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EPIDEMIOLOGY

Identifying socio-demographic and clinical characteristics associated with medication beliefs about aromatase inhibitors among postmenopausal women with breast cancer

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Abstract

Purpose Non-adherence/persistence to adjuvant endocrine therapy can negatively impact survival. Beliefs about medicines are known to affect adherence. This study aims to identify socio-demographic and clinical characteristics associated with medication beliefs among women taking aromatase inhibitors (AIs).

Methods Women completed an online survey on beliefs about AI therapy [Beliefs about Medicines Questionnaire (BMQ)], beliefs about breast cancer [Assessment of Survivor Concerns scale (ASC)], and depression [Personal Health Questionnaire depression scale (PHQ-8)]. Socio-demographic and clinical characteristics were collected. Bivariate analyses and linear regression models were performed to investigate relationships between variables.

Results A total of 224 women reported currently taking AI therapy and were included in the analysis. Significantly higher concern beliefs were found among women who had at least mild depression, experienced side effects from AIs, and previously stopped therapy with another AI. Significant correlations were found between concern and necessity beliefs and cancer and health worry. Women age 70 and older displayed less fear of cancer recurrence and health worry, and a trend towards lower necessity and concern beliefs. No differences were found for other variables. In the regression model, greater necessity beliefs were found with increases in the number of current prescription medications ($B = 1.06$, 95% CI 0.31–1.81, $p = 0.006$) and shorter duration of current AI therapy ($B = -0.65$, 95% CI -1.23 to -0.07, $p = 0.029$), whereas greater concern beliefs were associated with higher depression scores ($B = 1.19$, 95% CI 0.35–2.03, $p = 0.006$).

Conclusions Medication necessity and concern beliefs were associated with a definable subset of patients who may be at higher risk for non-persistence.

Keywords Medication adherence · Adjuvant endocrine therapy · Aromatase inhibitor · Beliefs about medicines · Socio-demographic characteristics · Persistence

Introduction

Breast cancer accounts for approximately one of three diagnosed cancer cases among women in the United States, and it is the second most common type of cancer in women associated with mortality [1]. About two-thirds of breast cancer tumors are estrogen receptor-positive, primarily affecting postmenopausal women [2]. Following

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completion of local therapies and chemotherapy, as indicated, treatment with adjuvant endocrine therapy, which may include an aromatase inhibitor (AI), such as letrozole, anastrozole, or exemestane, or the selective estrogen receptor modulator (SERM) tamoxifen, is recommended. Both AIs and tamoxifen are indicated for postmenopausal women; however, AIs are considered the preferred choice of treatment as they have shown to significantly reduce recurrence rates and improve overall survival compared to tamoxifen [2, 3].

The current recommended guideline for the length of adjuvant endocrine treatment is 5–10 years [2, 4]. A 5-year treatment with AIs reduces the 10-year breast cancer mortality by 40%, compared to no treatment [5]. Adherence to the full course of treatment is critical to reduce the risk of breast cancer recurrence and to improve mortality [6–9]. Because of the potential negative clinical consequences that non-adherence has for breast cancer outcomes, it is anticipated that patients would be highly motivated to follow the regimen for the recommended duration. However, adherence to AIs has been shown to be suboptimal, ranging from 50 to 91% over 1–5 years of therapy [10]. Previous studies conducted with postmenopausal women with breast cancer on adjuvant endocrine therapy showed that lower adherence was associated with several socio-demographic characteristics, including extremes of age (>70–80 and <40 years), being non-white, not married, and having lower income [10–14], but not with education level [10].

An important factor known to affect medication adherence is medication beliefs [15–17]. High necessity and low concern beliefs have been associated with better adherence for a variety of chronic conditions [18]. Within the oncology field, adherence to endocrine therapy has been associated with beliefs in the efficacy of the medication in quantitative and qualitative research [19–22]. On the other hand, worry about long-term effects or concerns about side effects have been associated with non-adherence to endocrine treatment [23]. Fink et al. [20] found that women who perceived therapy with tamoxifen to have greater benefits than risks were more likely to be adherent to their treatment, while those holding neutral or negative beliefs were more likely to discontinue tamoxifen. Grunfeld et al. [21] observed very similar findings where nonadherent women were more likely to report a belief that there was nothing to be gained from taking tamoxifen. In regards to therapy with AIs, a recent study applied the Health Belief Model framework to assess the relationship between health beliefs and adherence to AIs and demonstrated that patients who perceived greater barriers to AI treatment were more likely to take breaks or stop treatment [24]. Perceived susceptibility to breast cancer and perceived benefits of AIs, however, were not found to be predictive of adherence in this study [24]. Specific medication beliefs towards AIs, namely high necessity and concern beliefs, were also found to be associated with higher fear of cancer recurrence [25], which has been reported as one reason that explains adherence behavior [26].

