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Risk-reducing salpingo-oophorectomy among diverse patients with *BRCA* mutations at an urban public hospital: a mixed methods study

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ABSTRACT

Objectives To assess the association of socioeconomic demographics with recommendation for and uptake of risk-reducing bilateral salpingo-oophorectomy (rrBSO) in patients with *BRCA1* and *BRCA2* (*BRCA1/2*) mutations.

Design Retrospective cohort, semistructured qualitative interviews.

Setting and participants *BRCA1/2* mutation carriers at an urban, public hospital with a racially and socioeconomically diverse population.

Intervention None.

Primary and secondary outcomes The primary outcomes were rate of rrBSO recommendation and completion. Secondary outcomes were sociodemographic variables associated with rrBSO completion.

Results The cohort included 167 patients with *BRCA1/2* mutations of whom 39% identified as black (n=65), 35% white (n=59) and 19% Hispanic (n=32). Over 95% (n=159) received the recommendation for age-appropriate rrBSO, and 52% (n=87) underwent rrBSO. Women who completed rrBSO were older in univariable analysis (p=0.05), but not in multivariable analysis. Completion of rrBSO was associated with residence in zip codes with lower unemployment and documented recommendation for rrBSO (p<0.05). All subjects who still received care in the health system (n=79) were invited to complete interviews regarding rrBSO decision-making, but only four completed surveys for a response rate of 5.1%. Themes that emerged included menopause, emotional impact and familial support.

Conclusions In this understudied population, genetic counselling and surrogates of financial health were associated with rrBSO uptake, highlighting genetics referrals and addressing social determinants of health as opportunities to improve cancer prevention and reduce health inequities. Our study demonstrates a need for more culturally centred recruiting methods for qualitative research in marginalised communities to ensure adequate representation in the literature regarding rrBSO.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study evaluates providers' adherence to evidence-based guidelines for ovarian cancer prevention and patient adherence to those recommendations among a population of racially, ethnically and socioeconomically diverse *BRCA1* and *BRCA2* mutation carriers who are under-represented in the literature.
⇒ Sociodemographic factors were identified within the constraints of the electronic medical record.
⇒ Patient advocates participated in designing the qualitative portion of this study and recruitment methods.
⇒ The response rate to qualitative surveys was low and did not reflect the diverse study population, which demonstrates the need for better culturally centred recruiting methods for qualitative research in marginalised communities.

INTRODUCTION

Risk-reducing bilateral salpingo-oophorectomy (rrBSO) is recommended for patients with germline *BRCA1* and *BRCA2* (*BRCA1/2*) mutations by the National Comprehensive Cancer Network (NCCN) because it provides an 80% reduction in ovarian cancer risk.[1–3] Despite these recommendations, reported uptake of rrBSO in *BRCA* mutation carriers is only 51–70%.[2 4–6] Premature menopause from rrBSO has an impact on health and quality of life, and clinical trials are underway to test the efficacy of other methods such as risk-reducing salpingectomy with delayed oophorectomy, radical fimbriectomy, intensive surveillance and chemoprevention to avoid morbidity of premature menopause.[7–9]

Decision-making factors for *BRCA1/2* mutation carriers considering rrBSO include age, menopausal status, childbearing history, a personal or family history of breast cancer and having a first-degree relative die of breast or ovarian cancer.[2–4 6 10 11] However, these study populations consisted of 85–94% Caucasian women and 65–95% with some college

education or higher, and one study reported 71% Ashkenazi Jewish women.[6]

Only half of the studies in the published literature on rrBSO decision-making report sociodemographics like race and education level of the study population.[6 10 11] In contrast, the UPTAKE study investigated rrBSO decision-making in a population of 100 Latina patients with *BRCA1/2* mutations. Older age, personal history of breast cancer, higher income and not having a full-time job were significantly associated with increased rrBSO uptake in this population.[12] More research like the UPTAKE study is needed to fill crucial gaps in the literature regarding diverse *BRCA1/2* populations, especially when considering that rates of referral to genetic testing for women at high risk of ovarian cancer are low among women of colour and those on public insurance,[7 13 14] and these populations received lower rates of guideline-adherent care.[15–17]

Our objective was to address this gap in the literature by examining providers' adherence to evidence-based guidelines for recommending rrBSO, patient adherence to those recommendations and the decision-making considerations identified as important to *BRCA1/2* mutation carriers. Uniquely, we performed this study at an urban, public academic centre whose population is racially and socioeconomically diverse.

