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Recruiting families at risk for hereditary breast and ovarian cancer from a statewide cancer registry: a methodological study

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Abstract

Purpose Cancer genetic services (counseling/testing) are recommended for women diagnosed with breast cancer younger than 45 years old (young breast cancer survivors—YBCS) and at-risk relatives. We present recruitment of YBCS, identification and recruitment of at-risk relatives, and YBCS willingness to contact their cancer-free, female relatives.

Methods A random sample of 3,000 YBCS, stratified by race (Black vs. White/Other), was identified through a population-based cancer registry and recruited in a randomized trial designed to increase use of cancer genetic services.

Baseline demographic, clinical, and family characteristics, and variables associated with the Theory of Planned Behavior (TPB) were assessed as predictors of YBCS' willingness to contact at-risk relatives.

Results The 883 YBCS (33.2% response rate; 40% Black) who returned a survey had 1,875 at-risk relatives and were willing to contact 1,360 (72.5%). From 853 invited at-risk relatives (up to two relatives per YBCS), 442 responded (51.6% response rate). YBCS with larger families, with a previous diagnosis of depression, and motivated to comply with recommendations from family members were likely to contact a greater number of relatives. Black YBCS were more likely to contact younger relatives and those living further than 50 miles compared to White/Other YBCS.

Conclusion It is feasible to recruit diverse families at risk for hereditary cancer from a population-based cancer registry. This recruitment approach can be used as a paradigm for harmonizing processes and increasing internal and external validity of large-scale public health genomic initiatives in the era of precision medicine.

Keywords Young breast cancer survivors · At-risk relatives · Cancer registry · Recruitment · Public health genomic trials

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Introduction

Public health action leveraging family history is needed to reach a large number of individuals at risk for hereditary cancer [1]. An important public health intervention is the promotion of cancer genetic services (counseling and testing) in families at risk for hereditary breast and ovarian cancer syndrome [2, 3]. Germline genetic testing identifies mutation carriers and enables personalized

cancer risk management. Cascade genetic testing among at-risk relatives can also confirm the non-inheritance of a well-characterized mutation and prevent unnecessary early onset screening and healthcare costs among "true negative" relatives [4]. Clinical guidelines recommend genetic assessment for all first- and second-degree relatives of women diagnosed with breast cancer younger than 50 years [5].

Reaching a large number of at-risk individuals, let alone at-risk families, has been a long-standing challenge for researchers. Using cancer registries has been one way to address this challenge. Studies in the US [6–9] and internationally [10–13] have used population-based cancer registries, hospital-based registries [14, 15], or both [16] often with random sampling for patients who met eligibility criteria [7, 13–15, 17]. Response rates from hospital-based registries varied, depending on clinicians' time and motivation to recruit patients [7, 9, 16]. Recruitment from population-based registries yielded more participants, but without targeted sampling [13, 14, 18], minority, rural, and hard-to-reach patients were underrepresented due to low response rates.

Breast [6, 7, 11–13, 15, 19] and colorectal cancer patients [8, 16, 17] have often been recruited from cancer registries. Identifying cancer survivors with the early onset disease is critical for identifying at-risk relatives and promoting genetic testing and cancer screening due to possible hereditability of a cancer syndrome [7, 8, 11, 15, 16, 18]. Survivors have often been asked to allow the research team to contact at-risk relatives directly, which ensures that the latter receive the invitation [6, 8, 11, 13, 16]. One study asked cancer survivors whether they would like to recruit at-risk relatives themselves, or they would rather allow the research team to do this on their behalf, but did not report response rates for either recruitment method [17].

It is unclear to what extent women affected by breast cancer at a young age are willing to contact at-risk relatives for promoting screening and cancer genetic services, and factors associated with their willingness to do so. Moreover, little is known about using cancer registries to recruit at-risk families affected by the early onset breast cancer. Young breast cancer survivors (YBCS) is a growing clinical population for which there is paucity of information; recruiting at-risk relatives who could benefit from advances in genomic medicine is also an emerging priority research area. To address this gap, in our knowledge, this paper presents methodological details about using a population-based cancer registry to identify and recruit young breast cancer survivors (YBCS) and at-risk relatives. The study also explored predictors of YBCS' willingness to contact at-risk relatives.

Methods

Design, setting, sample, and procedures

Identifying and recruiting YBCS and at-risk relatives were examined with baseline data from a prospective randomized trial designed to increase cancer surveillance and use of genetic services in families with the early breast cancer onset [20]. All appropriate Institutional Review and Scientific Advisory Boards approved the study protocol.