In addition to their effect on adherence, negative beliefs about the efficacy of endocrine therapy play a key role in the decision of not initiating therapy [20, 21, 27]. As many as 30% of women are not convinced of the efficacy of endocrine therapy and about 15% do not believe endocrine therapy is necessary [28]. Consistent with previous literature, the findings by Heisig et al. [29] show that women with greater concern than necessity beliefs have lower expectations about the efficacy of endocrine therapy, reporting lower intention to start treatment.

Previous studies examined socio-demographic characteristics associated with specific medication beliefs in other medical conditions [30–32]. A former study sought to identify correlates of treatment expectations in patients with breast cancer before the start of endocrine therapy [29]. Brier et al. [24] recently studied socio-demographic characteristics associated with health beliefs (using the Health Belief Model framework) among women taking AIs, as a secondary aim of their main study. However, to the best of our knowledge, no studies to date have focused on the differences in medication necessity and concern beliefs across women with different socio-demographic and clinical characteristics taking AIs, which is important for designing future strategies to address non-persistence to AIs. Therefore, the aim of this study was to identify socio-demographic and clinical characteristics associated with medication beliefs among postmenopausal women currently taking AIs.

Methods

Design and subjects

This was a cross-sectional, observational study conducted between October 2014 and February 2015. Patients fulfilling the following inclusion criteria were identified from the University of Michigan (UM) Cancer Registry and recruited into the study: (1) female at least 50 years old with a diagnosis of hormone receptor-positive stage I–III breast cancer (invasive carcinoma of the breast, status post-surgical resection, and axillary assessment) between September 1, 2009 and September 30, 2013; (2) therapy with an AI (anastrozole, letrozole, or exemestane) for 6–48 months; (3) completed prior surgery, radiation therapy, and chemotherapy, as indicated, for breast cancer; (4) not having had breast cancer recurrence; and (5) having consulted with a breast cancer specialist at the UM

Comprehensive Cancer Center within 6 months before enrollment in the study. Patients who did not self-report being on therapy with an AI at the time of contact regarding study participation were excluded from the study.

A total of 934 eligible patients prescribed AI therapy were identified from the UM Cancer Registry, of which 600 were randomly selected for recruitment into the study using Microsoft Excel. The 600 randomly selected individuals were mailed a letter with information about the study, a $2 incentive to increase response rate, and a link to the online survey on Qualtrics.

The study was approved by the University of Michigan (UM) Institutional Review Board (IRBMED). Informed consent was obtained from every participant prior to beginning the online survey by having participants agree with the terms of the study before being directed to the survey questions.

Data collection

An online survey was used to collect patient responses to validated questionnaires as well as socio-demographic, clinical, and treatment characteristics as described below.

Beliefs about medicines were assessed using the specific subscale of the beliefs about medicines questionnaire (BMQ) [17, 33], which contains five items to assess medication necessity beliefs and five items to assess medication concern beliefs. Examples of items from the necessity scale include: “My health, at present, depends on my medicines” and “My medicines protect me from becoming worse.” Examples of items from the concern scale include: “Having to take my medicine worries me” and “I sometimes worry about the long-term effects of my medicines.” Each item is scored on a five-point Likert scale, ranging from 1 = strongly disagree to 5 = strongly agree. Scores obtained for the individual items within each scale are summed to yield a scale score. Total scores for the necessity and concern scales range from 5 to 25, with higher scores indicating stronger beliefs in the concepts represented by each scale.

Disease beliefs were assessed using the Assessment of Survivor Concerns Scale (ASC) [34]. This scale is comprised of five items scored on a 4-point scale (not at all, a little bit, somewhat, very much) that measure fears about cancer recurrence and health concerns in cancer survivors. The 5-item ASC tool is specific to cancer and showed good reliability and validity [34].