METHODS

This is a mixed methods study combining retrospective cohort analysis of the electronic medical record (EMR) of patients with an identified hereditary breast and ovarian cancer (HBOC) gene mutation with prospectively collected qualitative interviews. The research team members have no conflicts of interest to disclose. Subjects were identified from a database of patients seen at the University of Illinois Hospital (UIH) Familial Cancer Program from 1 January 2008 through 31 December 2019. To ensure inclusion of patients who receive care at UIH but may have been diagnosed with a gene mutation outside the Familial Cancer Program, International Classification of Diseases Ninth Revision (ICD-9) and ICD-10 codes (online supplemental file 1) were used to identify and retrieve medical records for patients diagnosed with a hereditary genetic syndrome putting them at increased risk of ovarian cancer.

Eligible patients for the retrospective cohort study had an increased risk of ovarian cancer due to pathogenic mutations in *BRCA1* or *BRCA2* and were old enough that they should have undergone rrBSO based on NCCN age-specific recommendations (ie, *BRCA1* mutation carriers under 35 years and *BRCA2* mutation carriers under age 40 were excluded). Patients with *BRCA1/2* mutation variants of undetermined significance were excluded given no strong evidence or recommendation for risk-reducing surgery. Patients who already had a diagnosis of ovarian, Fallopian tube or peritoneal cancer prior to diagnosis of a *BRCA* mutation were also excluded.

The primary endpoints for the retrospective cohort study were documentation of guideline-concordant recommendations for risk-reducing surgery, and guideline adherence in completing rrBSO. EMR was reviewed to collect these data, along with the following data: age, gravidity and parity, self-identified race/ethnicity, self-identified education level, insurance status, zip code, medical history, family cancer history, date of rrBSO (if applicable), ovarian cancer screening participation and documentation of an encounter with a genetic counsellor.

Publicly available census data for subjects' zip codes were used as surrogate markers of exposure to food insecurity, unemployment, poverty and crime. These variables were defined as the rate of food stamp or Supplemental Nutrition Assistance Program (SNAP) benefit utilisation, unemployment, living below 150% of poverty line and violent crime within the zip code. Per the Federal Bureau of Investigation in the USA, 'violent crime' refers to crimes using force or the threat of force and includes aggravated assault, sexual assault, robbery and murder or non-negligent manslaughter.[18]

Univariate differences between rrBSO groups were determined by χ^2 analyses, Fisher's exact test and t-tests, where appropriate. ORs and 95% CIs were calculated using multivariable logistic regression. Two models were performed that controlled for increasing levels of measured covariates. Model 1 is a model examining baseline characteristics adjusted for categorical age, mutation, parity, race/ethnicity, insurance and highest achieved education. Model 2 additionally adjusted for factors predicted to affect decision-making, including socioeconomic status (SES) information, personal and family history of cancers and rrBSO recommendations. Level of statistical significance was set at <0.05. All statistical analyses were performed using SPSS V.27. Raw data are available in an online, open access repository.[19]

The prospective qualitative study was designed to determine the decision-making factors in this cohort. Living patients with a documented HBOC gene mutation who were still receiving care at UIH (as defined by an encounter with any UIH provider in the prior 18 months) were identified from the study population. Invitations to participate in a structured interview were sent in both English and Spanish by mail or EMR messaging, and patients could respond to the research team to indicate their interest or decline further contact. As our data collection largely took place during the COVID-19 pandemic and public health emergency, interviews were conducted over the phone in accordance with social distancing. A member of the research team reviewed the purpose and procedures of the interview with the participant. Given the need for social distancing and the barriers that electronic written consent can pose, verbal consent was acquired and audio recorded. No identifying information was included in these recordings. After providing verbal informed consent, participants completed a survey by telephone that was made up of nine semistructured questions (online supplemental file 2). Thematic content

analysis of interview transcripts was performed by two investigators, who coded and analysed transcripts independently, and agreed by consensus on emerging themes identified.

