not covered by the Genetic Information Nondiscrimination Act (GINA) [51].

1.6. Additional considerations regarding genetic testing of patients with gynecologic cancer

The laboratory and technological options available for performing hereditary cancer germline genetic testing have changed dramatically over the past several years. Technical improvements in genetic testing methodology started with the introduction of BRACAnalysis Rearrangement Testing (BART) in 2006, clinical multi-gene panel testing using next-generation sequencing in 2013, improvements to testing for *PMS2* to account for the presence of pseudogenes, and the evaluation of the Boland inversion (exons 1–7) in *MSH2*, which have become clinically available in recent years. Not all clinical testing laboratories have the same or equivalent technical capabilities for genetic testing. This is relevant to ensure that patients with gynecologic cancer receive appropriate and comprehensive genetic testing, and that gynecologic cancer survivors have access to opportunities for additional testing as technology continues to improve.

Changes in genetic testing technology, analysis of multiple genes, and improved access to genetic testing among diverse populations have increased the frequency of uncertain or conflicting results. Given the lack of data available from underserved and diverse patient communities, in part due to historic lack of inclusion in research and lower rates of clinical genetic testing, uncertain results (i.e., identification of variants of uncertain significance) are more likely to be obtained in the testing of ethnic or racial minority populations [52]. In addition to the identification of uncertain results, discrepancies may arise in the interpretation of these results across clinical laboratories, thereby increasing the ambiguity of findings and the potential risk for clinical misinterpretation and inappropriate clinical intervention with irreversible results, such as unnecessary premenopausal salpingo-oophorectomy or mastectomy [53]. Clinical genetic testing laboratories take different approaches to reporting uncertain results, determining whether variant reclassification is applicable, and distributing amended classifications to health care providers. Medically underserved communities and

minority racial and ethnic populations are therefore at higher risk for the burden of uncertainty when undergoing genetic testing. Accordingly, awareness of laboratory processes regarding variant interpretation and reclassification are important to consider when offering genetic testing in diverse patient populations.

1.7. Current barriers to cascade testing

The barriers to cascade testing of at-risk relatives are not well established. Communication of positive genetic testing results, a key initial step, presents its own challenges. In a survey of genetic counselors, almost half (46%) reported having had a patient refuse to notify an at-risk relative [54]. The most commonly reported reasons for patient non-disclosure of results to relatives included psychosocial considerations, such as estranged relationships and risk or fear of changing the family dynamics, and practical considerations, such as insurance or employment discrimination [54]. Communication of genetic test results with relatives may also be inhibited by proband-specific factors, such as lower levels of confidence in one's ability to share results, scoring highly on measures of depressive symptoms, and the perception that relatives are not in favor of hearing the results [55]. Although up to 80% of probands share their genetic testing results and advise relatives to seek genetics assessment, sharing of detailed risk information, medical implications, and risk management recommendations, as demonstrated by the relative's awareness of this information, may occur much less frequently [56]. For example, one study reported that less than half (45%) of surveyed relatives confidently knew of the availability of predictive gene testing, and only 37% had good or complete awareness of potential preventative options available to individuals with a BRCA1/2 mutation; awareness was lower among more distant relatives [56]. A study of families with LS investigated what information was actually shared by probands, and found that the genetic counseling note was shared 53% of the time, whereas additional information, such as testing laboratory information, online resources, or information about genetics referral, were given to fewer than 33% of relatives. Females and first-degree relatives were more likely to be given additional material [39]. The baseline medical literacy necessary to convey results, as well as understand the results' implications for relatives, may be a significant limitation for many medically underserved groups. Additionally, the gender of the proband may impact the communication barriers experienced; men reported greater difficulty disclosing genetic test results with at-risk family members, whereas women expressed more emotional distress associated with discussion of results [57].

The majority of patients express the desire to share their genetic testing result information with their relatives themselves. Unfortunately, studies of mechanisms used by health care professionals' to support proband result disclosure have exhibited mixed utility. One study found lower uptake of cascade testing following a physician's referral for genetics evaluation than after relative's self-referral to genetics services [58]. Health care provider–driven interventions aimed at improving family communication, including telephone discussions or mailed information, have also yielded mixed results [59–61]. Letters from the genetics service improved the proportion of at-risk relatives who got cascade testing from 23% to 40% in one study, and a study that used multiple follow-up calls did show improvement in the outcome, i.e., contact with genetic services [61]. In contrast, another study reported that a telephone counseling program made no significant change in the rate at which at-risk relatives contacted genetic services for appointment or testing [59,60].