Depression was assessed using the Patient Health Questionnaire depression scale (PHQ-8) [35], an 8-item questionnaire that assesses severity of depression. Each of the eight items is scored from 0 to 3 and then summed to yield a final score. The PHQ-8 scale defines depression at a score of $\geq$10. A score of 10 or greater is considered major depression, and a score of 20 or more is deemed major severe depression.

Demographic information including age, race, marital status, household income, and education level, and clinical information comprising AI currently taking, previously stopped therapy with another AI, length of current AI therapy, experience of side effects from AIs, total number of prescription medications currently taking, disease stage, and prior chemotherapy received were collected from the patient or abstracted from the medical record. Experience of side effects from AIs was assessed with a yes/no answer to the question “As a result of taking this medication, did you experience any side effects at all?”.

Data analyses

Descriptive statistics were used to describe demographic and clinical variables, with absolute values and relative frequencies being reported for categorical variables (age, race, household income, marital status, education level, number of prescription drugs, disease stage, prior chemotherapy received, AI currently taking, length of current AI therapy, previously stopped therapy with an AI, depression category and experiencing side effects from AIs) and means and standard deviations for continuous variables (BMQ scores and ASC scores). The household income variable was categorized as $\leq$\$30, \$30,001–50, \$50,001–90, and $\geq$\$90,001K for the purpose of the analysis.

Bivariate analyses were applied to investigate the relationship between socio-demographic and clinical characteristics and medication necessity and concern beliefs. *T*-tests and ANOVA were used to compare means of continuous variables across two or more groups, respectively. Pearson correlation coefficients were calculated to estimate the relationship between medication (BMQ) and disease beliefs (ASC). Multivariate linear regression analyses were applied to ascertain the associations of socio-demographic and clinical variables with necessity and concern beliefs. Variables entered into the model included: age, race, education, household income, marital status, number of prescription medicines, AI currently taking, experience of side effects from AIs, length of current AI therapy, depression, and disease beliefs (cancer worry and health worry). In this model, the variable ‘AI currently taking’ was converted to a dummy variable with the comparator being anastrozole. Statistical analyses were performed using SPSS for Windows, Version 23.0 Chicago, SPSS Inc. All tests were two-tailed, and statistical significance was defined as $p < 0.05$.

Results

Of the 600 recruitment letters sent, a total of 279 (response rate 47%) women completed the survey, of which 224 (80.3%) reported being currently on therapy with an AI. The largest proportion of respondents was between 60 and 70 years old, 90.2% were white, 60.8% had college/postgraduate education, and 75% were married/partnered. A third of the respondents were on therapy with anastrozole (67.4%), and a similar proportion of the remaining respondents were on letrozole (17.4%) or exemestane (15.2%). A total of 47 (21.0%) women were on therapy with their second AI medication (Table 1). About 30% of women in this study reported at least mild depression, and 153 (69.2%) reported that they had experienced side effects from therapy with AIs. The mean (SD) BMQ scores for the necessity and concern subscales were 14.7 (4.2) and 11.0 (4.2), respectively, indicating higher necessity than concern beliefs towards AIs. The mean (SD) ASC score for cancer and health worry was 7.7 (2.6) out of 12 and 4.5 (1.9) out of 8, respectively.

Since one-third of enrolled patients were over the age of 70, differences in beliefs with age as a dichotomous variable (<70 and ≥70) were examined. Significant differences in disease beliefs were found, with women age 70 and older displaying less fear of cancer recurrence (6.7 (2.5) vs. 8.1 (2.6), $p < 0.001$) and less health worry (4.0 (1.5) vs. 4.8 (2.0), $p = 0.001$) compared to those younger than 70. Likewise, there was a trend towards lower necessity (14.0 (4.5) vs. 15.0 (4.0), $p = 0.077$) and lower concern beliefs (10.2 (3.9) vs. 11.3 (4.2), $p = 0.062$) among older compared to younger women.

