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ORIGINAL ARTICLE

Biomarker profiling for breast cancer detection: translational research to determine acceptance of a novel breast cancer screening technique

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ABSTRACT

The current study seeks to determine how the psychosocial predictors of the health belief model are related to willingness to adopt biomarker screening practices among women above and below current screening age recommendations, as biomarker profiling can potentially detect cancer much earlier than current breast cancer detection methods. Patients (N = 205) at an Obstetrician/Gynaecology office in a mid-sized Midwest city. Participants completed a survey in the waiting room before their doctor appointment. Results revealed that benefits ($p < .001$), barriers ($p = .02$), cancer worry severity ($p = .01$), and self-efficacy ($p = .002$) were significant predictors of willingness to adopt biomarker profiling, and susceptibility was marginally related ($p = .09$). The direct effects are qualified by two interactions between psychosocial predictors of the health belief model and participants' age. The model predicted willingness to adopt biomarker screening well (R^2 = 28%), and may be used successfully as a framework to assess the diffusion of biomarker screening acceptability.

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Biomarker profiling represents a promising tool for breast cancer prevention risk assessment and screening. Broadly defined, biomarkers can signify normal or pathogenic biological processes, or pharmacological responses (Committee on Policy Issues in the Clinical Development & Use of Biomarkers for Molecularly Targeted Therapies, 2016), and are typically identified in biofluids (blood, urine), or through tumour biopsy (Van Poznak et al., 2015). Research on genetic biomarkers has identified genomic mechanisms that facilitate or inhibit specific subtypes of cancer (Marcotte et al., 2016). Currently, the American Society of Clinical Oncology (ASCO) recommends three genetic biomarkers for breast cancer that have proven clinical utility (*ER, PR*, and *HER2*) to guide treatment decisions (Krop et al., 2017; Van Poznak et al., 2015). A promising newer focus involves the identification of salient metabolites that can serve as indicators of a potential malignancy (Huang et al., 2016; Slupsky et al., 2010). Preliminary findings suggest that metabolite or protein-based biomarker profiling can be highly sensitive to the presence of breast cancer and may actually be superior to surgical biopsies in some cases, potentially allowing for earlier and more accurate detection (Kloten et al., 2013; Spratlin, Serkova, & Eckhardt, 2009; Wu & Qu, 2015).

The continued identification of cancer biomarkers is central to the advancement of the precision medicine initiative and a key priority of the national Cancer Moonshot (Cancer Moonshot Blue Ribbon Panel, 2016; Collins & Varmus, 2015). In this regard, behavioural research is necessary to facilitate the adoption of biomarker profiling techniques among the general public as they become available. Existing behavioural research in this area has focused on identifying factors that lead to the acceptability, diffusion, and accurate interpretation of genetic testing information. Findings suggest that a host of individual-level factors, including awareness, knowledge, attitudes and beliefs, and social factors, including culture and acculturation, can impact the acceptability of genomic biomarker information in the prevention of disease (Kaphingst & Goodman, 2016). Similar research has prioritised the identification of factors predicting biospecimen banking consent, or the donation of biological tissue samples which can be used to identify and

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study cancer biomarkers. Much research in this area is focused on identifying demographic and cultural correlates of consent as well as focus group interviews to understand motivations for donating biologic samples to tissue banks (Drake et al., 2016; Drake, Boyd, Carter, Gehlert, & Thompson, 2017; Kaphingst, Janoff, Harris, & Emmons, 2006).

The present study extends this area of research by identifying belief-based correlates of biomarker profiling acceptability. Specifically, we assess perceptions of risks, benefits, and barriers, and whether they are associated with acceptability of biomarker profiling technology. Behavioural research in this area has identified several knowledge-based and structural barriers to biomarker profiling uptake, including general lack of awareness about test availability, concerns about potential privacy violations, cost, transportation issues, and the need for childcare (Andersen et al., 2007; Kinney et al., 2014; Ramirez et al., 2015). A survey of physicians from 35 countries suggests that lack of funding and access to molecular sequencing technology were the largest barriers to physician recommendation (Gingras et al., 2016). Still, little is known about the attitudinal and belief-based constructs that can affect biomarker profiling decision-making.