The Michigan Cancer Surveillance Program is a population-based cancer registry and was searched for YBCS cases from 1998 onward. Eligible YBCS were (1) female, 25–64 years old; (2) diagnosed with unilateral or bilateral invasive breast cancer or *ductal carcinoma in situ* (DCIS) between 20 and 45 years old; (3) lived in Michigan when diagnosed; and (4) were not pregnant, incarcerated, or institutionalized during recruitment. A random sample of 3,000 YBCS was identified out of 7,866 cases included in the registry. Most people (93%) in Michigan are self-identified as Black or White. To ensure adequate representation and have enough Black participants in the final sample of the randomized trial, YBCS were stratified according to registry-recorded race (1,500 Black vs. 1,500 White/Other) [21]. The 7% of YBCS of other ethnic/racial background were grouped with White YBCS, because they could not be included as a separate stratum. The cancer registry cross-referenced mortality data for deceased YBCS [20].

The Michigan Cancer Surveillance Program mailed the reporting facility and the physician of record requesting, for any reason, the YBCS should not be contacted for the study. A non-response within 30 days was taken as an agreement for contacting the YBCS. This contact method is consistent with patient preferences [22] and provides the opportunity for physician input, while eliminating barriers of requesting permission for patient contact [23]. The cancer registry mailed an invitation letter, an informed consent form, and the self-administered baseline survey to YBCS. Contact information for Institutional Review Boards, the Director of the cancer registry, the Principal Investigator, and the Cancer-Genomics Program at the Michigan Department of Health and Human Services were also provided.

A staff person from the cancer registry (50% FTE for six months) carried out contacting duties, starting with the letter to the facility and physician of record and recruitment letters. YBCS were identified between February and April 2012; letters to facilities/ physicians were sent in June 2012. YBCS were sent up to three recruitment letters between August and November 2012. A search through Accurint, a LexisNexis database with coverage across the US, obtained new addresses for YBCS not reached with the initial letters. A new series of letters was sent if an alternate address was located. Less than 20 YBCS contacted the registry

with questions about being included in the database. YBCS accepting participation returned a signed consent and the baseline survey to the cancer registry and received a $10 gift card as a token of appreciation.

Identifiable information for YBCS was not released from the cancer registry to the research team until the YBCS accepted participation. Two board-certified genetic counselors from the Cancer-Genomics Program at the Michigan Department of Health and Human Services reviewed surveys to ascertain YBCS eligibility. If the YBCS reported a known mutation, such as *BRCA1, BRCA2*, or a known hereditary cancer syndrome, such as *Lynch, PTEN Hamartoma Tumor, Li-Fraumeni, or Peutz-Jeghers syndromes*, the genetic counselors made three attempts to contact her and verify the response. YBCS with a confirmed hereditary cancer syndrome were excluded from the randomized trial, because the intervention was not applicable to them. Their relatives were not recruited in the study; instead, YBCS were mailed printed material from the National Cancer Institute, the Centers for Disease Control and Prevention, and from FORCE (Facing Our Risk of Cancer Empowered) to distribute to them.

The genetic counselors used YBCS' baseline surveys to identify relatives who were eligible to participate in the study. Identification of eligible relatives followed a protocol that involved a pedigree-based algorithm. YBCS were asked (1) to list anonymously all their first- and second-degree female relatives, e.g., sister, maternal aunt, etc.; (2) who were unaffected by cancer; (3) the relative's age; (4) whether she lived in Michigan; (5) whether she lived within 50 miles from the YBCS; and (6) whether the YBCS was willing to contact her. The study recruited only relatives that the YBCS was willing to contact. Relatives eligible to participate had to be female, between 25 and 64 years old, unaffected by any type of cancer, first-degree relative or second-degree relative of the YBCS, US resident, able to read English and provide informed consent, and not currently pregnant, incarcerated or institutionalized. Recruitment priority was given to first- vs. second-degree relatives, and to younger vs. older women. Genetic counselors could contact YBCS for additional information regarding eligibility of relatives.

Each participating YBCS was mailed a letter suggesting up to two of her female relative(s) to invite in the study, along with consent forms, surveys, and postage-paid envelopes to pass on to them. A Project Navigator was available by phone to discuss concerns about this procedure. The research team did not have direct contact with relatives until they returned a signed consent accepting participation. Approximately 25% of at-risk relatives did not respond within six to eight weeks to the initial invitation to the study. In these cases, the Project Navigator contacted the YBCS to select an alternate relative. Relatives' baseline surveys were returned to the Cancer-Genomics Program and were reviewed by two genetic counselors to ascertain eligibility. Identification, recruitment, and collection of data from relatives occurred between November 2012 and May 2013.