Patient and public involvement

To inform a culturally appropriate survey design for the qualitative arm of this project, a focus group of patient advocates was held. Participants were recruited by a patient advocate and community organiser known to the research team and included ovarian cancer survivors and/or patients with a *BRCA* mutation. Recruitment strategies, general study themes and specific survey questions were revised and approved by focus group participants in order to minimise the burden of participation for study subjects.

RESULTS

The study sample consisted of 214 patients. Of these, 204 had a pathogenic *BRCA1* or *BRCA2* mutation, and 167 were eligible for analysis (figure 1). Demographics and characteristics of the study sample are presented in table 1. Approximately half of the study sample carried a *BRCA1* mutation (52%, n=86), and half a *BRCA2* mutation (46%, n=77). The remaining 3% (n=5) of the population had a documented *BRCA* mutation without specifying *BRCA1* versus *BRCA2* in the EMR. A majority self-identified as racial and ethnic minorities with 39% identifying as black (n=65) and 19% non-black Hispanic (n=32). About a third of the sample identified as Caucasian (35%, n=59), and 7% self-identified as none of the above. About 5% of patients reported known Ashkenazi Jewish heritage. Regarding insurance, 38% of the population was insured by Medicaid or Medicare (n=64), and 5% was uninsured (n=8).

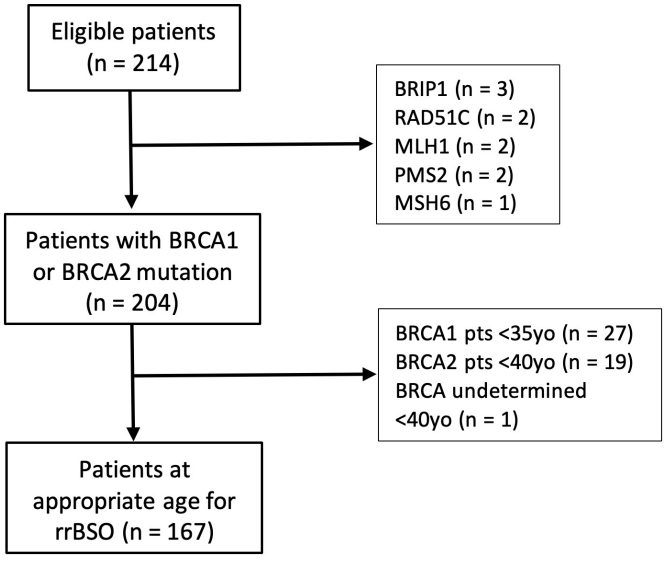

Figure 1 Eligibility screening of study population. After screening 214 patients, 167 were eligible for multivariable regression analysis. rrBSO, risk-reducing bilateral salpingo-oophorectomy.

About 95% (n=159) had a documented recommendation for age-appropriate rrBSO. This recommendation was withheld in clinically appropriate scenarios (ie, previous BSO for other indications, recent metastatic breast cancer diagnosis). About half (52%, n=87) are known to have undergone rrBSO (table 1).

Ashkenazi Jewish heritage was statistically associated with not completing rrBSO (table 1); however, this conclusion is limited by a small cohort of Ashkenazi patients that was insufficient for further analysis.

Table 2 presents both the baseline model 1 and fully adjusted model 2 multivariable logistic regressions. The association with individuals above the age of 50 (a surrogate marker for the age of menopause) having a greater than expected rate of undergoing rrBSO was no longer significant in multivariable analyses. We did not note that other baseline characteristics, most SES risks inherent in the zip code of residence and family/self-history of cancer were predictive of rrBSO. In model 2, however, we noted a significant reduction in the odds of rrBSO when unemployment rates were higher in the zip code of residence (OR=0.83, 95% CI 0.73 to 0.95) (table 2).