To address this, the current study uses the health belief model (HBM) as a theoretical framework to assess perceptions of acceptability of biomarker profiling in the context of breast cancer. The HBM suggests that five constructs can predict whether an individual will engage in a recommended health behaviour: (1) susceptibility, or the perception of vulnerability to a particular harm, is positively associated with protective behaviours; (2) severity, or magnitude of harm, is positively associated with protective behaviours; (3) perceived benefits of enacting the behaviour are positively associated with protective behaviours; (4) perceived barriers to enact the behaviour, which are negatively associated with protective behaviours; and (5) self-efficacy, or beliefs in one's ability to enact a protective behaviour, which are positively associated with protective behaviours (Rosenstock, Strecher, & Becker, 1988). Historically, the HBM has been used to investigate the relationship between health beliefs and behavioural intentions or behaviours, and a recent meta-analysis has supported this use, providing empirical evidence that the components of the HBM are predictive of health intentions and behaviours (Sheeran et al., 2016). The HBM has frequently been used to evaluate beliefs surrounding breast cancer screening behaviours (e.g., Abolfotouh et al., 2015; Lee, Stange, & Ahluwalia, 2015; Vandyke & Shell, 2016) and has more recently been used in assessing attitudes and behaviours surrounding biomarker screening behaviours (e.g., Valdovinos et al., 2015). As such, the HBM is an appropriate framework for providing insight into factors that impact acceptance or rejection of biomarker profiling. Four separate critical reviews of the model detailing the results of 89 studies across various populations suggest that susceptibility, severity, benefits, and self-efficacy all have positive relationships with health outcomes whereas perceived barriers is negatively related to outcomes (Carpenter, 2010; Harrison, Mullen, & Green, 1992; Janz & Becker, 1984; Zimmerman & Vernberg, 1994).

This study represents an effort to match translational research efforts with forthcoming advancements in prevention, diagnosis, and treatment; understanding women's motivations and impediments to biomarker profiling now will allow for a more purposeful and effective delivery of future health information. In doing so, the present investigation hypothesises that the variables of the health belief model will significantly predict people's willingness to adopt biomarker profiling as a screening tool for breast cancer.

Another relevant factor to consider is age. Although breast cancer is diagnosed less frequently among women under 40, metastatic breast cancer incidence is rising in this population and younger women tend to be diagnosed with more aggressive cancers and face lower survival rates (Anders et al., 2008, 2011; Johnson, Chien, & Bleyer, 2013). Currently, there are no efficacious screening tools for women under 40. Biomarker profiling may make it possible to effectively monitor genetic risk factors and screen for breast cancer indicators among this population in the future. In this regard, it may be important to explore how women younger than current screening guidelines (<40 years) react to biomarker profiling as well as those at or above current screening guidelines.

1. Methods

1.1. Participants and procedure

Convenience sampling was utilised to collect data from patients of an Obstetrician/Gynaecology (OB/GYN) practice. The practice is one of the largest providers of women's healthcare in Indiana, United States. All recruitment and study participation took place at participants' OB/GYN office. Upon checking in for their appointments, a member of the research team approached potential participants and asked if they would like to take a survey on breast cancer while waiting for their appointment. There were no inclusion/exclusion criteria specified, all female patients interested in participation were allowed entry into the study. Those who agreed were handed a clipboard with an information sheet detailing biomarker profiling, the survey, and a $2 bill. The instructions indicated that participants could keep the $2 even if they declined participation. The information sheets consisted of study information and a one-page informational sheet that defined the biomarker profiling, discussed its potential application for breast cancer, described how the test is conducted, and detailed other potential disease applications using this technique.

Surveys were completed on site and returned to the researchers. Data collection occurred over two days. Study protocol was approved by the Purdue University institutional review board. In total, 220 surveys were distributed and 205 surveys were returned. On average, participants were 37.8 years old (SD = 14.2) and Caucasian (89.3%; see full descriptive statistics in Table 1).

1.2. Measures

1.2.1. Control variables

Age and *previous cancer history* (0 = no, 1 = yes) were measured as control variables.