Measures

YBCS' and relatives' surveys included identical scales, except for scales assessing YBCS' responses to breast cancer (e.g., fear of cancer recurrence, self-efficacy dealing with cancer diagnosis, etc). These scales did not apply to relatives who were unaffected by cancer. The behavior of interest in this paper is the number of relatives that YBCS was willing to contact. Predictors of intention to perform a behavior were chosen according to the Theory of Planned Behavior (TPB), i.e., knowledge and attitudes, subjective norms, and perceived control [24]. Family support facilitates decisions for genetic testing [25] and was added to the model. Measures were reliable (Cronbach's alpha > 0.71) and publicly available.

Predictors of willingness to invite at-risk relatives included YBCS's characteristics, relatives' characteristics as reported in the YBCS survey, and predictors related to the adapted TPB. Specifically, these predictors were (1) YBCS' demographics (age; race; education; income; insurance; marital status; lives alone; has a routine source of care; cannot access care due to high out-of-pocket costs); (2) YBCS' clinical characteristics (years since diagnosis; invasive breast cancer vs. DCIS; unilateral or bilateral breast surgery; family history of cancer; having genetic counseling and/or testing; number of relatives with breast cancer; and the previous diagnoses of depression and anxiety); (3) Relatives' characteristics assessed in YBCS' surveys (first- or second-degree relatives; age; lives in Michigan; lives within 50 miles from YBCS). Predictors from the adapted TPB were (4) knowledge and attitudes (perceived breast cancer risk; fear of cancer recurrence; knowledge of breast cancer risk factors; and breast cancer genetics); (5) subjective norms (family members expect engagement in preventive behaviors; healthcare providers expect engagement in preventive behaviors; motivation to comply with family members' suggestions; and motivation to comply with healthcare providers' suggestions); (6) perceived control (breast cancer self-efficacy); and (7) family support (communication; support in illness; and hardiness); and number of female relatives as a proxy of YBCS' family size. Most predictors from the adapted TPB were assessed on 7-point Likert scales ranging from one "Strongly Disagree" to seven "Strongly Agree." Perceived breast cancer risk was assessed with one item asking participants to rate their chances of getting breast cancer on a 10-point Likert scale with verbal anchors ("Definitely will not" to

"Definitely will"). Items assessing knowledge of breast cancer risk factors and knowledge of breast cancer genetics could be answered as "True", "False", or "Do not Know."

Data analyses

Data analyses were performed in the R software (Version 3.2.2, R Core Team, 2015).

Means, standard deviations, and frequencies were used to describe the sample. A Poisson regression was used to model predictors of number of relatives YBCS were willing to contact based on the distribution of the dependent variable. Power analysis determined that a sample of $n = 352$ would achieve 80% power for the Poisson regression with two tailed alpha set at $p < .05$. Missing values were less than 18% of the survey data, and involved primarily values in multi-item scales assessing concepts of the adapted TPB. Missing values were addressed with multiple imputations using the R software *mi* package [26, 27]. For each copy of the imputed data set ($m = 10$), we conducted a variable selection based on the LASSO method [28] using the R software glmnet package [27]. A ten-fold cross-validation determined the value of the tuning parameter λ in LASSO. The final Poisson regression model was identified using the λ value with the smallest cross-validation error. The final model included predictors with non-zero coefficients in the fitted LASSO model. The means and standard errors of estimates for each imputed data set were then pooled to create a combined estimate based on Rubin's rules [29].

Results

Overall, 883 YBCS accepted participation (33.2%); 353 were identified from the cancer registry as Black (27.5%) and 530 as White/Other (38.6%) (Fig. 1). Most YBCS ($n = 778$, 88.1%) resided in Michigan and 11.9% in 23 other states (data available upon request). The most common reason for no participation was lack of current address for YBCS ($n = 252$), most commonly for Black YBCS (69% of invalid addresses). Accurint enabled locating 91.6% of the initial YBCS cohort. Other known reasons for non-participation were: YBCS was deceased ($n = 66$); the reporting physician advised against contact ($n = 22$); YBCS was incarcerated ($n = 3$). From 883 participating YBCS, 24 were ineligible, because they were not diagnosed younger than 45 years old ($n = 10$), were pregnant ($n = 9$), and returned their survey too late ($n = 5$). There was "no response" from 832 Black (55%) and 663 White/Other YBCS (44%).

