Short-term (1–2 months) Hormone Therapy Cessation Before Mammography

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Abstract

Background—Some health care providers recommend hormone therapy (HT) cessation before mammography to improve performance.

Methods—We performed a randomized clinical trial, the Radiological Evaluation And breast Density (READ) study within an integrated health plan (2004–2007). Women aged 45–80 who used HT at their most recent screening (index) mammogram, were due for a screening (study) mammogram, and were still using HT, were invited to participate. Randomization groups were: 1) no, 2) one-month, or 3) two-month cessation. Women's willingness to participate was evaluated by age, race, ethnicity, education, hysterectomy, type of HT (unopposed estrogen, ET, estrogen plus progestin, EPT), duration of HT use, body mass index (BMI), breast cancer risk, and breast density.

Results—5861 women were invited to participate; 2999 refused. An additional 169 women agreed to participate, but withdrew before data collection. Compared to women who participated (N=1535), nonparticipants (N= 3168; 2999+169; 54%) were older, were less educated, and had lower BMI (all p<0.05). Among nonparticipants, 1876 (59,2%) were unwilling to stop HT. Among EPT users, women with a first degree relative with a history of breast cancer had lower odds of refusal than women without a family history of breast cancer (aOR=0.71, 95%CI 0.54, 0.93).

Conclusions—Most women were unwilling to stop HT, even for a short period when the intent was to improve mammographic accuracy, and even when informed they could restart HT at any time during the 2-month study. Some factors predicted willingness to stop HT; the magnitude of the differences may not be clinically meaningful.

Keywords

hormone therapy cessation; mammographic screening; mammography performance; estrogen therapy (ET) cessation; estrogen and progestin therapy (EPT) cessation

INTRODUCTION

Currently, some physicians encourage women to stop hormone therapy (HT) before receiving a mammogram in the hopes that short-term cessation will improve mammographic sensitivity and specificity, [1, 2] but little is known about the characteristics of women who might be willing to consider short-term HT cessation. Women who use postmenopausal estrogen plus

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progesterone (EPT) [3] for 4 or more years and women who have been using estrogen therapy (ET) for extended periods of time may be at increased risk for breast cancer. [4–6] In addition, postmenopausal HT has been shown to increase breast density and increased breast density is a strong risk factor for breast cancer. [7–11]

We performed a randomized clinical trial to test the hypothesis that HT cessation for one or two months before a screening mammogram would improve mammographic performance by decreasing breast density and mammography recall rates (recall for additional imaging). This report describes our recruitment experience and women's willingness to participate in the study. Our trial started recruitment following the publication of findings from the Women's Health Initiative that EPT increases breast cancer risk. [5] We hypothesized that women who continued HT use in the wake of these findings, particularly women at higher risk for breast cancer, would be interested in, and willing to participate in, a study involving a short-term intervention designed to improve mammographic performance. We also hypothesized that women with more severe menopausal symptoms before starting HT might be less willing to participate, although our recruitment materials specifically stated that any woman who agreed to participate and was randomly assigned to HT cessation but became intolerant of symptoms during the study, could immediately restart her HT.

METHODS

Study Setting

The Radiological Evaluation And breast Density (READ) randomized clinical trial was conducted at Group Health, an integrated health plan in Washington State (US) with approximately 550,000 members. Group Health has a population-based Breast Cancer Screening Program (BCSP) that women are invited to join when they turn 40 years old or when they join Group Health and are age 40 years old or greater.[9, 11–13] Demographic and breast cancer risk factor information are gathered via a self-administered questionnaire when women enter the BCSP and then at each subsequent screening mammogram. [9]

We used automated administrative data to identify and recruit women aged 45–80 years who were due for a screening mammogram. To be eligible, women had to have had a screening mammogram ("index") at Group Health within the past two years at which time they reported current HT use on a self-administered questionnaire. Women had to be due for a screening mammogram ("study" mammogram) and to have evidence of continued HT dispensing from Group Health pharmacies in the 6 months before study recruitment. We required that women self report use of HT (denying use of HT was an exclusion criteria) and they were required to have at least 2 fills of a prescription of HT in the prior 6 months to be included in the study. Thus, we had evidence from 2 different sources regarding HT use. Estrogen dose was defined as: medium − 0.0625 mg conjugated estrogens, 1 mg oral estradiol, 0.050 mg transdermal estradiol; low - all doses less than medium; and high - all doses greater than medium.