Significantly higher concern beliefs were found among women with ‘mild’ and ‘moderate to severe’ depression compared to ‘no depression’ (mean (SD) 12.4 (4.4) and 15.7 (3.9) vs. 10.1 (3.8), $p = 0.011$ and $p = 0.005$, respectively). Similarly, women who experienced side effects from AIs displayed significantly higher concern beliefs compared to those who did not experience side effects (mean (SD) 11.3 (4.3) vs. 10.0 (3.7), $p = 0.023$). As well, women who previously stopped therapy with another AI had significantly higher concerns than those who never stopped an AI before (mean (SD) 12.2 (4.3) vs. 10.5 (4.0), $p = 0.01$). When assessing whether women who previously stopped therapy with another AI experienced more side effects than those who never stopped one, no significant differences appeared. No statistically significant differences were found for concern beliefs for all other demographic and clinical variables, including: age (3 categories), race, marital status, household income, education level, number of prescription drugs, disease stage, prior chemotherapy received, and length of current AI therapy

Table 1 Demographic and clinical characteristics of women included in the study ($n = 224$)

Characteristic	*N* (%)
Age (years)	
<60	43 (19.2)
60 to <70	101 (45.1)
≥70	80 (35.7)
Race	
White	202 (90.2)
Non-white	22 (9.8)
Household income	
≤$30K	32 (16.4)
$30,001–50K	33 (16.9)
$50,001–90K	65 (33.3)
≥$90,001K	65 (33.3)
Marital status	
Not married/not partnered	56 (25.0)
Married/partnered	168 (75.0)
Education	
High school or less OR GED	30 (13.4)
Some college	58 (25.9)
College	68 (30.4)
Postgraduate	68 (30.4)
Number of prescription drugs	
1	32 (14.6)
2	51 (23.3)
3–5	97 (44.3)
+5	39 (17.8)
Disease stage	
0	9 (4.0)
I	114 (50.9)
II	82 (36.6)
III	17 (7.6)
Prior chemotherapy received	
Yes	(47.8)
AI currently taking	
Anastrozole	151 (67.4)
Letrozole	39 (17.4)
Exemestane	34 (15.2)
Length of current AI therapy	
0.5–1 year	84 (37.8)
>1 to ≤2	52 (23.4)
>2 to ≤3	44 (19.8)
>3	42 (18.9)
Total number of AIs previously taken (excluding current)	
1	47 (21.0)
2	6 (2.7)
PHQ-8 (depression)	
No depression	151 (69.6)
Mild depression	48 (22.1)

Table 1 continued

Characteristic	*N* (%)
Moderate depression	11 (5.1)
Moderately severe depression	6 (2.8)
Severe depression	1 (0.5)

AI aromatase inhibitor, *PHQ* patient health questionnaire

(data not shown). No statistically significant differences were found for necessity beliefs for all demographic and clinical variables tested (data not shown).

A positive correlation was found between medication and disease beliefs. BMQ concern beliefs were significantly positively correlated with cancer worry (Pearson correlation coefficient $r = 0.31, p < 0.001$) and health worry ($r = 0.32$, $p < 0.001$). Likewise, BMQ necessity beliefs were positively correlated with both cancer worry ($r = 0.20$, $p = 0.003$) and health worry ($r = 0.20, p = 0.004$).

The multivariate linear regression model predicting concern beliefs predicted 15.5% of its variance and showed that greater concern beliefs were associated with higher depression scores ($B = 1.19$, 95% CI 0.35–2.03, $p = 0.006$) (Table 2). Increased reporting of side effects and greater BMQ concern beliefs appear to be related, but the coefficient was not statistically significant ($B = 1.28$, 95% CI −0.04 to 2.60, $p = 0.058$). Greater necessity beliefs were found with increases in the number of prescription medications women reported currently taking ($B = 1.06$, 95% CI 0.31–1.81, $p = 0.006$) and shorter duration of current treatment with an AI ($B = -0.65$, 95% CI −1.23 to −0.07, $p = 0.029$) (Table 2). The regression models predicting necessity beliefs explained 7.1% of variance.