YBCS race was recorded based on registry data, since this was a criterion for sample stratification before random selection, while race of relatives was based on self-report. Thus, the race of family members is not the same in

20 family units. YBCS were on average 11 ± 4 year post-diagnosis. They were approximately 10 years older than relatives, less educated, and had fewer barriers to access healthcare services compared to relatives. About one in four YBCS reported multiple breast cancers and/or other cancers, such as ovarian. Most had a family history of breast cancer (Tables 1, 2).
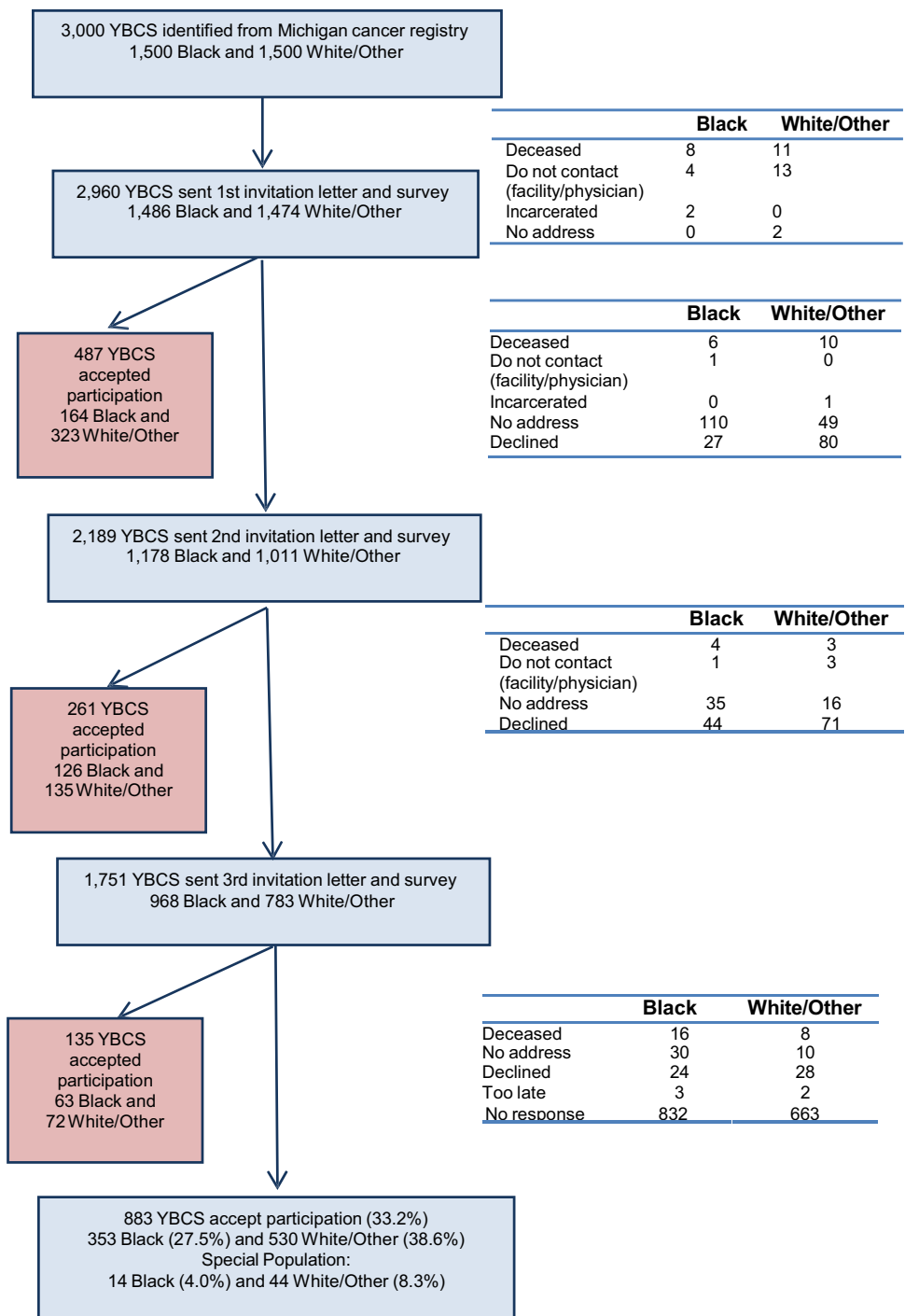
Among 859 eligible YBCS, approximately one in three reported having genetic counseling and/or genetic testing. The majority of these YBCS reported having a negative test result, meaning that a mutation connected to cancer was not identified. Only 58 YBCS reported a *BRCA1* ($n = 19$) or *BRCA2* ($n = 14$), or other mutation ($n = 7$); having a family member with a known mutation ($n = 6$); having a known hereditary cancer syndrome (e.g., *Li Fraumeni*) ($n = 12$). These 58 YBCS were excluded from the randomized trial and their data are not included in the Poisson regression, because their willingness to contact at-risk relatives may be different from other YBCS. There were 801 eligible YBCS whose data are included in the Poisson regression.

