Genetic Testing and Surveillance of Young Breast Cancer Survivors and Blood Relatives: A Cluster Randomized Trial

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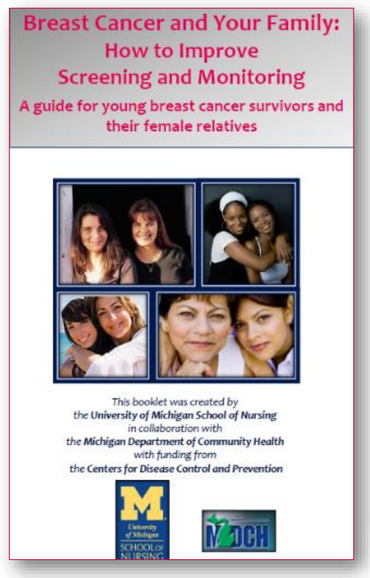
Background

- Women w/ breast cancer younger than 45 years old (YBCS) are about 25% of new cases; more likely to be hereditary breast and ovarian cancer (HBOC) syndrome cases
- National guidelines for YBCS recommend genetic evaluation (counseling and testing) to determine HBOC and annual clinical breast exams (CBE) and mammograms
- Underutilization of cancer genetic services and mammography, especially for Black YBCS
- 1º- and 2º - relatives of YBCS have a 2.3 and 1.5 increased relative breast cancer risk respectively. Relatives of HBOC cases should initiate MRI screening at age 25 (MRI) or earlier based on family history.
- The challenges concerning YBCS and at-risk relatives are
  - identify them in large numbers and racially diverse sample
  - low-resource ways to inform about genetic evaluation and cancer surveillance



Aims

Compare efficacy of two low-resource interventions delivered via postal mail, including targeted (more generic) versus tailored (person-specific) messages

The outcomes presented are

- Initiation of genetic testing for YBCS and cascade genetic testing for relatives
- Surveillance (CBE and mammography) based on national guidelines for YBCS and relatives
- Satisfaction, acceptance, and perceived usefulness of the interventions

Methods

Two-arm cluster randomized trial (RCT)
Stratified sample of 3,000 YBCS (1500 Black vs. 1500 White/other)
Random selection from Michigan Cancer
Registry w/ computer algorithm

- 25-64 y.o. at the time of study
- 20-45 y.o. diagnosed w/ invasive breast cancer or DCIS
- Michigan residents at the time of diagnosis
- Able to read English, provide informed consent
- Willing to invite one of their 1º or 2º-female relatives

Relatives had to be:

- Female and Cancer-free
- 25-64 y.o. at the time of the study
- Able to read English, provide informed consent

Outcomes assessed at baseline and 8-month follow-up

Ethics approval: University of Michigan (HUM00055949) and
Michigan Department of Health and Human Services (201202-09-EA)

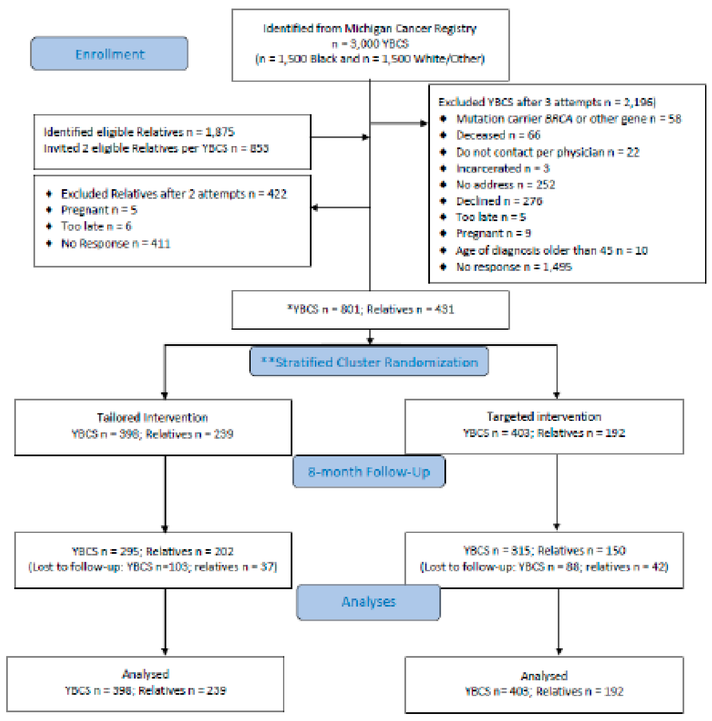


Figure 1. Consort diagram. * YBCS = young breast cancer survivor; ** Stratified randomization of YBCS according to race (Black vs. White/Other); relatives follow randomized arm of YBCS.