1.2.2. HBM constructs

Susceptibility, benefits of screening, barriers to screening, and self-efficacy measures were adapted from previous breast cancer research (Champion, 1999; Champion & Skinner, 2003; Champion, Skinner, & Menon, 2005) to measure perceptions about biomarker profiling. All measures demonstrated acceptable reliability (Cronbach's $\alpha > .86$ for all measures). Most people believe that breast cancer is a severe disease (Jensen et al., 2014), which may lead to ceiling effects in measures of severity. Thus, *cancer worry severity* was measured as a proxy for severity. A four-item measure of dispositional cancer worry severity was used to measure this construct (Jensen, Bernat, Davis, & Yale, 2010).

Table 1. Sample descriptive statistics.

	N	%
Age		
Below ACS recommended screening age (17–39)	125	61.0
Above ACS recommended screening age (40+)	75	36.6
Unreported	5	2.4
Race/Ethnicity		
African American	4	2.0
Asian/Pacific Islander	1	0.5
Caucasian	183	89.3
Latino	5	2.4
Unreported	12	5.9
Has someone significant to you had breast cancer?		
No	111	54.1
Yes	88	42.9
Unreported	6	2.9
Have you had breast cancer before?		
No	196	95.6
Yes	2	1.0
Unreported	7	3.4
Have you had any kind of cancer before?		
No	190	92.7
Yes	10	4.9
Unreported	5	2.4
Had a Mammogram		
No	1	1.3
Yes	74	98.7
If yes, when was most recent mammogram?		
More than 2 years	1	1.4
Within past 2 years	39	97.2
Not sure	1	1.4
Had abnormal biopsy		
No	67	91.8
Yes	6	8.2
Had hormone replacement therapy (HRT)		
No	44	61.1
Yes	28	38.9

1.2.3. Willingness to adopt

Five items were used to assess willingness to adopt biomarker profiling: the desire for more information about it, plans to utilise it, would utilise even without insurance, would use it if insurance only covered one yearly breast cancer screening test, and desire to participate in biomarker profiling clinical trials. Scores were on a 10-point scale ranging from "very certain 'no'" to "very certain 'yes.'" As many of the distributions for the individual items were skewed and/or kurtotic, a scale that approximated a normal distribution and had acceptable reliability ($\alpha = .86$) was created using all five items (all survey items can be seen is Appendix A).

2. Results

Approximately 5.88% of the data were missing, replaced using maximum likelihood procedures. Table 2 shows means, standard deviations, and bivariate relationships between HBM constructs and willingness to adopt biomarker profiling. Hierarchical regression was used in SPSS 21. In this case, hierarchical regression allows us to understand the effects of the HBM variables while controlling for demographic covariates. Age and previous cancer history were entered into the first block of the regression equation as controls and the HBM constructs were entered into the second block (see Table 2). The controls accounted for about 9.1% of variation in willingness to adopt, F (2, 197) = 9.87, $p < .001$. Of these, only age was significantly related to willingness to adopt, $b = .04$, $p < .001$. The second block accounted for an additional 28% of the variance in willingness to adopt, F (7, 192) = 16.15, $p < .001$. Four of the five predictors were significantly associated with willingness to adopt: benefits ($b = .84$, $p < .001$), cancer worry severity ($b = .21$, $p = .01$), barriers ($b = -.51$, $p = .02$), and self-efficacy ($b = .80$, $p = .002$). As perceived benefits, cancer worry severity, and self-efficacy increased, willingness to adopt was more favourable. As perceived barriers to conventional screening increased, willingness to adopt decreased. Susceptibility was marginally associated with willingness to adopt biomarker screening ($b = .29$, $p = .09$), such that as susceptibility increased, willingness to adopt increased.

The difference in willingness to adopt between women who are above the recommended screening age (40 years old) and those below may be of particular interest to researchers, as these groups may report differing motivations and barriers to biomarkers uptake. As such, five interaction analyses were conducted to determine how psychosocial predictors of the HBM differed across age. In each model, one predictor of the HBM was entered as the focal predictor, age was entered as a moderator,

Table 2. Hierarchical linear regression model predicting biomarker profiling intentions.

