Differential Association of Modifiable Health Behaviors with Hot Flashes in Perimenopausal and Postmenopausal Women

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OBJECTIVE: **To determine the association of modifiable factors, such as smoking, body mass index, and alcohol use, with hot flashes, and to ascertain whether the association with hot flashes varies by menopausal stage.**

DESIGN: **A written survey completed by perimenopausal and postmenopausal women enrolling in a randomized, controlled trial of a menopause risk management program in 1999. Survey items included questions on demographics, health status, and health behaviors.**

SETTING: **A Massachusetts-based health maintenance organization.**

PATIENTS/PARTICIPANTS: **Female members, age 40 to 65, excluding women with chronic conditions precluding study participation, were randomly selected from an automated medical record system.**

MEASUREMENTS AND MAIN RESULTS: **The majority of the 287 postmenopausal and 468 perimenopausal women participating in the study were white, college educated, and nonsmoking. Approximately 30% of both groups reported experiencing hot flashes. Separate multivariable logistic regression models were developed for perimenopausal and postmenopausal women to identify correlates of reporting any versus no hot flashes. After controlling for age, race, oral contraceptive use, hormone replacement therapy use, and depression, correlates of hot flashes in perimenopausal women were body mass index ≥25 kg/m^2 (odds ration [OR], 2.00; 95% confidence interval [CI], 1.28 to 3.12) and alcohol use of 1 to 5 drinks per week (OR, 0.52; 95% CI, 0.31 to 0.86). The only significant correlate of hot flashes in the postmenopausal population was high dietary fat intake (OR, 0.35; 95% CI, 0.15 to 0.81).**

CONCLUSION: **Although study respondents were from similiar sociodemographic groups and received their health care in the same health maintenance organization, modifiable factors associated with hot flashes were different for perimenopausal and postmenopausal women.**

KEY WORDS: **menopause; hot flash; BMI; alcohol; smoking; diet.**
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As many as 80% of women experience hot flashes during the menopause transition, with greater than 50% of these women reporting hot flashes for at least 5 years.[1,2] Although many women do not require therapy, 30% to 50% seek pharmacologic treatment for vasomotor symptoms.[3] Of available therapies, estrogen with or without progestin has been the dominant treatment for more than 6 decades.

In 2002, the estrogen-progestin arm of the Women's Health Initiative, a national randomized, controlled trial assessing the effects of hormone replacement therapy (HRT), was prematurely stopped because women taking estrogen and progesterone were more likely to develop breast cancer, thromboembolic events, and cardiac events than women taking placebo.[4] News of these life-threatening side effects enacted a wave of change, with both patients and clinicians seeking alternative methods to HRT for the management of hot flashes.

Although considerable prior research has evaluated treatment alternatives to HRT, epidemiologic studies have not provided a consensus as to whether modifiable health behaviors and characteristics, such as smoking, drinking, and being overweight, have an impact on the likelihood of experiencing hot flashes. Moreover, because menopause is not one homogeneous life event, but rather a transition marked by physiologic stages, health behaviors could affect hot flash prevalence differently depending on menopausal stage.[5]

We used questionnaire data to assess the effect of health behaviors, health characteristics, and demographic factors on the likelihood of reporting bothersome hot flashes, and to evaluate whether any effect might vary by menopausal status. If modifiable health behaviors are associated with vasomotor instability, women and clinicians would have an alternative to managing symptoms—avoidance of behavioral triggers at appropriate stages in the menopausal transition. In the post-Women's Health Initiative era, such an alternative approach would represent an important adjunct to symptom management.

METHODS

Study Population

Study participants were recruited from a mixed-model health maintenance organization serving approximately 800,000 Massachusetts residents. Six thousand women, age 40 to 65, were randomly selected to participate in a randomized trial if they had continuous membership for at least 1 year prior to study enrollment. Women with a diagnosis of dementia, organic brain syndrome, or

Alzheimer's disease were excluded. Once eligible women were identified, investigators obtained permission from the women's primary care providers to invite the patients to participate in a yearlong, randomized, controlled trial of a menopause risk management program.