Women were ineligible if they had a history of myocardial infarction, angina treated with medication, coronary revascularization surgery, stroke, blood clots, breast cancer, mastectomy or breast implants, or dementia or cognitive impairment. We further excluded women with any dispensings of tamoxifen or raloxifene from a Group Health pharmacy because of their potential influence on breast density. Women who had a breast density rating of "entirely fat" (BI-RADS density = 1) on either breast at their index mammogram were also excluded since their density was not likely to influence mammography performance on or off HT.

This study was reviewed and approved by the Institutional Review Boards at Group Health and the United States Department of Defense.

Recruitment and Refusal to Participate

We recruited potentially eligible women over a 35-month period from November 2004 through September 2007; enrolling a median of 49 (range 33–75) women per month. Women were initially contacted by mail with an introductory letter and study brochure. They were given the option to call a toll-free number if they did not want to be contacted further by the study team. We contacted potentially eligible women by telephone, invited them to participate, and further screened them for eligibility. We considered a participant enrolled after we verified her eligibility, she returned her consent form and Health Insurance Portability and Accountability Act (HIPAA) authorization, and she was randomized to one of the study groups: 1) no, 2) one-month, or 3) two-month HT cessation.

During telephone screening, we asked women who refused participation to report the main reasons for refusal which included: "not willing to stop HT", "too busy", "physician recommended not stopping HT", "concerned about risks", "too ill", "other" and "reason not specified". Women were classified as "refused participation" if they refused and were never randomized or if they were consented and randomized, but then withdrew before any baseline data were obtained (with the exception of information on reasons for nonparticipation). We grouped these women into two categories: 1) those who refused participation because they were "unwilling to stop HT", and 2) those who refused participation for all "other reasons". We only collected one primary reason for refusal for each woman. Since women may have had more than one reason for not wanting to participate, there is likely overlap between the refusal groups. Final percentage of eligible subjects could not be determined as many women refused prior to determining final eligibility.

We modified recruitment materials 12 months into the study to emphasize to women that we welcomed their participation even if they were not sure they could maintain HT cessation, and that they could restart their HT if their symptoms proved intolerable, or for any other reason they ultimately wanted to withdraw from the study.

Data collection

We used self-reported demographic characteristics, duration of HT use, and breast cancer risk information from the Group Health Breast Cancer Surveillance questionnaire [14] completed at the time of the index mammogram, and prior to randomization. Years of enrollment and age were obtained from automated databases. Lifetime Gail model risk score was based on breast cancer risk factors collected at the index mammogram and was calculated using the National Cancer Institute's (NCI) Breast Cancer Risk Assessment Tool. [15] Reasons for declining study participation were collected and maintained in the study recruitment records. Reasons for taking HT were recorded among study participants: to manage symptoms (including vasomotor symptoms, sleep disturbances, mood, vaginal bleeding, vaginal dryness, and sense of well being), prevent or treat osteoporosis, prevent heart disease, doctor told me to, and "other".

Outcome

Factors associated with willingness to stop HT 1–2 months before screening mammogram were evaluated including age, race, ethnicity, years of education, hysterectomy, type and duration of HT use at time of recruitment (ET versus EPT), body mass index (BMI), and breast cancer risk (lifetime Gail model risk score; first degree relative with breast cancer). In addition, we evaluated differences in mammographic breast density (using BI-RADS categories) between participants and nonparticipants.