A cohort of 79 patients were eligible for the prospective qualitative portion of this study and were invited to participate by MyChart (patient medical record portal) when possible (57%, n=45) or postal service (43%, n=34). Invitations were sent in Spanish to the 9% (n=8) of eligible patients who identified Spanish as their preferred language. More than half (56%, n=44) had undergone rrBSO. Five of the invited participants responded, and four surveys were completed, for a response rate of 5.1%. Per patient self-identification in the EMR, two respondents were white, one was black and one was Asian. All four respondents had undergone rrBSO and were postmenopausal when they had their surgery. Table 3 reports the emergent themes with representative quotes. Themes including menopause, concern for ovarian cancer risk and following medical advice contributed to patients' decision-making.

DISCUSSION, STRENGTHS AND LIMITATIONS

We report strong provider adherence to evidence-based guidelines for recommending age-appropriate rrBSO in an under-represented population of *BRCA1/2* mutation carriers at an urban, public hospital. The uptake of rrBSO in our population was 52%, which is within range of rates reported in the literature. The findings reported here also suggest that social determinants of health such as low unemployment rates in their zip code of residence are associated with patients undergoing risk-reducing surgery. This study adds to the growing body of evidence that social determinants of health must be understood and addressed in ongoing research towards eradicating disparities in cancer prevention.

A major strength of this study is adding to the literature the experience of an under-represented population made up of racial and ethnic minorities and/or vulnerable SES

Table 1 Demographics of study population

	rrBSO n (%)	No rrBSO n (%)	Total n (%)	Value	df	P value
Total population	87 (52)	80 (48)	167			
Age at time of study (years)				7.63	2	0.02
<40	10 (11)	14 (18)	24 (14)			
41–49	28 (32)	38 (48)	66 (83)			
50 and older	49 (56)	28 (35)	77 (46)			
Mutation				1.63	2	0.52
BRCA1	44 (51)	41 (51)	85 (51)			
BRCA2	39 (45)	38 (48)	77 (46)			
BRCA unspecified*	4 (5)	1 (1)	5 (3)			
Parity at time of study				6.535	3	0.088
0	11 (13)	12 (15)	23 (17)			
1–2	38 (44)	27 (34)	65 (39)			
3 or more	26 (30)	18 (23)	44 (26)			
Not documented	12 (14)	23 (29)	35 (21)			
Race/ethnicity				0.81	3	0.85
Caucasian	29 (33)	30 (38)	59 (35)			
Black	34 (39)	31 (39)	65 (39)			
Hispanic	17 (20)	15 (19)	32 (19)			
None of the above	7 (8)	4 (5)	11 (7)			
Ashkenazi Jewish heritage						0.02
Yes	1 (1)	7 (9)	8 (5)			
No	86 (99)	73 (91)	159 (95)			
Preferred language						0.22
English	75 (86)	74 (93)	149 (89)			
Other	12 (14)	6 (8)	18 (11)			
Insurance type				0.72	2	0.698
Private insurance	47 (54)	48 (60)	95 (57)			
Medicaid/Medicare	36 (41)	28 (35)	64 (38)			
Uninsured	4 (5)	4 (5)	8 (5)			
Educational attainment				4.74	3	0.19
Below high school	6 (7)	2 (3)	8 (5)			
High school/GED	12 (14)	5 (6)	17 (10)			
At least some higher education	18 (21)	20 (25)	38 (23)			
Undocumented	51 (59)	53 (66)	104 (62)			
Mean % of zip code using food stamps or SNAP benefits (SD)	19% (±12%)	21% (±13%)	20% (±12%)	0.97	165	0.34
Mean % of zip code unemployed (SD)	9% (±5%)	11% (±6%)	10% (±6%)	1.91	165	0.060
Mean % of zip code living below 150% of poverty line (SD)	27% (±13%)	29% (±14%)	28% (±13%)	1.08	165	0.281
Mean violent crime rate of zip code per 100 000 population (SD)	770 (±801)	881 (±801)	823 (±800)	0.90	165	0.37
PMH of breast cancer	61, 70%	46, 58%	107, 64%	2.88	1	0.09
FH of ovarian or peritoneal cancer	20, 23%	23, 29%	43, 26%	0.72	1	0.40
FH of other *BRCA*-related cancers	72, 83%	69, 86%	141, 84%	0.39	1	0.53

X^2, Fisher's exact test and two-sided t-test were used where appropriate.
*A small subset of patient's charts referenced a BRCA mutation but did not specify BRCA1 versus BRCA2.
FH, family history; GED, General Educational Development test; PMH, past medical history; rrBSO, risk-reducing bilateral salpingo-oophorectomy; SNAP, Supplemental Nutrition Assistance Program.