Patients who enrolled in the trial completed a self-administered, baseline survey in 1999. The analysis reported in this manuscript is based on responses to this initial mailed questionnaire. We analyzed survey results from women describing themselves as perimenopausal or postmenopausal. Perimenopause was defined as a change in menstrual cycle frequency, duration, quantity, or associated premenstrual syndrome-like symptoms during the previous 3 to 11 months. Postmenopause was defined as cessation of periods for 12 months or more,[3] or history of a hysterectomy without oophorectomy and age 55 years or older.

We excluded women with breast, ovarian, or endometrial cancer, bilateral oophorectomy, women missing data for menopausal status or hot flashes, or women younger than 55 with a history of a hysterectomy.

Measurements

The survey contained 38 questions addressing sociodemographic, health behavior, and health status domains. The primary outcome of interest, a self-reported measure of hot flashes, was measured using a single question adapted from the Hunter Women's Health Questionnaire:[6] "Please indicate how bothered you are now and in the past few days by hot flashes: not at all, a little bit, quite a bit, or extremely." Given the small frequencies of women in our sample who experienced hot flashes "quite a bit" or "extremely," the outcome was treated as a dichotomous variable: women not bothered by hot flashes versus women bothered at any level by hot flashes.

Eight self-reported covariates were included in the analysis: body mass index (BMI), alcohol, education, exercise, dietary fat, multivitamin use, parity, and smoking. Body mass index,[7–11] alcohol use,[12–14] education,[11,14–17] exercise,[9,17,18] parity,[8,14] and smoking[9,10,13–16,19,20] were included due to conflicting literature reporting possible associations between these factors and hot flashes. Multivitamin use was included due to conflicting recommendations that vitamin E may improve hot flashes.[21] Dietary fat intake was included to investigate the possible association between elevated BMI and hot flashes.

Body mass index, defined as weight in kilograms divided by height in meters squared, was dichotomized into $<25\ kg/m^2$ and $\geq 25\ kg/m^2$ to identify normal weight and overweight patients, respectively. Underweight patients (BMI $<18.5\ kg/m^2$) comprised 1% of the postmenopausal women and <3% of the perimenopausal women. Inclusion of these women in the "normal weight" category for dichotomous BMI did not alter effect estimates in the final analysis by greater than 10%.[22] Alcohol use was categorized as no alcohol, 1 to 5 drinks per week, and >6 drinks per week. Education was categorized as high school or less, 2 years of college, 4 years of college, and graduate school. Two questions were used to assess exercise on the questionnaire. Moderate exercise was defined as "exercise or work lasting 30 minutes or more without stopping." Weight-bearing exercise was defined as "exercise where your legs bear your body weight, such as walking, jogging, dancing, or weight training." Any exercise was categorized as never, less than once per week, 1 to 2 times per week, and at least 3 times per week. High dietary fat was assessed by intake of red meat, dairy products, saturated oils, fried foods, and baked goods, and was analyzed according to frequencies of daily, 3 times per week, and 1 per week or less. Multivitamin intake and smoking were dichotomous, both measuring current use.

Statistical Analysis

Chi-square and Wilcoxon rank-sum tests were used to compare characteristics of the perimenopausal and postmenopausal women. Unadjusted logistic regression was used to evaluate the relationship between covariates and hot flashes in the perimenopausal and postmenopausal groups. Independent variables associated with reporting hot flashes at the $P \leq .05$ level in the perimenopausal group were introduced into a multivariable logistic regression model for perimenopausal women. A separate model for postmenopausal women, including variables associated with hot flashes at the $P \leq .05$ level in the postmenopausal group, was also developed. This stratification approach was chosen based on the hypothesis that different covariates are associated with hot flashes in each of the two groups, and that effect estimates differ greatly. Although including both sets of women in a single model is technically possible, it would hinder interpretation with little gain in efficiency.