Responses from YBCS' baseline surveys helped to identify 1,875 at-risk relatives; YBCS were willing to contact 1,360 relatives (72.5%). We examined that characteristics of relatives YBCS were not willing to contact. There was no difference between first- vs. second-degree relatives and whether the relative resided in Michigan. Black YBCS were significantly more likely to not be willing to invite older relatives. The mean age for no-contact relatives from Black YBCS was 47.6 ± 11.7 vs. 44.0 ± 13 from White/Other ($p = .001$). Black YBCS were also significantly more likely to not be willing to contact relatives that lived within 50 miles ($n = 124$) vs. White/Other ($n = 99$) ($p = .027$).

To have comparable family units in terms of participating members, the study invited up to two relatives per YBCS (total $n = 853$ at-risk relatives) (Fig. 2). Greater emphasis was placed on recruiting first-degree relatives (440 sisters; 231 daughters; 25 mothers) compared to second-degree relatives (89 nieces; 36 half-sisters; 32 aunts). Overall, 442 relatives accepted participation (51.5%); some were ineligible due to pregnancy ($n = 5$) or survey returned too late ($n = 6$). A total of 431 relatives enrolled 231 sisters (53.6%); 123 daughters (28.5%); 9 mothers (2.1%); 41 nieces (9.5%); 14 half-sisters (3.2%); and 13 aunts (3.0%). Most relatives ($n = 313$, 72.6%) resided in Michigan; 27.4% resided in 27 other states (data available upon request).

Out of the 19 predictors selected by LASSO, five predictors were significantly associated with the number of relatives YBCS who were willing to contact in the Poisson regression (Table 3). The exponentiated coefficients indicate the multiplicative difference between willingness and unwillingness to contact relatives. YBCS with larger families were 26% more likely to contact at-risk relatives.

Fig. 1 Consort diagram—YBCS enrollment by race

Figure content (flow diagram boxes):

- 3,000 YBCS identified from Michigan cancer registry
  1,500 Black and 1,500 White/Other

- 2,960 YBCS sent 1st invitation letter and survey
  1,486 Black and 1,474 White/Other

- 487 YBCS accepted participation
  164 Black and 323 White/Other

- 2,189 YBCS sent 2nd invitation letter and survey
  1,178 Black and 1,011 White/Other

- 261 YBCS accepted participation
  126 Black and 135 White/Other

- 1,751 YBCS sent 3rd invitation letter and survey
  968 Black and 783 White/Other

- 135 YBCS accepted participation
  63 Black and 72 White/Other

- 883 YBCS accept participation (33.2%)
  353 Black (27.5%) and 530 White/Other (38.6%)
  Special Population:
  14 Black (4.0%) and 44 White/Other (8.3%)

	Black	White/Other
Deceased	8	11
Do not contact (facility/physician)	4	13
Incarcerated	2	0
No address	0	2

	Black	White/Other
Deceased	6	10
Do not contact (facility/physician)	1	0
Incarcerated	0	1
No address	110	49
Declined	27	80

	Black	White/Other
Deceased	4	3
Do not contact (facility/physician)	1	3
No address	35	16
Declined	44	71

	Black	White/Other
Deceased	16	8
No address	30	10
Declined	24	28
Too late	3	2
No response	832	663

YBCS reporting greater motivation to comply with suggestions from family members were 6% more likely to contact relatives. YBCS with a previous diagnosis of depression, those with a greater number of relatives diagnosed with breast cancer, and those reporting less motivation to comply with healthcare providers were approximately 16, 8, and 8% less likely to contact relatives.

Discussion

We present the feasibility of using a state cancer registry to identify and recruit at-risk families in a trial designed to increase surveillance and use of cancer genetic services. The study assessed methods to integrate unaffected relatives with a possible predisposition to hereditary cancer to an efficacy trial and circumvent typical barriers associated

Table 1 Demographic characteristics

859 family units	YBCS (n = 859)		Relative (n = 431)	
549 (64%) w/1 (YBCS)				
189 (22%) w/2 (YBCS + 1Relative)				
121 (14%) w/3 (YBCS + 2Relatives)				
Age (years)	51.0 ± 5.9 (30–63)		43.4 ± 11.9 (25–64)	
Time since Dx (years)	11.2 ± 4.0		n/a	
Black[a]	YBCS (n = 859)		Relative (n = 431)	
	39.6% (registry)		20.5% (self-report)	
	Black	White/other	Black	White/other
Education ≤ high school	30.4%	18.9%*	28.0%	14.3%***
Household income ≤$60,000	65.4%	34.3%*	75.4%	47.2%***
Has medical insurance	90.6%	95.4%*	75.9%	89.8%**
Has routine source of care	90.4%	94.8%*	95.1%	91.2%
Cannot access care 12 m—cost	25.1%	12.4%**	28.2%	16.9%*
Married or partnered	36.2%	76.2%**	33.3%	66.5%**
Lives alone	24.9%	12.4%**	18.4%	12.8%