Table 2 Multivariate linear regression model predicting necessity and concern beliefs towards aromatase inhibitors (AI)

	BMQ necessity ($n = 176$)				BMQ concern ($n = 179$)			
	B	95% CI Adjusted $R^2 = 0.071$	Beta	*p*-value	*B*	95% CI Adjusted $R^2 = 0.155$	Beta	*p*-value
Age[a]	−0.84	−1.82 to 0.14	−0.14	0.091	−0.27	−1.17 to 0.64	−0.05	0.558
Race[b]	1.99	−0.29 to 4.26	0.13	0.086	1.71	−0.37 to 3.79	0.12	0.106
Education[c]	−0.11	−0.80 to 0.58	−0.03	0.748	−0.27	−0.92 to 0.37	−0.06	0.407
Income[d]	0.24	−0.47 to 0.94	0.06	0.511	−0.31	−0.97 to 0.35	−0.08	0.354
Marital status[e]	−1.02	−2.63 to 0.59	−0.10	0.212	−0.39		−0.04	0.610
Number of Prescription drugs[f]	1.06	0.31 to 1.81	0.23	**0.006***	−0.18	−0.86 to 0.51	−1.89 to 1.11	0.608
							−0.04	
Length of current AI therapy[g]	−0.65	−1.23 to −0.07	−0.17	**0.029***	0.18	−0.36 to 0.72	0.05	0.515
Letrozole[h]	0.31	−1.38 to 2.00	0.03	0.717	1.33	−0.25 to 2.92	0.12	0.098
Exemestane[h]	0.26	−1.52 to 2.03	0.02	0.776	0.19	−1.45 to 1.83	0.02	0.819
Side effects[i]	0.04	−1.38 to 1.45	0.004	0.959	1.28	−0.04 to 2.60	0.14	0.058
ASC Cancer worry[j]	0.15	−0.25 to 0.55	0.09	0.469	0.12	−0.25 to 0.49	0.08	0.526
ASC Health worry[k]	0.11	−0.46 to 0.67	0.05	0.707	0.33	−0.20 to 0.86	0.15	0.217
Depression[l]	0.07	−0.82 to 0.97	0.01	0.874	1.19	0.35 to 2.03	0.22	**0.006***

AI aromatase inhibitor, *ASC* assessment of survivor concerns, *BMQ* beliefs about medicines questionnaire

* Statistical significance $p < 0.05$

[a] categorical variable: 1 = <60, 2 = 60 to <70, 3 = ≥70

[b] categorical variable: 0 = non-white, 1 = White

[c] categorical variable: 1 = High school or less OR GED, 2 = Some college, 3 = College, 4 = postgraduate

[d] categorical variable: 1 = <30k, 2 = 30 to <50K, 50 to <90K, 4 = ≥90K

[e] categorical variable: 0 = not married/not partnered, 1 = married/partnered

[f] categorical variable: 1 = 1 med, 2 = 2 meds, 3 = 3–5 meds, 4 = >5 meds

[g] categorical variable: 1 = ≤1 year, 2 = >1 to ≤2 years, 3 = >2 to ≤3 years, 4 = >3 years

[h] dummy variable: comparator = Anastrozole

[i] categorical variable: 0 = no, 1 = yes

[j,k] continuous variables

[l] categorical variable: 1 = no depression, 2 = mild, 3 = moderately, 4 = moderate to severe

Discussion

Greater medication concern beliefs have previously been shown to be associated with increased non-adherence with medications. Few studies in the literature have focused on understanding the characteristics associated with necessity and concern beliefs towards AIs. In this cross-sectional study, we identified a number of patient factors that were associated with increased medication concern beliefs. This knowledge will help health care professionals target-specific patients for interventions to address non-adherence and non-persistence to AIs.

Higher concern and necessity beliefs towards AIs were found to correlate positively with worry about cancer, similar to what has been previously reported [25]. One study examining the relationship between medication beliefs and fear of cancer recurrence found that both holding high concerns and greater beliefs in the necessity of taking AIs was associated with greater fear of cancer recurrence [25]. Greater fear of cancer recurrence was in turn reported as one of the reasons for patients to be adherent to adjuvant endocrine therapy [26]. Interestingly, however, factors associated with higher risk of breast cancer recurrence, including higher disease stage and previous treatment with chemotherapy, were not associated with medication beliefs in our study. This suggests that degree of fear of recurrence and medication beliefs may need to be specifically elicited from patients and cannot be assumed based on disease factors.