Table 2 Results of multivariable regression analyses

	n	Model 1 OR (95% CI)	Model 2 OR (95% CI)
Age at data collection (years)			
≤40	24	Reference	Reference
41–49	66	0.94 (0.33 to 2.70)	1.07 (0.34 to 3.36)
50+	77	2.59 (0.92 to 7.31)	2.72 (0.84 to 8.81)
Mutation			
BRCA1	85	Reference	Reference
BRCA2	77	0.89 (0.44 to 1.80)	1.18 (0.52 to 2.65)
BRCA unspecified	5	4.04 (0.37 to 43.93)	18.21 (0.88 to 377.07)
Parity			
0	23	Reference	Reference
1–2	65	1.10 (0.39 to 3.08)	1.48 (0.48 to 4.53)
3+	44	0.89 (0.29 to 2.75)	1.19 (0.35 to 4.08)
Not documented	35	0.45 (0.14 to 1.38)	0.55 (0.16 to 1.85)
Race/ethnicity			
Caucasian	59	Reference	Reference
Black	65	0.76 (0.33 to 1.76)	2.03 (0.59 to 6.98)
Hispanic	32	1.10 (0.42 to 2.87)	1.66 (0.54 to 5.12)
None of the above	11	1.35 (0.31 to 5.82)	1.35 (0.26 to 7.08)
Insurance type			
Private insurance	95	Reference	Reference
Medicaid/Medicare	64	1.28 (0.60 to 2.71)	1.35 (0.58 to 3.14)
Uninsured	8	0.62 (0.11 to 3.53)	0.30 (0.05 to 1.99)
Educational attainment			
High school/GED	17	Reference	Reference
Below high school	8	2.07 (0.24 to 17.71)	2.42 (0.25 to 23.81)
Some higher education	38	0.48 (0.12 to 1.96)	0.67 (0.13 to 3.39)
Not documented	104	0.40 (0.12 to 1.40)	0.36 (0.09 to 1.44)
Zip code SES data			
% on food stamps/SNAP	–	–	1.05 (0.93 to 1.18)
% unemployed	–	–	**0.83 (0.73 to 0.95)**
% below 150% of poverty line	–	–	0.98 (0.89 to 1.07)
Violent crime rate	–	–	1.00 (1.00 to 1.00)
History of cancer			
PMH of breast cancer	107	–	1.81 (0.77 to 4.26)
FH of ovarian or peritoneal cancer	43	–	0.78 (0.32 to 1.94)
FH of other *BRCA*-related cancer	141	–	0.65 (0.22 to 1.93)
BSO recommendation	**159**	–	13.58 (0.96 to 192.81)

Model 1 adjusts for baseline characteristics while model 2 adjusts for other variables and community factors predicted to affect decision-making. Significant values are in bold.
BSO, bilateral salpingo-oophorectomy; FH, family history; GED, General Educational Development test; PMH, past medical history; SES, socioeconomic status; SNAP, Supplemental Nutrition Assistance Program.

groups. Distinct from other studies of rrBSO adherence decision-making, the majority of our study population identifies as black or Hispanic, and a large proportion of subjects use public insurance. Per Federal Census data, 35% of this population lives in zip codes where at least 25% of the population uses food stamps or SNAP benefits. Per the US Bureau of Labor Statistics, the national unemployment rate in December 2019 (end of study period) was 4%.[20] However, in our study population, 76% of subjects live in zip codes with greater than 5% unemployment. Furthermore, 65% of the study population live in areas where greater than 20% of the population are living below 150% of the poverty line, and 36% live in zip codes with a violent crime rate of at least 1000 per