Analysis

We conducted two main comparisons to evaluate the characteristics of: 1) all participants versus nonparticipants; and 2) participants versus the two main groups of non-participants (refused to stop HT; refused for other reason). Chi-square tests were used to compare differences between categorical variables, Wilcoxon rank-sum and Kruskall-Wallis tests for ordinal variables and t-tests and ANOVA for continuous variables. We used multinomial logistic regression models to estimate the odds ratios for each of our two non-participant groups relative to participants (referent group). Logistic regression models were also used to estimate the odds ratios for refusal for the combined non-participant group relative to participants, controlling for those factors that were associated with non-participation in the univariate analyses (p<0.05). All analyses were run both with and without stratification by HT type (ET, EPT) in the 6 months prior to recruitment to the study. Finally we assessed whether modifications to our recruitment materials influenced who was willing to participate.

RESULTS

Of the 5861 women contacted to participate, 2999 refused (Figure 1). An additional 169 women agreed to participate and were randomized, but withdrew before data collection and are also considered nonparticipants for this analysis (total nonparticipation 54.1%); 125 of the 169 were unwilling to stop HT. Unwillingness to stop HT was most often cited as the reason for non-participation (n=1876;1751+125) and accounted for 59.2% of 3168 nonparticipants. Other common reasons for refusal were not interested or too busy (15.6%). Nearly one in three potentially eligible women invited to participate (N=1876, 32%) refused or withdrew before any participation because they were unwilling to stop HT use. Of those who enrolled in the study, 47% reported that they had tried to quit taking HT in the past and approximately 75% used at least standard doses of estrogen. There were 247 women (16.1%) who did not list a specific symptom as a reason for HT use. Rather, they stated the reason for HT use as: "to prevent or treat osteoporosis", "to prevent heart disease", "doctor told me to", or "other". There were 33 women (2.1%) who did not respond to the question about reason for HT use – it is unknown whether this group of women was taking HT for symptoms.

There were few remarkable distinctions between women who agreed to participate and women who refused, although statistically significant differences were noted (Table 1). Overall, the mean age was 61 years, most women were white with an average BMI of 27.3 kg/m^2, most were taking ET (61%), and 52% had had a hysterectomy. Overall characteristics of participants were no different from non-participants with respect to Hispanic race, HT type (ET vs EPT), dose of ET, family history of breast cancer, and mammographic breast density. Women taking EPT were slightly less willing to discontinue use for 1–2 months prior to mammogram as compared to those women taking ET, but differences were not significant (31.5% EPT vs. 33.4% ET, p=0.18). All other factors did differ between the two groups, but the magnitudes of the differences were not clinically important. Overall, compared to participants, non-participants were older, had less education and lower BMI.

Univariate analyses evaluated the odds of refusal to participate by HT type and by reason for refusal (Table 2). Type of HT used (ET vs. EPT) did not yield different findings with a few minor exceptions - the confidence intervals were wide; any apparent differences should be interpreted cautiously. Among ET users, older aged women, women with lower BMI, non-Caucasian women, or women with high school education or less were more likely to refuse participation, but the latter two findings were only true for women who refused participation for "other reasons". Similarly, among women taking EPT, non-Caucasian women or women with high school education or less were more likely to refuse participation for "other reasons". Women taking EPT had a greater likelihood of participation if they had a first degree relative with breast cancer as compared to those who did not.

After controlling for other factors, the odds of participation did vary by type of HT used (ET vs. EPT) with respect to age, BMI, education and first degree relative with breast cancer, but not by race (Table 3). Among women taking ET, older women (≥71 years) or women with low BMI (<25 kg/m^2) had higher odds of being unwilling to participate as compared with younger women (≤ 50 years) or women with higher BMI (≥25 kg/m^2), respectively. This association was not observed among women taking EPT. Conversely, among women taking EPT, those with a high school education or less had higher odds of refusal compared to women with a graduate school education, and women with a first degree family history of breast cancer had lower odds of refusal compared to women without a family history, These associations were not observed among ET users. Again, the confidence intervals for the estimated OR in the stratified multivariable analysis overlapped, and differences by HT type should be interpreted cautiously.