	M (*SD*)	*r*	*b* (*SE*)	*t*	95%CI	ΔR^2
Block 1: Controls						.09
Age	37.8 (14.2)	.30***	.04 (.01)	4.37***	[.02, .06]	
Cancer history	–	.24***	−.20 (.64)	−0.31	[−1.46, 1.07]	
Block 2: HBM constructs						.28
Benefits	4.00 (.75)	.43***	.84 (.16)	5.19***	[.52, 1.16]	
Barriers	1.53 (.65)	−.35***	−.51 (.22)	−2.29*	[−.94, −.07]	
Susceptibility	2.47 (.74)	.15*	.29 (.17)	1.72†	[−.04, .61]	
Worry severity	3.94 (1.49)	.11	.21 (.08)	2.55**	[.05, .37]	
Self-Efficacy	4.40 (.53)	.39***	.80 (.26)	3.14**	[.30, 1.31]	

Notes: *r* is the bivariate correlation between predictor and willingness to adopt biomarker profiling. *b* represents the unstandardised regression coefficient for the effect of each predictor on willingness to adopt biomarker profiling. ΔR^2 is the change in R^2 associated with each block of predictors. Cancer History operationalised as 0 = No, 1 = Yes.†$p < .10$.
*$p < .05$; **$p < .01$; ***$p < .001$.

willingness to adopt was entered as the dependent variable, and all remaining HBM variables and breast cancer history were entered as covariates. Hayes and Matthes (2009) technique for probing interactions was utilised to assess these relationships. The moderation effect of age was probed at +1*SD* (52 years old) and −1*SD* (23.6 years old) from the mean age.

Of the five models assessed, age was a significant moderator of two HBM variables: barriers, and cancer worry severity (see Figure 1). Although barriers were negatively related to willingness to adopt across all values of age, this relationship was strongest among participants below the current recommended screening guidelines, $b = -.69$, $p = .008$, 95% CI = −1.20, −.19. Specifically, as perceptions of barriers increased, younger participants reported reduced willingness to adopt, whereas perceived barriers to screening did not significantly influence willingness to adopt for those above the recommended screening age. Of the specific individual barrier items that were assessed, the three that had the strongest bivariate relationship with willingness to screen were: the time it takes to get screened ($r = -.31$), forgetting to schedule a screening appointment ($r = -.34$), and having other problems more important than breast cancer screening ($r = -.34$). Among older participants, an increase in cancer worry severity resulted in significantly higher willingness to adopt, $b = .33$, $p = .007$, 95%CI = .09, .55. In short, as cancer worry severity increased among older participants, willingness to adopt significantly increased.

3. Discussion

The present study used the HBM to assess women's willingness to adopt biomarker profiling as a breast cancer detection practice. Findings reveal that in general, as perceptions of the benefits of screening, susceptibility to- and severity of breast cancer, and self-efficacy to engage in screening increase, willingness to adopt increased. Likewise, as perceptions of barriers to screening increased, willingness to adopt decreased. These findings are consistent with the HBM, suggesting that this model may be an appropriate framework from which to model biomarker uptake intentions and behaviour. This type of research is increasingly important; conducting basic behavioural translational research can better target and tailor public health campaigns to disseminate new health innovations and recommendations. Additionally, these findings highlight the types of variables that campaign researchers should target to increase biomarker screening when the practice completes clinical trials.

This study also investigated the psychosocial differences between younger participants who were below the age limit for traditional screening recommendations