These findings indicate that knowledge, awareness, and family dynamics play important roles in communication of results and recommendations for cascade testing. However, there remain significant access barriers associated with social determinants of health, such as access to care and health literacy factors. Moreover, only a few studies have directly described or addressed genetic counseling and genetic testing barriers among probands and their relatives from medically underserved populations.

1.8. Approaches to decreasing disparities in genetic counseling and genetic testing

The findings described above emphasize the need for tailored and culturally appropriate interventions aimed at increasing the awareness of, access to, and uptake of genetic counseling and genetic testing in medically underserved and diverse populations at risk for hereditary predisposition to cancer.

Improvements in awareness of hereditary cancer, availability of local genetics services, and communication of the importance of genetics evaluation may be effectively driven by efforts in the healthcare setting; however, community-based public health campaigns and awareness efforts may have a greater reach. In the health care setting, pilot studies suggest that closer collaboration between cancer genetics services, primary care providers, and cancer care providers may improve patient access, especially when tailored to local populations [62]. In addition, increased genetic knowledge and provision of tools and support for delivery of familial cancer risk assessment among physicians and nurses caring for patients from racial and ethnic minority populations may improve patient awareness of genetics services and cancer risk perceptions [63]. Community-based interventions have demonstrated some benefit, and may warrant further evaluation. Previously reported interventions have included community awareness raising, cultural events, use of local newspapers and radio, and a website supported by leaflets, as well as locating services within the target community; collectively, these approaches have effectively improved awareness of hereditary cancer and collection of family history [44].

Strategies for increasing patient access to genetics services include telegenetics (telemedicine technology to provide clinical genetic services), group counseling sessions, integrating or embedding services within specialty oncology clinics, initial genetic testing performed by non-genetics clinicians, direct-to-consumer genetics education and testing, quality improvement initiatives, and other clinic support tools such as video education, computer-assisted family history collection, and patient navigation [64–66]. Alternative service delivery models for the provision of guideline-compliant genetics services have been proposed, and initial research has been performed; however, knowledge of the effectiveness, benefits, and risks of some delivery models remains limited. The best-studied alternative service delivery model for genetics services is the use of telephone genetic counseling, which may reduce geographic barriers for patients. A recent randomized non-inferiority trial demonstrated that delivery of telephone genetic counseling led to outcomes that were non-inferior to standard in-person genetic counseling for hereditary breast and ovarian cancer. However, women who were randomized to telephone counseling were less likely to complete BRCA1/2 testing than those randomized to in-person counseling [67]. Subsequent analyses of this trial revealed that patient's race and ethnicity moderated the association between randomization group and testing, and that women from minority populations who received telephone counseling were least likely to complete testing. Implementation of alternative service delivery models may reduce some difficulties faced by medically underserved communities, but additional research is needed to determine whether providing such alternatives effectively address all barriers and improve equitable access to genetics care.

At the same time that alternative service delivery models have attempted to reduce barriers to genetic counseling, the barriers to genetic testing have also been reduced. Cost of genetic testing and lack of insurance coverage have been significant challenges to patients completing testing; however, in recent years the cost of genetic testing has decreased in part due to technological advances, health insurance payer policies regarding test coverage, and the Affordable Care Act's inclusion of BRCA1/2 testing as a covered service [50]. Additionally, many

clinical genetic testing laboratories offer financial assistance programs to patients who are uninsured or underinsured, which help to defray most or all of the out-of-pocket costs of genetic testing. Reducing financial barriers to genetic testing may improve access to this service, especially among medically underserved, uninsured, or impoverished patients.

Future research on awareness, referral, and use of genetics services, including cascade testing among families, should include evaluation and reporting of patient race and ethnicity status, as well as socioeconomic factors. As highlighted in Table 1 and Table 2, many studies do not include evaluation of these patient factors, limiting awareness of disparities and obscuring opportunities for improvement.

2. Conclusions

Underserved and minority communities in the U.S., including populations with low socioeconomic status, are significantly less likely to receive the guideline-recommended genetic counseling and genetic testing to identify hereditary predispositions to ovarian and endometrial malignancies. Low rates of referral for genetic counseling and testing are compounded by lack of patient awareness of genetics services and barriers to their utilization, including access to care, socioeconomic factors, poor familial communication, inaccurate risk perception, or other cultural factors. Further research is needed to specifically identify barriers to receipt and use of cancer genetics services among underserved gynecologic cancer patient populations and their families, to serve as a foundation for the design of tailored and appropriate interventions to improve care and ultimately prevent cancer in high-risk families.

Disclosure of interests

The authors declare that there are no conflicts of interest.

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Author contribution

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