*p < .05 **p < .001

[a] Demographic information is presented separately for Black and White/Other YBCS and Relatives. The sample was stratified by race and examining racial differences was an important element of the study design. Statistical comparisons above are based on Chi-square tests and represent significant racial differences between Black vs. White/Other YBCS and Black vs. White/Other Relatives

Table 2 Clinical characteristics—YBCS

	Black YBCS (n = 340) (%)	White/other YBCS (n = 519) (%)	Total YBCS (n = 859) (%)
Invasive breast cancer	59.8	53.5	53.7
DCIS**	39.4	58.4	50.9
Ovarian cancer	0.9	1.0	0.9
Other cancer (thyroid, melanoma, etc.)	7.6	10.0	9.1
Number of breast cancer diagnoses			
One	86.2	72.6	78.2
Two	12.4	23.7	19.1
Three +	1.8	3.7	2.9
Double mastectomy**	11.5	23.7	18.9
Family history			
Any cancer	79.9	85.3	83.2
Breast cancer*	45.3	53.2	50.1
Ovarian cancer	16.8	12.5	14.2
Male breast cancer	2.1	1.9	2.0
Had genetic counseling**	27.0	36.9	32.9
Had genetic testing**	20.0	33.9	28.9
Anxiety (prior diagnosis)	27.0	31.1	29.5
Depression (prior diagnosis)	30.4	30.1	30.2

Statistical comparisons above are based on Chi-square tests represent significant racial differences between Black vs. White/Other YBCS

*$p < .05$, ** $p < .001$

with collection of family history and participant recruitment. Although family history is typically assessed during medical visits in clinics or hospitals, lack of time, and shortage of personnel in these settings prevent collection of detailed family information and limit follow-up. Clinical sites are seldom large enough to target and reach at-risk populations. Cancer registries are an efficient alternate to implement family studies due to their greater outreach capacity. They contain data of reported malignancies within a particular population and can help establish family based registries.

Using the database of the Michigan Cancer Surveillance Program enabled targeting a large number of YBCS, a growing clinical population for which there is paucity of information. Response rate among YBCS was approximately 33%, similar to other studies that recruit participants via mailed invitation letters [12–15]. YBCS stratification enabled recruitment of a large number of Black YBCS. Response rate among Black YBCS was lower, often because the cancer registry did not have a current address and possibly because the sample had been diagnosed on average 11 years prior to attempted contact. Updating contact information on a regular basis should be considered. YBCS reported multiple signs in their personal history which could be indicative of hereditary cancer, e.g., multiple primary breast cancers, ovarian cancer, and male breast cancers. Using age of onset (≤45 years old) as the primary selection criterion identified survivors who should be evaluated genetically according to current guidelines [5]. This approach could be used for population-based recruitment for biobanks and family studies evaluating the penetrance of newly identified mutations [30].