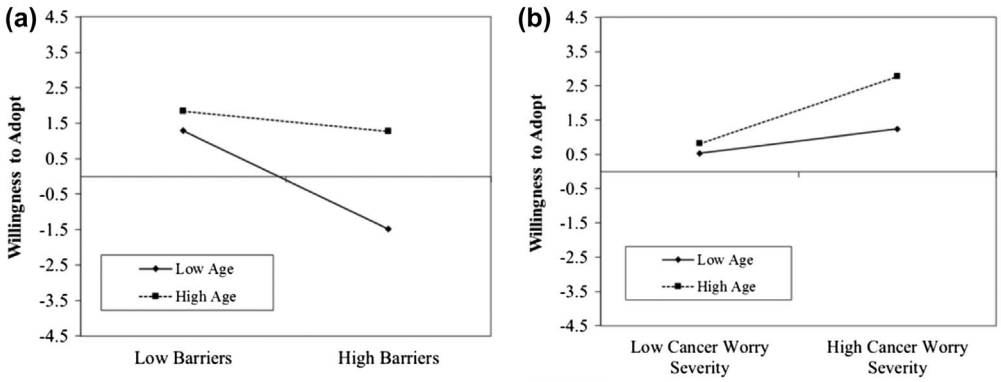

Figure 1. How age moderates the association between predictors and willingness to adopt biomarker-profiling. Low age (23.6) and high age (52) were operationalised as ±1SD from the mean age (37.8).

and older participants who should already be engaged in some form of breast cancer screening. Examining factors that influence younger women's willingness to adopt is crucial. For example, if advances in diagnostic tools –like biomarker screening– can reliably detect breast cancer earlier than conventional screening techniques, this may lead to a readjustment of the recommended screening age to include younger women. One key finding was that although barriers to breast cancer screening did not meaningfully affect older women's willingness to adopt, there was a decrease in willingness to adopt among younger participants as perceived barriers increased. On the surface, biomarker screening should be easier and less invasive for women to enact than conventional screening methods, suggesting that people who perceive higher barriers to breast cancer screening methods may be open to the idea of biomarker profiling. This does not appear to be the case among younger women, whose willingness to adopt actually decreased as perceptions of breast cancer screening barriers increased. Two of the barriers that had the strongest negative relationship with willingness to adopt (embarrassment and unnecessary radiation exposure) are less of an issue with biomarker screening compared to conventional screening. Future interventions should focus on highlighting the ways in which biomarker screening improves upon current screening techniques, particularly to younger audiences.

Among older women, willingness to adopt increased markedly as perceptions of severity increased, however this relationship was not as strong among younger women. Taken together, these findings for barriers and severity are not surprising. As younger women do not currently fall within the recommended screening age, it makes sense that the relationship between HBM constructs and willingness to adopt is not as strong compared to older women. Still, it is necessary to understand the psychosocial factors that influence screening intentions for women both above and below the recommended screening age in an effort to facilitate the translation of new advancements in breast cancer screening to the general public.

3.1. Limitations and future research

As the present sample was recruited from an OB/GYN office, we were unable to recruit people who do not regularly visit their health care provider, which may not be representative of the overall US population. Moreover, many of the women included in this sample have previously had a mammogram; it is unclear if this impacts their decisions about utilising different screening options, such as biomarker profiling. Perhaps the results found here may be different among an audience that has not had a mammogram. Another limitation of the present investigation is that currently biomarker screening for breast cancer is in the clinical trial phase and is not widely available unless one has the means to pay for this screening out-of-pocket. Additionally, the risk of premenopausal breast cancer is higher among African–American women (Carey et al., 2006), making this population ideal for biomarker profiling. Future research should focus explicitly on potential barriers and facilitators of biomarker profiling uptake among African–American women. Unfortunately under-served racial/ethnic groups such as African–American and Hispanic women were underrepresented in this sample, limiting subgroup analysis. Finally, there were no items explicitly measuring family history of breast cancer; although one item asked if "someone significant to you had breast cancer", it is not possible to discern actual family history from this indicator.

Results of the present study may only generalise to the US health system. To illustrate, women in other countries and health systems may have different barriers to screening that are more or less salient than the ones identified here. Other health systems may not yet be able to utilise biomarker screening. Therefore, the adaptation of the present study to other countries and health systems may be limited. Future research in this area should also focus on inductive, qualitative research to understand the facilitators and barriers that may be unique to biomarker profiling. While the present findings detail the importance of perceived barriers on biomarker profiling acceptability, future work in this area should focus on identifying specific salient barriers that can be addressed in subsequent intervention research. Finally, future research should more closely examine the factors that may influence biomarker profiling for women both above and below the current recommended screening age, as biomarker profiling may allow for earlier and more accurate breast cancer diagnoses, which could impact the monitoring or treatment of breast cancer from earlier ages.