Table 3 Notable quotations and emerging themes from qualitative interviews

Theme	Example quotations
Menopause	'I was in my late 50s when I had it, so I wasn't as worried about the hormone impact 'cause I was already going through menopause.' 'If I'm in my 20s—maybe my decision, maybe changed? Yeah, but you know, chemotherapy already caused menopause, and I don't have a plan to have a child or anything.'
Ovarian cancer risk	'They told me (and I already knew) that ovarian cancer is very difficult to find in early stage. Once they find the cancer [it is] already kind of late stage or something. So I totally agree to reduce my risk.' 'I wanted to reduce those risks as far as I can reduce them, because I, you know, I eventually want to see grandchildren, right?' 'So I said OK, since I've just seen my sister go through ovarian cancer, I'm like no—let's just get rid of it. We don't need it.'
Ease of decision	'[You] have to do what you feel is best for you and you think that's the right decision for you. You make that decision. If you don't, wait until you feel its right for you.' 'That was easy, that was. You know done real quick and easy, you know.' 'It was nothing to discuss… they told me what it was and it was just and I was already in [breast cancer] stage—I think it was 3 or 4, so there was nothing to discuss.'
Seeking support from loved ones	'I talked to my sister… I talked to, you know some friends, just friends in general, but nobody that had actually gone through it.' 'My husband has always been a little um—he's been supportive but not overly involved.' 'This is my practical patient thing is, you know try to take someone with you. I always felt like write your notes out, write your questions out before you go in. Have someone go with you and listen and write the answers down because a lot of times when you're talking to your health care professional, you can't always remember after you walk out.'
Following medical advice	'Essentially this decision I just have to go through…I have to just trust the medical staff.' 'I was very confident in my surgical team. I was very confident in the doctor that followed me after the surgery.' '[My doctor] felt like it was imperative, but based on the research. But I felt like, you know, I was in good hands with her…so I felt like it was a good thing for me to do.'
Previous medical experiences	'I just don't want to go through again another chemotherapy or other complicated situation, so because I already have a complicated breast cancer.'
Increasing personal understanding	'Have someone go with you and listen and write the answers down because a lot of times when you're talking to your health care professional, you can't always remember after you walk out.' '[The medical staff] gave me information and you know, like. [I got] information from the Internet and stuff like that.'
Emotional impact	'[I wish I had] more information on the impact of it and the emotional impact it had. It did hit me hard when I had the oophorectomy and… I deal with depression and it just seemed to make it that much more worse.' '[I felt] mainly nervous. Unsure of the unknown.' 'I was fully unprepared for the diagnosis of the *BRCA*.' 'I feel better knowing now that, you know, I've reduced my risks.'

100 000 population. Figure 2 compares the average rates of these SES metrics among the study population versus national averages,[18 20–22] demonstrating that our study population faces greater social and economic stressors known to adversely affect health. Nonetheless, evidence-based age-specific recommendations were made consistently throughout this population, and uptake of rrBSO is similar to studies of more affluent populations, suggesting that access to genetic counselling is a key component to closing health equity gaps in cancer prevention.

We sought to explore the lived experiences of this patient population and to understand decision-making regarding rrBSO at the individual level with the qualitative portion of this study. Our findings are concordant with the current body of literature with themes such as age, menopausal status and family history factoring into decision-making.[2–4 6] However, our recruitment efforts were unsuccessful at engaging with the communities represented in our population, which limits the conclusions of these data. Only one black woman completed the survey, and no Latina patients responded, so our vulnerable communities remain under-represented regarding decision-making for rrBSO. Based on our experience, we recommend partnering with trusted community organisations for outreach, engagement and recruitment into culturally competent and patient-centred qualitative research.

Limitations of this study also include those inherent to retrospective data collection including the inability to determine causality as well as a low sample size and a clearly low response rate to our survey. The low response rate, however, is data in and of itself perhaps reflecting the lack of engagement or uptake of resources in this underserved sample. Furthermore, sociodemographic factors were identified within the constraints of the EMR. Namely, multiple-choice options for race/ethnicity may not accurately reflect a person's racial identity, and educational attainment was rarely reported in the EMR. Census data for zip codes may not accurately describe an individual's SES. Addresses may be transient, and zip codes may not align accurately with community areas or residence. Improved documentation of social determinants of health in the EMR would provide more reliable information for purposes of research, and, importantly, could highlight opportunities for intervention for healthcare providers. These efforts are being made with the implementation of