Experiencing side effects was found to be significantly associated with higher concern beliefs towards AIs in the bivariate analyses, and this association approached significance in the regression analyses. In addition, as expected, women who had previously switched from one AI to another had higher concerns about the medication, even though they were not more likely to report side effects from the current AI medication at the time of the survey. These findings were in line with a previous study in heart failure showing that patients with an adverse drug event held more negative beliefs about their illness and more concerns about their medication than patients without an adverse drug event [36]. These findings suggest the need to evaluate whether more aggressive management of AI toxicity or prevention of development of side effects will result in either lower medication concern beliefs or to a better ability to manage these concerns over time.

Women with some degree of depression had significantly higher concern beliefs in both the bivariate and regression analyses. Similarly, a study examining changes in medication beliefs during long-term care for ischemic heart disease found that depression was associated with increased concerns [37]. Fewer concerns about treatment and low levels of depression have been associated with better quality of life in cancer and thalassemia patients [38, 39]. This highlights the importance of health care professionals assessing and addressing depressive symptoms, as previous reports also showed that depression in cancer survivors can be a significant barrier to health care utilization [40]. However, it is yet to be established that treating depression results in the reduction of concern beliefs towards AIs. Other emotional alterations such as high levels of distress cause patients to more likely be concerned about their medications and those who are anxious about their cancer hold both high concern and high necessity beliefs about cancer medications [41].

Higher necessity beliefs were found with shorter length of current AI therapy in our study, which may reflect increased perception of benefit from therapy closer to initial diagnosis of the disease [42, 43]. Higher necessity beliefs were also associated with greater number of prescription medications currently taken. This is consistent with findings from previous studies showing that patients with more prescription medications at baseline were less likely to discontinue tamoxifen [44]. Similarly, Neugut and colleagues [45] demonstrated that women who were adherent to medication for other chronic conditions prior to initiating hormonal therapy were less likely to be non-adherent to their subsequent hormonal therapy. Altogether, these findings support that necessity beliefs held towards medications in general play a role in patient adherence behavior and predict adherence to future therapy, even if the new medication is given to treat a different medical condition. We have not accounted for non-prescription medications in this study; however, a recent study in patients with breast cancer showed that higher concerns about the physical effects of chemotherapy, lower beliefs in the benefits of chemotherapy and higher expectations of adverse effects from chemotherapy were associated with high levels of complementary and alternative medicine use [46]. Specifically for endocrine therapy, women using complementary or alternative medicines were found to be more likely to discontinue their AI treatment [47]. Therefore, in addition to obtaining an accurate and complete medication history to avoid drug–drug interactions, this information may also be useful for assessing whether a patient is at increased risk of non-persistence with endocrine therapy.

Prior studies have demonstrated decreased adherence to AI therapy in patients over the age of 70 [10]. In our cohort, although older patients taking AI therapy reported having fewer medication concerns, which are often associated with increased adherence, they reported decreased fear of recurrence and lower belief in the necessity of the medication, both of which are associated with increased risk of decreased adherence. Interventions to reframe the necessity beliefs may be required to improve adherence in this patient population.

The findings from this study are important to guide healthcare providers to focus on the need to target this population for development of interventions to improve adherence and persistence. Prior studies evaluating education interventions for improving AI adherence have not shown them to be effective [48, 49]. Our findings suggest that an alternate approach that addresses concern beliefs by reframing them, rather than just reiterating the benefits of therapy, may result in improved treatment adherence, as lower concerns have been linked with better adherence [18].

A limitation of our study is that we cannot generalize the results given that the sample only comprised women from one institution, and the majority of patients reported relatively high income and education level. A further limitation is the cross-sectional design of the study that precludes causal interpretation of the associations found and inability to assess change in beliefs over time. Our analysis was also limited to patients who had been on AI therapy for at least 6 months and two-thirds of our sample had been on therapy for more than a year. Therefore, the results are not generalizable to those just starting treatment with an AI or at the time of treatment decision-making, which could have biased the results towards patients more likely to tolerate the medications.

Conclusion

Patient characteristics were associated with either concern beliefs or necessity beliefs, and both concern and necessity beliefs correlated positively with cancer and health worry. Assessment for beliefs about medications could potentially identify patients at higher risk of nonadherence or early discontinuation of AI therapy. Future research should focus on developing strategies to improve quality of life and adherence/persistence with endocrine therapy for these high-risk patients.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This study was approved by the University of Michigan (UM) Institutional Review Board (IRBMED). Written informed consent was obtained from all individuals before completing the survey.

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