4. Conclusion

The current study was a translational research effort to assess the utility of the HBM as a theoretical framework to study the diffusion of biomarker screening acceptability as a tool for detecting breast cancer. Results suggested that the HBM predicted willingness to adopt biomarker profiling reasonably well (R^2 = 28%). The analysis also uncovered psychosocial differences that impacted willingness to adopt between women younger than and within the current recommended screening ages. These differences are discussed in terms of their ability to influence the acceptability of biomarker screening in advance of its general availability.

Disclosure statement

No potential conflict of interest was reported by the authors.

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Appendix A. Measures

Susceptibility

Measured on a 5-pt scale ranging from "strongly disagree" to "strongly agree."

(1) It is likely that I will get breast cancer.
(2) My chances of getting breast cancer in the next few years are great.
(3) I feel I will get breast cancer sometime during my life.

Worry severity

Measured on a 7-pt scale ranging from "strongly disagree" to "strongly agree."

(1) I am afraid of the physical consequences of getting cancer
(2) I worry about my health because of my chances of getting cancer
(3) I feel anxiety when I think of the possible consequences of getting cancer
(4) I brood about the physical consequences of getting cancer

Benefits

Measured on a 5-pt scale ranging from "strongly disagree" to "strongly agree."

(1) My family will benefit if I am screened for breast cancer.
(2) If I get screened for breast cancer and nothing is found, I do not worry as much about breast cancer.
(3) Getting screened for breast cancer will help me find breast lumps early.
(4) If I find a lump through an annual breast cancer screening, my treatment for breast cancer may not be as bad.
(5) Getting screened for breast cancer is the best way to find a very small lump.
(6) Getting screened for breast cancer will decrease my chances of dying from breast cancer.

Barriers

Measured on a 5-pt scale ranging from "strongly disagree" to "strongly agree."

(1) I am afraid to have breast cancer screening because I might find out something is wrong.
(2) I am afraid to have breast cancer screening because I don't understand what will be done.
(3) I don't know how to go about getting screened for breast cancer.
(4) Getting screened for breast cancer is too embarrassing.
(5) Getting screened for breast cancer takes too much time.
(6) People doing breast cancer screenings are rude to women
(7) Getting screened for breast cancer exposes me to unnecessary radiation.
(8) I can not remember to schedule a breast cancer screening.
(9) I have other problems more important than getting screened for breast cancer.
(10) I am too old to need a routine breast cancer screening.
(11) Getting screened for breast cancer is too painful.

Self-Efficacy
Measured on a 5-pt scale ranging from "strongly disagree" to "strongly agree."

(1) You can arrange transportation to get screened for breast cancer.
(2) You can arrange other things in your life to have a breast cancer screening.
(3) You can talk to people at the screening centre about your concerns.
(4) You can get screened for breast cancer even if you are worried.
(5) You can find a way to pay for breast cancer screening.
(6) You can make an appointment for breast cancer screening.
(7) You know for sure you can get breast cancer screening if you really want to.
(8) You know how to go about getting screened for breast cancer.
(9) You can find a place to have a breast cancer screen.

Willingness to adopt biomarker profiling
Items were measured two ways: First, participants were asked to respond "yes/no" to each item, then they were presented with a 5-point scale asking how positive they were in their response, ranging from "not very positive" to "very positive."
These scores were combined to create an index. "No" responses were coded negatively, with scores ranging from -1 (not very positive) to -5 (very positive). "Yes" responses were coded positively, with scores ranging from 1 (not very positive) to 5 (very positive). This resulted in a 10-point scale of participants' willingness to adopt biomarker profiling.

(1) I would be interested in more information about metabolite profiling.
(2) I plan to utilise metabolite profiling once it is available.
(3) I would consider using metabolite profiling, even if it wasn't covered by insurance.
(4) I would consider using metabolite profiling, even if my insurance only covered one breast cancer screening test a year (i.e., mammography or metabolite profiling).
(5) I would participate in metabolite profiling clinical trials.