Results

Outcomes for YBCS* Tailored n=398 Targeted n=403	Baseline		Follow-up**		Tailored vs. Targeted p value[A] (95% CI)	Change from Baseline to Follow-up p value[B] (95% CI)	
	Tailored	Targeted	Tailored	Targeted		Tailored	Targeted
Had Genetic Testing	79 (19.85%)	107 (26.55%)	99 (24.87%)	127 (31.52%)	1.00 (-0.030 - 0.031)	**≤0.001[b]** (0.031 - 0.077)	**<0.001[b]** (0.031 - 0.076)
Had CBE according to NCCN*** Guidelines	342 (85.92%)	333 (82.63%)	361 (90.70%)	356 (88.33%)	0.66 (-0.040 - 0.023)	**<0.001[b]** (0.029 - 0.074)	**<0.001[b]** (0.037 - 0.084)
Had mammography according to NCCN*** Guidelines[1]	298 (87.64%)	292 (87.16%)	315 (92.65%)	302 (90.15%)	0.17 (-0.009 - 0.055)	**<0.001[b]** (0.029 - 0.079)	**0.002[b]** (0.014 - 0.054)
Outcomes for Relatives Tailored n=239 Targeted n=192	**Baseline**		**Follow-up****		**Tailored vs. Targeted p value[A] (95% CI)**	**Change from Baseline to Follow-up p value[B] (95% CI)**	
	Tailored	**Targeted**	**Tailored**	**Targeted**		**Tailored**	**Targeted**
Had Genetic Testing	9 (0.04%)	4 (0.02%)	17 (0.07%)	5 (0.03%)	0.08[a] (-0.001 - 0.058)	**0.008[b]** (0.015 - 0.065)	1[b] (0.000 - 0.029)
Had CBE according to NCCN*** Guidelines	179 (74.89%)	146 (76.04%)	204 (85.36%)	161 (83.85%)	0.44 (-0.032 - 0.085)	**<0.001** (0.069 - 0.151)	**<0.001[b]** (0.044 - 0.125)
Had mammography according to NCCN*** Guidelines[2]	109 (69.87%)	87 (71.31%)	126 (80.77%)	96 (78.69%)	0.43 (-0.039 - 0.110)	**<0.001[b]** (0.065 - 0.168)	**0.004[b]** (0.034 - 0.135)

*YBCS=young breast cancer survivor
**Intention to Treat
***NCCN=National Comprehensive Cancer Network
[A] Two-proportions z-Test or [a]Fisher's Exact Test
[B] McNemar's test or [b] McNemar's Exact Test

1. Tailored n = 340 and Targeted n = 335 after excluding YBCS with double mastectomy who do not receive mammograms per NCCN guidelines (excluded Tailored n = 58; Targeted n = 68)
1. Tailored n = 156 and Targeted n = 122 after excluding relatives younger than 35 years old AND relatives between 35 to 40 with Gail lifetime risk <20% who do not receive mammograms per NCCN guidelines (excluded Tailored n = 83; Targeted n = 70)

Outcomes for YBCS* Black n=324 White/Other n=447	Baseline		Follow-up**		Black vs. White/ Other p value[A] (95% CI)	Change from Baseline to Follow-up p value[B] (95% CI)	
	Black	White/ Other	Black	White/ Other		Black	White/ Other
Had Genetic Testing	52 (16.05%)	134 (28.09%)	68 (20.99%)	158 (33.12%)	0.92 (-.0038 - 0.054)	**<0.001[b]** (0.028 - 0.079)	**<0.001[b]** (0.035 - 0.079)
Had CBE according to NCCN*** Guidelines	268 (82.72%)	407 (85.32%)	286 (88.27%)	431 (90.36%)	1 (-0.033 - 0.036)	**<0.001[b]** (0.033 - 0.086)	**<0.001[b]** (0.035 - 0.079)
Had mammography according to NCCN*** Guidelines[1]	244 (83.28%)	346 (90.58%)	259 (88.40%)	360 (94.24%)	0.46 (-0.020 - 0.049)	**<0.001[b]** (0.029 - 0.083)	**<0.001[b]** (0.020 - 0.061)
Outcomes for Relatives Black n=87 White/Other n=344	**Baseline**		**Follow-up****		**Black vs. White/ Other p value[A] (95% CI)**	**Change from Baseline to Follow-up p value[B] (95% CI)**	
	Black	**White/ Other**	**Black**	**White/ Other**		**Black**	**White/ Other**
Had Genetic Testing	2 (2.30%)	11 (3.20%)	4 (4.60%)	18 (5.23%)	1.00[a] (-0.035 – 0.039)	0.5[b] (0.003 - 0.081)	**0.016[b]** (0.008 - 0.041)
Had CBE according to NCCN*** Guidelines	63 (72.41%)	262 (76.16%)	71 (81.61%)	294 (85.47%)	1.00 (-0.076 - 0.068)	**0.008[b]** (0.041 - 0.173)	**<0.001** (0.064 - 0.129)
Had mammography according to NCCN*** Guidelines[2]	39 (65.00%)	157 (72.02%)	45 (75.00%)	177 (81.19%)	1.00 (-0.085 - 0.102)	**0.031[b]** (0.038 - 0.205	**<0.001[b]** (0.057 - 0.138)

*YBCS= young breast cancer survivor
** Intention to Treat
***NCCN= National Comprehensive Cancer Network
[A] Two-proportions z-Test or [a]Fisher's Exact Test
[B] McNemar's test or [b]McNemar's Exact Test
[1]Tailored n = 293; Targeted n = 382, after excluding YBCS with double mastectomy (excluded Tailored n = 31; Targeted n = 95)
2. Tailored n = 60; Targeted n = 218, after excluding relatives younger than 35 years old AND relatives between 35 to 40 with Gail lifetime risk <20% according to NCCN guidelines (excluded Tailored n = 27; Targeted n = 126)

Conclusions

- Uptake of genetic testing in both arms increased approximately 5% (short-term follow-up, lack of referral from a healthcare provider, YBCS on average 11 years post diagnosis)
- YBCS in the tailored arm more likely to report higher self-efficacy for genetic testing (not shown)
- Cascade genetic testing depends on YBCS having genetic testing first and identified with an HBOC-associated pathogenic variant
- 5% to 10% increase in CBE and mammography rates for YBCS and relatives
- Black YBCS reported higher self-efficacy and intention for genetic testing, higher satisfaction with intervention materials (data not shown)

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