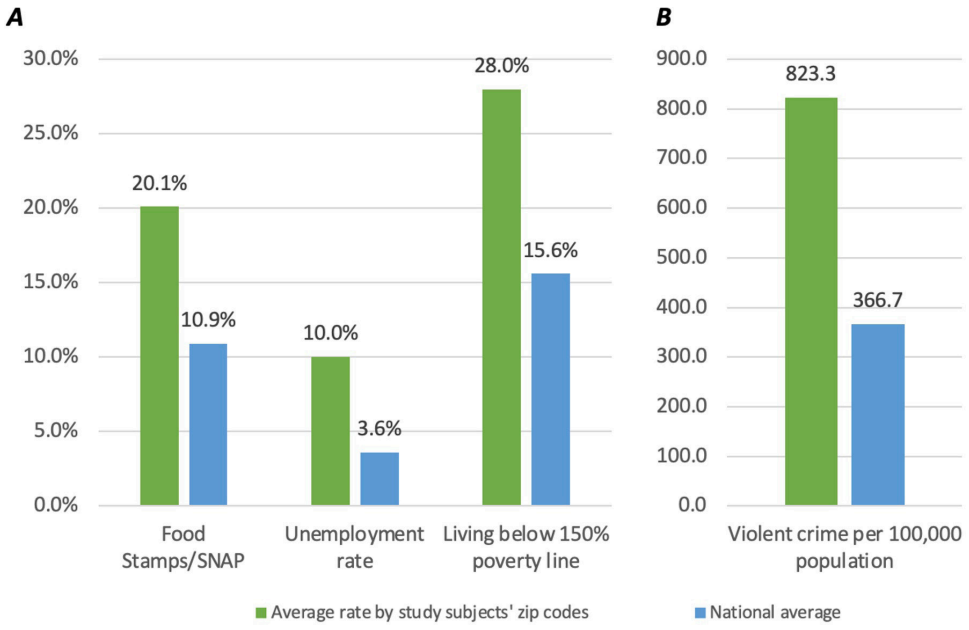

Figure 2 Socioeconomic status (SES) metrics: study population versus national average. (A) Average rates of food stamp/Supplemental Nutrition Assistance Program (SNAP) benefit usage, unemployment and living below 150% of poverty line among study subjects' zip codes versus national averages.[19–21] (B) Average rate of violent crime per 100 000 of population in study subjects' zip codes versus national average.[18]

a new EMR in the UI Health system. Notably, Medicare is improving reimbursement in a paradigm shift from fee-for-service to value-based care models, which will improve feasibility of this line of research for ours and other institutions.[23]

CONCLUSION

By focusing on patients who are under-represented in research and vulnerable to high rates of non-guideline-adherent cancer care, this study fills gaps in our knowledge regarding cancer prevention in patients with HBOC genetic mutations. We demonstrate that genetic counselling is significantly associated with recommendation for rrBSO in this population, which further highlights the need to address inequities in referring to genetic counselling for those at a high risk for breast and ovarian cancers. We also reveal the association of sociodemographic factors such as neighbourhood unemployment rates with the uptake of cancer prevention strategies despite appropriate counselling, thereby demonstrating the importance of identifying and addressing social determinants of health to improve cancer prevention and care delivery. Our study also demonstrates a need for more culturally centred recruiting methods for qualitative research in marginalised communities to ensure adequate representation in the literature regarding rrBSO.

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Contributors AJL, NLS and SMD conceived the research and devised the project. AJL, LB, TM and KH contributed to quantitative data collection. AJL conducted the quantitative data analysis. AJL and SMD drafted the qualitative portion of the study with the input of KR. SS recruited the participants and conducted the semistructured interviews. SS, TM and AJL analysed the qualitative data. QAC guided the statistical considerations. AJL, QAC and SMD drafted the manuscript. All authors were involved in manuscript review. SMD is the guarantor of this study.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by the University of Illinois Chicago Institutional Review Board, Office for the Protection of Research Subjects (Research Protocol No 2020-0606). Participants gave informed consent to participate in the study before taking part.

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