The study involved YBCS to recruit relatives, with a response rate among relatives 51.5%, which supports the feasibility of this approach. Unique to this study was examining YBCS' overall willingness to make contact effort. The only information for non-participating relatives was available in YBCS' baseline survey and included their age, relationship with the YBCS, whether they live in Michigan, further than 50 miles from the YBCS, and whether the YBCS was willing to contact them. From data available in YBCS' surveys, we identified racial differences in YBCS' willingness to invite relatives, i.e., Black YBCS were more willing to invite younger vs. older relatives and those living further than 50 miles. YBCS with larger families were more willing to contact a greater number of relatives. There was a positive correlation between number of contacts an YBCS was willing to make and her family size, which was an expected finding. We considered using the proportion of relatives that YBCS were willing to contact (e.g., one relative out of five) as the dependent variable of the Poisson regression. However, this does not capture the "effort" needed by YBCS to contact each of her relatives. An
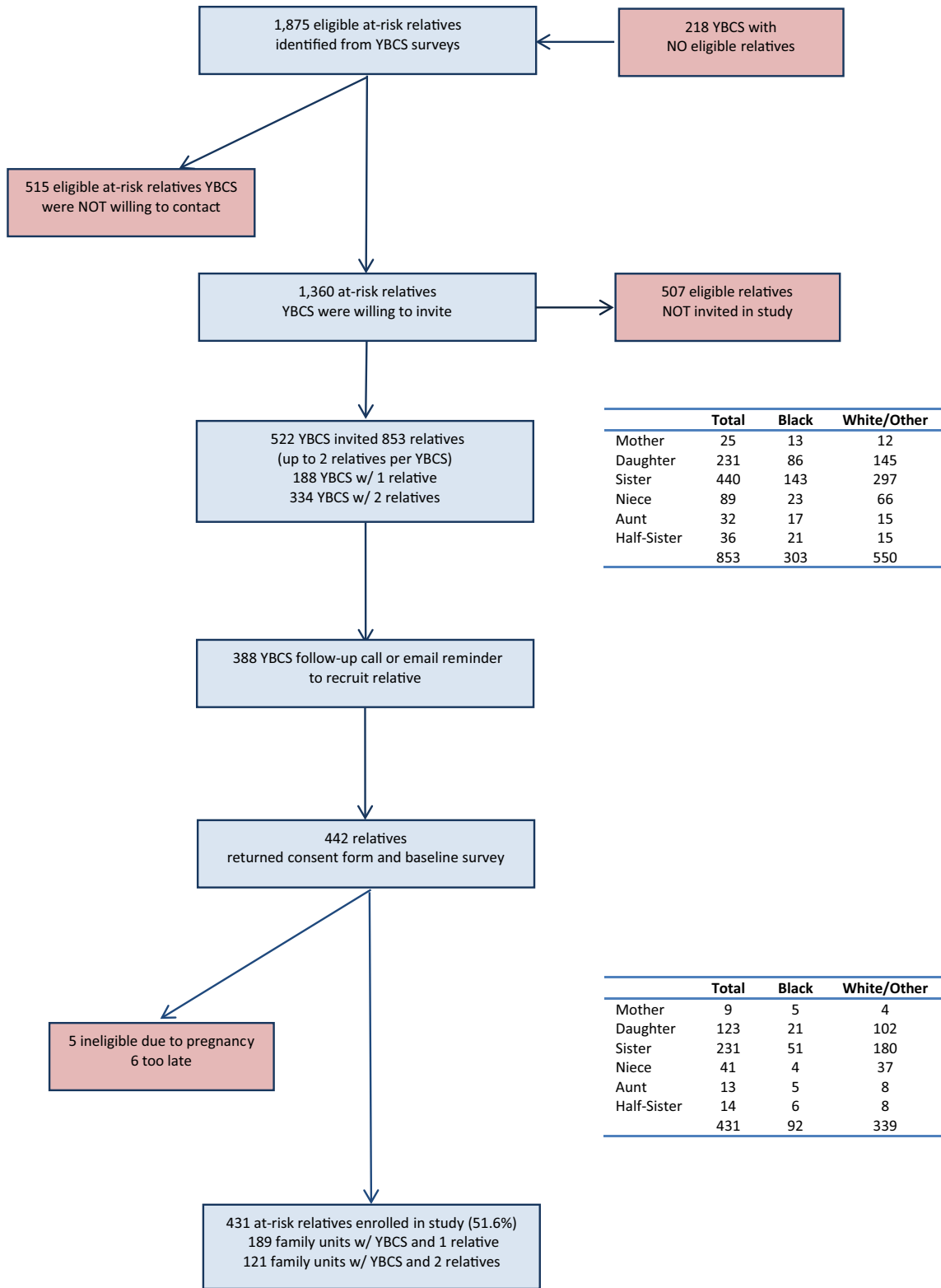
Fig. 2 Consort diagram—relative enrollment by race

Table 3 Fitted poisson regression model

Explanatory variable	Estimate	SD	*p* value	Exp (coef)
(Intercept)	−0.811	0.391	0.038	0.444
Black (vs. White/other)	−0.088	0.079	0.262	0.916
Education	0.031	0.034	0.366	0.970
Income	0.032	0.021	0.133	1.032
Insurance	0.057	0.143	0.692	1.058
Marital status	0.112	0.089	0.207	0.894
Lives alone	−0.155	0.103	0.132	0.857
Has routine source of care	0.069	0.147	0.641	0.934
Out-of-pocket cost barrier to care	−0.035	0.030	0.254	1.035
Years since first breast cancer diagnosis	0.015	0.008	0.061	1.015
Previous diagnosis of depression*	−0.154	0.072	0.033	1.166
Family history of cancer	0.129	0.097	0.185	1.137
Number of relatives with breast cancer*	−0.081	0.031	0.008	0.922
Perceived risk of another breast cancer	0.010	0.015	0.495	1.010
Knowledge of breast cancer risk factors	0.016	0.012	0.171	1.016
Motivation to comply recommendations Healthcare providers*	−0.078	0.033	0.018	0.925
Motivation to comply recommendations Family members*	0.058	0.0288	0.044	1.060
Family support in illness	0.008	0.037	0.819	1.009
Family coherence	0.053	0.050	0.288	1.055
Family size (number of relatives)*	0.231	0.014	<0.001	1.260

The outcome variable is the number of female at-risk relatives YBCS was willing to contact

*p < .05

YBCS who were willing to invite one out of two relatives shows 50% "effort." The same is true for an YBCS willing to invite five out of ten relatives, although she is willing to do more contact "effort."