In addition to statistically significant variables from the crude logistic regression analysis, both models included 6 possible confounders identified in the literature: diagnosis of depression,[16,23] depressive symptoms within the prior year,[24,25] current HRT use, current oral contraceptive (OCP) use, race/ethnicity,[8] and age.

Variables that did not achieve statistical significance in unadjusted logistic regression were entered individually into each of the two multivariable models. Order of model entry was determined by the effect estimate of each variable, with lowest priority given to those with effect estimates closest to 1.0. A variable was considered a confounder, and retained in the multivariable model, if its inclusion in the model altered the beta coefficient of any significant predictor by at least 10%.[26] Variables not identified as confounders and not achieving statistical significance when entered into the multivariable models were excluded.

To assess whether the effect size of correlates varied by severity of hot flashes, we conducted ordinal logistic regression including only women with hot flashes. We assessed the impact of each correlate on a 3-level outcome:

"a little bit bothered," "quite a bit bothered," and "extremely bothered" by hot flashes. Separate models were used for perimenopausal and postmenopausal women.

To identify effect modification, we used variables that were statistically significant in each model and evaluated interaction terms between them and all other variables in the models. Statistical analyses were performed using SAS for Windows, version 8.0 (SAS Institute, Inc., Cary, NC).

RESULTS

A total of 1,231 women enrolled in the randomized trial. Of those, 100% completed the baseline survey. Of the 948 perimenopausal and postmenopausal women who completed the survey, 755 women were eligible for analysis. Perimenopausal (*N* = 468) and postmenopausal (*N* = 287) groups differed with respect to age, education, fat intake, multivitamin use, and HRT use (Table 1).

In bivariable analyses of the perimenopausal group, smoking, alcohol use, BMI ≥25 kg/m^2, multivitamin use, and exercise were found to be significantly associated with reporting hot flashes and were included in the multivariable model. Education and exercise were retained in the model as confounders. Interaction terms to assess effect modification between smoking and BMI, depression, age, HRT, race, OCP use, exercise, multivitamin use, and alcohol use revealed a statistically significant interaction between depression and smoking in perimenopausal women. Perimenopausal women with depression who were smokers at the time of the interview were more likely to report bothersome hot flashes than smokers without a history of depression, nonsmokers with a history of depression, and nonsmokers without a history of depression. After adjusting for age, ethnic group, depression, OCP use, and HRT use, the significant correlates of reporting bothersome hot flashes in perimenopausal women were BMI ≥25 kg/m^2 and alcohol use of 1 to 5 drinks per week. Multivitamin use achieved borderline statistical significance (Table 2).

The only bivariable correlate of hot flashes for postmenopausal women was daily consumption of high-fat food.

Table 1. Baseline Characteristics of the Study Participants

	Perimenopausal *N* = 468 *n* (%)	Postmenopausal *N* = 287 *n* (%)	*P* Value[‡]
Age, y	46.5 (3.67)*	55.2 (4.74)*	<.0001
BMI	25.1 (5.89)*	25.8 (5.35)*	.20
BMI ≥25 kg/m^2	194 (41.5)	138 (47.9)	.08
Hot flash by severity			
Mild	119 (25.9)	64 (22.6)	.26
Moderate	32 (7.0)	24 (8.5)	
Extreme	15 (3.3)	4 (1.4)	
Ethnicity			
White	433 (92.5)	270 (93.8)	.56
African American	19 (4.06)	11 (3.82)	
Education			
High school or less	37 (7.92)	59 (20.5)	<.0001
College 2 to 4 years	185 (39.6)	115 (39.9)	
Graduate school	245 (52.5)	114 (39.6)	
Exercise[†]			
Never	43 (9.2)	33 (11.5)	.06
Less than weekly	84 (17.9)	36 (12.5)	
1 to 2 times weekly	158 (33.8)	85 (29.5)	
≥3 times weekly	183 (39.1)	134 (46.5)	
Daily multivitamin	225 (48.1)	165 (57.3)	.02
High dietary fat			
Once weekly or less	147 (31.6)	112 (39.6)	.03
Three times weekly	235 (50.4)	116 (41.0)	
Daily	84 (18.0)	55 (19.4)	
Weekly alcohol			
None	229 (48.9)	154 (53.5)	.49
1 to 5 drinks	161 (34.4)	92 (31.9)	
≥6 drinks	78 (16.7)	42 (14.6)	
Smoker	43 (9.2)	33 (11.5)	.32
HRT use	70 (15.0)	141 (49.0)	<.0001