Refining study materials to emphasize our interest in women who were willing to try to quit even if they had doubts about their ability to do so had no impact on who chose to participate (data not shown).

DISCUSSION

We conducted a randomized clinical trial among women due for a screening mammogram to test whether mammographic performance could be improved with short-term HT cessation. One in three potentially eligible women who were invited to participate, knowing that this study might improve mammography performance, refused. Very few differences distinguished women who agreed to participate versus those who refused, emphasizing that among current HT users, overall resistance to HT cessation is strong, even when there may be an immediate personal benefit.

Breast cancer is one of the greatest fears for women considering HT use [16], [17], and this same concern prompts many women to stop HT. [18] Thus, we presumed the majority of women, particularly those taking EPT, would be willing to attempt HT cessation for one or two months on the premise that improved breast cancer screening might be achieved. We were surprised that 54% of women invited to join the study refused and that 59% of women who refused participation did so because of unwillingness to stop HT for 1–2 months, despite recruitment materials explaining that they could resume HT at any time during the study. Perhaps unwillingness to stop HT could be explained by the fact that our study was performed 1–2 years following the major WHI publications describing the risks and benefits of HT. [6], [19] Our other studies have shown the prevalence of HT use in our health plan (and other health plans) fell dramatically after the WHI publications, [3] suggesting that continued HT users are very committed, and might be described as "hard core users". Indeed, 47% of those who agreed to participate had attempted HT cessation in the past and over 84% acknowledged taking HT for symptoms.

We noted only minor differences in the characteristics of women who refused participation based on use of ET versus EPT, and arguably any statistical differences between these groups were clinically insignificant. Women who refused participation had a lower BMI (predominantly ET) than those who agreed to participate. In addition, women who took EPT and agreed to participate had a higher risk of breast cancer (higher percentage of first degree relatives) than those who refused participation, whereas this finding was not observed among ET users. This finding might suggest that our patients have been educated regarding the Women's Health Initiative findings and understand that the WHI results showed an increased risk for breast cancer among EPT users and not among ET users. [5], [6], [19]

Symptom severity is the most common reason that women report for inability to stop HT. [20] Although the women in our study were not asked specifically if refusal to participate was due to concern for return of severe menopausal symptoms, the work of others would suggest that indeed this is commonly the case. [20, 21] Observational studies show that among women who have been on HT for over 1 year and try to quit, 25% resume HT within 6 months. [22] Ness and colleagues reported that reasons for continued HT use included severe symptoms (34%), personal preference (10%), gynecologist recommended (9%), not documented (11%) and other (3%).[21] Although these studies did not specifically address reasons associated with refusal to stop HT for short durations, they suggest that women continue HT use predominantly because of intolerable symptoms, despite known risks. Most likely women who continued or started to use HT following the WHI findings have already made a personal decision that symptom-benefits outweigh risks and potentially they view their personal risks as relatively low.

Others have shown that women who have had a hysterectomy are less likely to quit ET [20] as compared to women who have not had a hysterectomy and are using EPT. Contrary to these findings, we did not find that women taking EPT were more willing to discontinue use for 1–2 months prior to mammogram as compared to those women taking ET (p=0.18), although at baseline, more women overall were taking ET (62%) as compared to women taking EPT (38%). Interestingly, it is well recognized that the characteristics of women who take ET may vary from those of women who take EPT on multiple levels. Women who have had a hysterectomy are more likely to be nonwhite, have higher BMI, lower education and income, increased rates of hypertension, diabetes, hypercholesterolemia and depression, and to be less physically active (all P<0.01). [23,24] Despite these differences, we did not find major differences between those women willing to participate based on estrogen dose or type of HT use (ET versus EPT).

Our study has several limitations. We did not collect data on symptom severity before starting HT, as a number of women had been using HT for many years so we could not fully assess symptom severity as a reason for non-participation. We also did not assess women's understanding regarding HT risks and benefits, or to what degree they had made an informed decision whether to participate or not, based on their understanding of risks.