YBCS with more relatives diagnosed with breast cancer were willing to contact fewer of them, most likely because there were not many cancer-free relatives in their family. YBCS with a previous diagnosis of depression and those reporting less motivation to comply with healthcare providers were also less willing to contact relatives. Some YBCS likely did not invite relatives for logistic reasons (e.g., beginning of school year for children), while lack of open communication may also play a role in relatives' non-response to this invitation. In addition, response rates were lower among second-degree and Black relatives. Possibly, non-responding relatives perceived YBCS' breast cancer diagnosis not a threat to their own health. These findings highlight the need for healthcare and public health professionals to take an active role in encouraging contact within members of at-risk families and for identifying YBCS with a diagnosis of depression, who may benefit from supportive interventions to reach out to family members. Targeted and culturally sensitive interventions designed to increase awareness of breast cancer genetics are needed for at-risk and vulnerable populations.

Strengths and limitations

The study did not use a direct measure of willingness to contact at-risk relatives for genetic screening *per se*, but willingness to contact relatives for research. We consider this a reasonable proxy for the behavior of interest. YBCS' mutation status was based on self-report, although genetic counselors verified most of these reports. Self-reported genetic counseling and testing for breast cancer is generally accurate [31]. We examined YBCS overall willingness to contact relatives and not based on specific relative characteristics. Recruitment of at-risk relatives could have been compromised if the YBCS had not clearly understood instructions, or was hesitant to communicate information about breast cancer genetics. We did not recruit relatives from YBCS with an identified hereditary cancer syndrome, because we could not provide these families with appropriate intervention materials. In clinical practice, it would be important to contact these families and inform them about their cancer risk. The study "imposed" a recruitment scheme that involved only two relatives per YBCS (to have comparable family units), and favored first- vs. second-degree relatives and younger vs. older women, to reach relatives who could benefit the most from information about the possible hereditary nature of breast cancer in

their family. The downside of this recruitment scheme was that although YBCS' wishes were respected (invited only relatives she was willing to contact), YBCS were not really "free" to recruit the number and relatives of their choice to the study. Despite these limitations, the study recruited a large, random sample of at-risk families from a cancer registry database with an adequate representation of Black YBCS. Our recruitment method supports large-scale public health genomic studies.

Conclusions

Study findings are especially important in the era of the precision medicine initiative [32] which aims to develop a national cohort of one million or more U.S. participants and lead efforts in cancer-genomic research and other chronic diseases. The goal is to create a cohort reflecting the diversity of the U.S. population with participants from all age groups, health status, and from diverse social and racial/ethnic background, living in a variety of geographies, social environments, and economic circumstances. Our recruitment approach is supportive of such a large-scale public health genomic initiative. It can save resources and impact at-risk families by eliminating typical barriers associated with clinic-based recruitment. This method can also serve as a platform for standardizing nationwide recruitment efforts that support the internal and external validity of large-scale public health genomic efforts [33]. This recruitment method can also be used for studies aiming to increase genomic public health literacy [34], examine the effectiveness of genomic-based approaches in precision medicine [35], and using a "hybrid" approach bridging the gap between clinical and public health genomic research [36].

Compliance with ethical standards

Conflict of interest Maria C. Katapodi was the Principal Investigator of this study and received research support from DCD and RWJF. Debra Duquette declares that she has no conflict of interest James J. Yang declares that he has no conflict of interest. Kari Mendelsohn-Victor declares that she has no conflict of interest Beth Anderson declares that she has no conflict of interest. Christos Nikolaidis declares that he has no conflict of interest Emily Mancewicz declares that she has no conflict of interest Laurel L. Northouse declares that she has no conflict of interest Sonia Duffy declares that she has no conflict of interest. David Ronis declares that he has no conflict of interest Kara J. Mil-

liron declares that she has no conflict of interest. Nicole Probst-Herbst declares that she has no conflict of interest Sofia D. Merajver declares that she has no conflict of interest. Nancy K. Janz declares that she has no conflict of interest. Glenn Copeland declares that he has no conflict of interest. J. Scott Roberts declares that he has no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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