* *Mean (standard deviation) shown for continuous variables BMI and age.*
[†] *Weight-bearing exercise and moderate aerobic exercise combined.*
[‡] P *values represent comparison between perimenopausal and postmenopausal groups.*
BMI, body mass index; HRT, hormone replacement therapy.

Table 2. Multivariable Logistic Regression Model for Perimenopausal Women

	Odds Ratio*	95% Confidence Interval
Daily multivitamin	1.56	0.99 to 2.44
Smoker	0.64	0.19 to 2.14
Depression	0.87	0.54 to 1.41
High school or less	Reference	Reference
Two-year college	1.73	0.72 to 4.13
Four-year college	1.18	0.48 to 2.91
Graduate school	0.82	0.36 to 1.82
BMI >25 kg/m^2	2.00	1.28 to 3.12
Weekly alcohol		
None	Reference	Reference
1 to 5 drinks	0.52	0.31 to 0.86
>6 drinks	1.47	0.81 to 2.67
Exercise†		
>3 times weekly	Reference	Reference
1 to 2 times weekly	1.30	0.78 to 2.16
Less than weekly	0.76	0.40 to 1.44
Never	1.31	0.59 to 2.88
Interaction term		
Smoker with depression	7.88	1.71 to 36.2

** Adjusted for age, ethnicity, HRT use, OCP use, history of depression, and diagnosis of depression. Model includes the interaction term for depression and smoking.*
† Weight-bearing exercise and moderate aerobic exercise combined.
BMI, body mass index; HRT, hormone replacement therapy; OCP, oral contraceptive.

In the multivariable model, smoking was retained as a confounder. After adjusting for age, ethnic group, depression, OCP use, and HRT use, high dietary fat remained a significant correlate of a decreased likelihood of reporting hot flashes in postmenopausal women (Table 3).

Interaction terms for BMI and dietary fat, multivitamin use, exercise, smoking, and alcohol were entered into both models. No meaningful interactions were identified.

Ordinal logistic regression models of both perimenopausal and postmenopausal women, assessing whether the effect of correlates of hot flashes differed by hot flash severity, lacked adequate power to show any statistically significant findings.

Table 3. Multivariable Logistic Regression Model for Postmenopausal Women

	Odds Ratio*	95% Confidence Interval
High dietary fat		
Once weekly or less	Reference	Reference
Three times weekly	1.05	0.58 to 1.92
Daily	0.35	0.15 to 0.81
Smoking	0.66	0.26 to 1.67

** Adjusted for age, ethnicity, HRT use, OCP use, history of depression, and diagnosis of depression.*
HRT, hormone replacement therapy; OCP, oral contraceptive.

DISCUSSION

The findings from this cross-sectional survey of women age 40 to 65 suggest that potentially modifiable factors, such as BMI, alcohol intake, smoking, and dietary fat intake, may alter the risk of having hot flashes. The impact of these factors on hot flashes may differ by menopausal status.