Several strengths of the study are noted. Despite multiple publications regarding impact of HT discontinuation on breast density and possible mammographic performance, to our knowledge, no one has investigated women's willingness to stop HT before screening mammogram. We were careful to maintain details regarding study non-participation. Very little is known about whether a woman would be willing to stop HT for 1–2 months if she might have improved breast cancer screening as a result. Although our study did not find improved recall rates among women who stop HT for 1–2 months before mammogram, versus women who continued HT use, we did find a decrease in breast density, particularly among women who stop HT use for 2 months. [25] If a larger study were to find improved accuracy of mammogram screening with short-term HT cessation, our study is an important reminder that many women are unwilling to stop HT regardless of potential benefits. Currently, targeting HT discontinuation before mammogram to a sub-population of women does not appear feasible as most characteristics between those willing to stop HT for 1–2 months and women unwilling to stop HT varied little. However, with additional patient education regarding breast cancer risks, it is unknown whether high-risk groups (i.e. women on EPT with a first degree relative with breast cancer) might be more willing to attempt short term HT cessation prior to mammogram.

Acknowledgments

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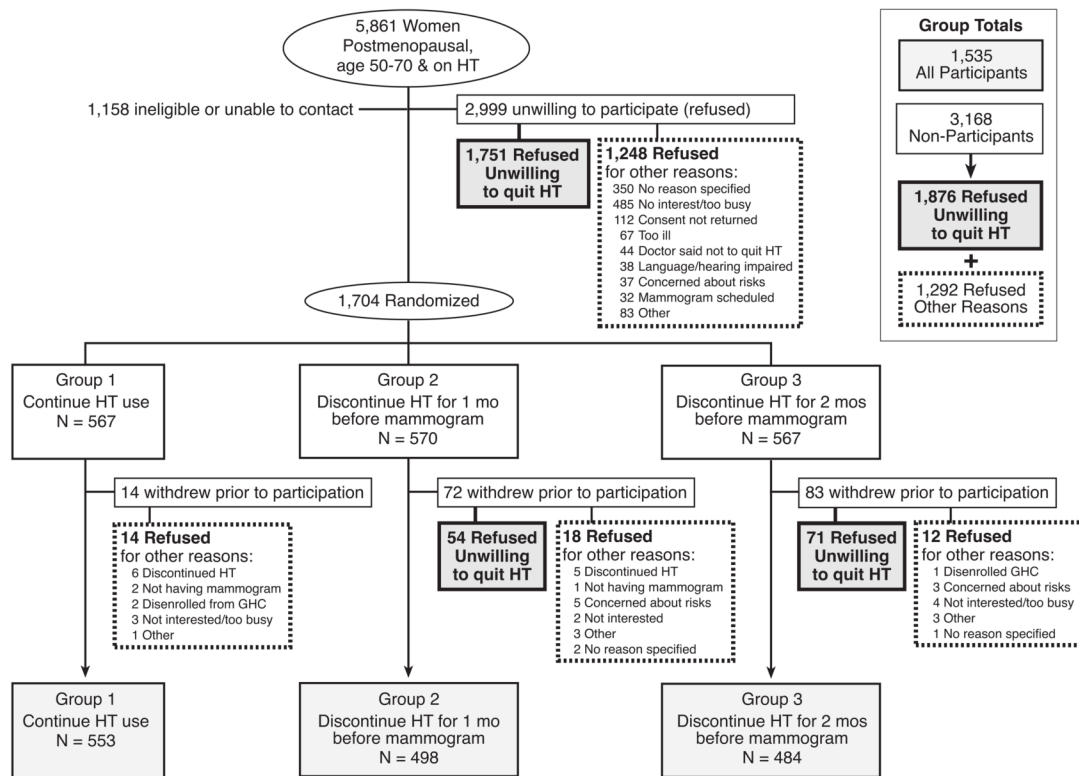
Figure 1.
The Radiological Evaluation And Breast Density (READ) study recruitment and participation
HT = hormone therapy

Table 1

Characteristics of women who refused to participate vs. those willing to participate in the Radiological Evaluation And Breast Density (READ) study.

Characteristics	Unwilling to quit HT	Refused: Other reason	Overall	Willing to Participate
	N = 1876	N= 1292	N = 3168	N = 1535
Age at recruitment, mean (SD)	60.9 (7.6)[†]	61.7 (8.0)[‡]	61.3 (7.7)[‡]	60.4 (7.3)
Age at recruitment				
≤ 55 years	26.5	22.3	24.8	26.7
56–60	28.1	28.2	28.2	29.6
61–65	18.1	21.0	19.3	20.9
66–70	14.6	11.7	13.4	12.3
71+	12.8	16.9	14.5	10.6
Race/ethnicity				
Caucasian	91.5	87.8[‡]	90.0	91.4
African American	2.7	2.3	2.5	2.2
Asian	2.1	5.6	3.6	2.0
Other	3.6	4.4	3.9	4.5
Hispanic				
Yes	2.4	3.3	2.8	2.5
Education				
≤High school	16.7	21.6[‡]	18.7[†]	14.5
Some college	38.8	37.4	38.3	40.7
College graduate	20.3	18.8	19.7	19.7
≥Graduate school	24.1	22.3	23.4	25.1
Hysterectomy				
Yes	50.8[†]	52.4	51.4	54.3
Type of hormone therapy				
Estrogen + progestin	40.1	38.9	39.6	37.6
Unopposed estrogen	59.9	61.2	60.4	62.4
Self-reported duration of HT use from BSRR at index mammogram				
≤ 2 years	9.3	9.3[†]	9.3[†]	10.3
3–4 years	10.8	10.6	10.7	11.7
5–9 years	23.5	19.7	21.9	22.7
10–14 years	19.6	22.1	20.6	20.1
15+ years	36.8	38.4	37.5	35.1
Estrogen dose [*]				
Low	24.8	22.2	23.8	25.3
Medium	58.7	63.4	60.6	62.5
High	16.5	14.4	15.6	12.2
Body mass index in kg/m^2, at index mammogram				
(mean, SD)	27.0 (5.7)[‡]	27.2 (6.0)	27.1 (5.8)[‡]	27.7 (5.7)
(median)	25.8	25.9	25.8	26.6
<25	42.3[‡]	42.7[†]	42.4[‡]	37.5
25 to <30	32.9	28.8	31.2	33.1
30+	24.8	29.5	26.3	29.4
Gail model risk score, lifetime				
<15%	92.2	92.5	92.3	91.3
15 – <20%	5.0	5.1	5.0	5.5
20 – <30%	2.2	1.8	2.1	2.2
≥ 30%	0.6	0.6	0.6	1.0
First degree family history				
Yes	18.1	16.8	17.6	18.2
Mammographic breast density at index mammogram[‡]				
Scattered fibroglandular	34.0	34.4	34.2	34.8
Heterogeneously dense	56.0	56.4	56.1	55.2
Extremely dense	10.0	9.3	9.7	10.0

[‡]p<0.01;

[†]p<0.05, comparing group to women willing to participate

[*] Estrogen dose: Medium = 0.0625 mg conjugated estrogens, 1 mg oral estradiol, 0.050 mg transdermal estradiol; Low = any doses < medium: High= any doses > medium.

Table 2

Likelihood of refusal to participate versus willing to participate in the Radiological Evaluation And Breast Density (READ) study.

	ET			EPT		
	Unwilling to quit HT	Refuse: Other reason	Overall	Unwilling to quit HT	Refuse: Other reason	Overall
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Age at recruitment						
≤55	1.00	1.00	1.00	1.00	1.00	1.00
56–60	0.89 (0.70, 1.14)	1.04 (0.79, 1.36)	0.95 (0.76, 1.18)	1.03 (0.79, 1.35)	1.27 (0.93, 1.73)	1.12 (0.87, 1.43)
61–65	0.83 (0.64, 1.07)	1.13 (0.85, 1.50)	0.94 (0.74, 1.18)	0.96 (0.70, 1.32)	1.33 (0.93, 1.90)	1.09 (0.82, 1.46)
66–70	1.06 (0.80, 1.41)	0.99 (0.72, 1.37)	1.04 (0.80, 1.34)	**1.62 (1.08, 2.42)**	1.58 (0.99, 2.51)	**1.60 (1.10, 2.34)**
71+	1.30 (0.98, 1.73)	**1.90 (1.40, 2.58)**	**1.52 (1.18, 1.97)**	1.00 (0.64, 1.59)	**1.85 (1.15, 2.96)**	1.31 (0.87, 1.96)
Caucasian						
No	0.98 (0.73, 1.31)	**1.42 (1.05, 1.90)**	1.15 (0.89, 1.49)	1.01 (0.65, 1.56)	**1.63 (1.06, 2.53)**	1.25 (0.85, 1.84)
Yes	1.00	1.00	1.00	1.00	1.00	1.00
Hispanic						
No	1.00	1.00	1.00	1.00	1.00	1.00
Yes	0.86 (0.50, 1.50)	1.46 (0.85, 2.49)	1.11 (0.69, 1.77)	1.21 (0.56, 2.60)	1.18 (0.51, 2.75)	1.20 (0.59, 2.42)
Education						
≤High school	1.14 (0.87, 1.51)	**1.67 (1.24, 2.25)**	**1.35 (1.05, 1.73)**	1.43 (0.97, 2.10)	**1.80 (1.20, 2.71)**	**1.57 (1.11, 2.23)**
Some college	1.03 (0.82, 1.30)	1.04 (0.80, 1.34)	1.04 (0.84, 1.27)	0.95 (0.73, 1.24)	1.06 (0.78, 1.43)	0.99 (0.78, 1.27)
College graduate	1.04 (0.79, 1.38)	1.10 (0.80, 1.50)	1.07 (0.83, 1.37)	1.11 (0.82, 1.51)	1.05 (0.74, 1.48)	1.09 (0.83, 1.44)
≥Graduate school	1.00	1.00	1.00	1.00	1.00	1.00
Self-reported duration of HT use from BSRR at index mammogram						
≤2 years	1.00	1.00	1.00	1.00	1.00	1.00
3–4 years	1.10 (0.69, 1.75)	0.92 (0.55, 1.56)	1.02 (0.67, 1.56)	0.97 (0.66, 1.43)	1.05 (0.68, 1.60)	1.00 (0.71, 1.42)
5–9 years	1.09 (0.73, 1.61)	0.97 (0.63, 1.50)	1.04 (0.73, 1.48)	1.23 (0.87, 1.75)	0.97 (0.65, 1.43)	1.13 (0.82, 1.55)
10–14 years	1.06 (0.72, 1.57)	1.22 (0.79, 1.87)	1.13 (0.79, 1.60)	1.16 (0.80, 1.68)	1.26 (0.84, 1.88)	1.20 (0.86, 1.68)
15+ years	1.22 (0.85, 1.75)	1.21 (0.82, 1.80)	1.22 (0.88, 1.68)	1.21 (0.82, 1.79)	1.42 (0.93, 2.17)	1.30 (0.91, 1.85)
Body mass index in kg/m², at index mammogram						
<25	1.00	1.00	1.00	1.00	1.00	1.00
25 to <30	**1.46 (1.18, 1.80)**	**1.26 (1.00, 1.59)**	**1.37 (1.13, 1.66)**	1.12 (0.84, 1.49)	1.01 (0.75, 1.38)	1.07 (0.83, 1.39)
30+	1.18 (0.95, 1.47)	0.94 (0.74, 1.19)	1.07 (0.88, 1.30)	1.12 (0.83, 1.52)	0.80 (0.57, 1.12)	0.98 (0.75, 1.30)
Gail model risk score, lifetime						
<15%	1.00	1.00	1.00	1.00	1.00	1.00
15 – <20%	1.10 (0.74, 1.64)	1.13 (0.74, 1.75)	1.12 (0.78, 1.60)	0.65 (0.41, 1.04)	0.66 (0.39, 1.12)	0.66 (0.43, 1.00)
20 – <30%	1.04 (0.59, 1.86)	0.99 (0.53, 1.87)	1.03 (0.61, 1.72)	1.02 (0.46, 2.23)	0.50 (0.17, 1.46)	0.81 (0.39, 1.70)
≥ 30%	0.71 (0.31, 1.66)	0.71 (0.28, 1.81)	0.71 (0.34, 1.50)	0.50 (0.08, 2.99)	0.37 (0.04, 3.56)	0.45 (0.09, 2.22)
First degree family history						
No	1.00	1.00	1.00	1.00	1.00	1.00
Yes	1.12 (0.89, 1.40)	1.10 (0.86, 1.41)	1.11 (0.90, 1.36)	0.83 (0.62, 1.11)	**0.64 (0.45, 0.90)**	**0.75 (0.57, 0.98)**
Mammographic breast density at index mammogram‡						
Scattered fibroglandular	1.00	1.00	1.00	1.00	1.00	1.00
Heterogeneously dense	1.00 (0.83, 1.20)	0.94 (0.77, 1.15)	0.97 (0.82, 1.15)	1.09 (0.85, 1.39)	1.22 (0.93, 1.60)	1.14 (0.91, 1.42)
Extremely dense	1.17 (0.84, 1.63)	0.90 (0.62, 1.31)	1.06 (0.78, 1.43)	0.87 (0.61, 1.25)	1.03 (0.69, 1.53)	0.93 (0.67, 1.29)

OR=Odds Ratio

Table 3

Multivariable model: likelihood of refusal to participate versus willing to participate in the Radiological Evaluation And Breast Density (READ) study.

	ET	EPT	Overall
	OR* (95% CI)	OR* (95% CI)	OR* (95% CI)
Age at recruitment			
≤ 55	1.00	1.00	1.00
56–60	0.94 (0.75, 1.18)	1.18 (0.91, 1.53)	1.03 (0.87, 1.23)
61–65	0.90 (0.71, 1.15)	1.12 (0.83, 1.52)	0.98 (0.81, 1.18)
66–70	1.00 (0.76, 1.31)	**1.65 (1.12, 2.43)**	1.15 (0.93, 1.44)
71+	**1.43 (1.09, 1.88)**	1.25 (0.82, 1.90)	**1.39 (1.11, 1.74)**
Caucasian			
No	1.17 (0.89, 1.53)	1.22 (0.81, 1.84)	1.18 (0.94, 1.48)
Yes	1.00	1.00	1.00
Education			
≤High school	1.22 (0.94, 1.58)	**1.51 (1.05, 2.17)**	**1.27 (1.04, 1.57)**
Some college	1.04 (0.84, 1.30)	1.00 (0.77, 1.28)	1.03 (0.87, 1.21)
College graduate	1.05 (0.81, 1.37)	1.08 (0.81, 1.44)	1.07 (0.88, 1.30)
≥Graduate school	1.00	1.00	1.00
Body mass index in kg/m², at index mammogram			
<25	**1.30 (1.06, 1.58)**	1.06 (0.81, 1.39)	**1.22 (1.04, 1.43)**
25 to <30	0.98 (0.80, 1.20)	0.98 (0.74, 1.30)	0.99 (0.84, 1.17)
30+	1.00	1.00	1.00
First degree family history			
No	1.00	1.00	1.00
Yes	1.08 (0.88, 1.33)	**0.71 (0.54, 0.93)**	0.94 (0.79, 1.10)

*OR= Odds ratio, adjusted for all other factors listed in the table