In our analysis, perimenopausal women with a BMI of ≥25 kg/m^2 were more likely to report hot flashes than women with a BMI of <25 kg/m^2. Body mass index was not associated with hot flashes in postmenopausal women. The observation that women with a BMI above normal range (18.5 to 24.9 kg/m^2) experience more bothersome hot flashes than women with a normal BMI is supported by multiple studies.[7–11] In three of these studies, high BMI was associated with hot flashes in perimenopausal women but not in postmenopausal women. In 1996, den Tonkelaar et al. found that women age 40 to 44 with a BMI ≥25 kg/m^2 experienced more hot flashes than women with a BMI <22 kg/m^2 (odds ratio [OR], 1.70; 95% confidence interval [CI], 1.30 to 2.21); hot flashes of women age 54 to 69 years were not associated with BMI (OR, 0.85; 95% CI, 0.52 to 1.36).[7] Similarly, in a subgroup analysis of the Study of Women Across the Nation (SWAN), early perimenopausal women with a BMI ≥27 kg/m^2 had an increased risk of hot flashes (OR, 1.15; 95% CI, 1.04 to 1.28), while the risk of hot flashes in postmenopausal and late perimenopausal women was not influenced by BMI.[9] More recently, Whitman et al. reported that perimenopausal women with a BMI >30 kg/m^2 were more likely to have any or daily hot flashes (OR, 2.1; 95% CI, 1.5 to 3.0) compared to women with a normal BMI. As in the two prior studies, the hot flashes of the postmenopausal women were not associated with BMI.[10]

In contrast to our findings, some studies have found an association between high BMI and fewer hot flashes,[27] as well as below normal BMI and greater risk of hot flashes.[14,28] Each of these studies included postmenopausal women only, while studies showing high BMI as a risk factor for hot flashes included both perimenopausal and postmenopausal women or perimenopausal women only.

The predominant form of estrogen in postmenopausal women is estrone, produced in adipose tissue by the conversion of androstenedione.[29] This connection between adipose tissue and estrogen production has been used to explain outcomes of studies showing an increased risk of hot flashes in women with low BMI.[14] However, studies evaluating the relationship between serum estrogen levels and hot flashes have shown that estrogen levels correlate poorly with hot flash activity.[23]

Estrogen is only one factor that may explain the association of BMI with hot flashes. Hypothalamic regulation of core body temperature may play a role in hot flash physiology[30,31] and has been shown to be related to menopausal status.[32] Serum androgen levels, shown to decrease as women transition to menopause[33] and in women with elevated BMI,[34] may also contribute to hot flash physiology.[35,36] Despite a lack of consensus in the literature, the majority of studies demonstrate an association between elevated BMI and increased hot flashes. Moreover, this association appears to vary by menopausal status.

In our analysis, perimenopausal women who consumed 1 to 5 alcohol-containing drinks per week reported hot flashes less often than women who drank no alcohol. Alcohol use was not significantly associated with hot flashes in the postmenopausal women. Prior studies have reported an association between alcohol use and hot flashes. In 2001, Freeman et al. found that weekly alcohol use increased hot flashes in perimenopausal women (OR, 1.10; 95% CI, 1.03 to 1.17).[8] Schwingl et al. found that postmenopausal women reporting ever drinking alcohol were more likely to have hot flashes than those who never drank; however, this trend was not statistically significant.[14] One additional study of 11 postmenopausal women found that alcohol use increased the duration and intensity of hot flashes.[13]

Although a causative link between alcohol and hot flashes is not well established, multiple processes exist by which alcohol could impact hot flashes. Estrogen deficiency, measured in women reporting chronic, heavy alcohol use has been attributed to direct toxic effects of alcohol on the ovaries and liver.[37] Mild to moderate alcohol use has also been shown to alter serum estrogen. In a randomized, controlled trial of postmenopausal women and alcohol use, women who drank 1 and 2 drinks per day for 8 weeks increased their serum estrone concentrations by 7.5% and 10.7%, respectively.[38] Alcohol may also affect hypothalamic temperature regulation[39] and serum androgen levels.[38,40,41] Although the mechanism by which alcohol affects hot flashes is unclear, our study suggests that the intake of 1 to 5 alcohol-containing drinks per week may reduce a perimenopausal woman's risk of hot flashes.

Perimenopausal women in our study who reported daily multivitamin use had 56% higher odds of reporting hot flashes compared to women who did not take a multivitamin. This observation was of borderline statistical significance (Table 2). One possible explanation for the tenuous association between multivitamin use and hot flashes may be that symptomatic women used vitamins to try and treat their hot flashes. Supplements, such as vitamin E, are recommended in the literature as adjunctive therapy for hot flashes.[21] However, one randomized, controlled trial in women with breast cancer found vitamin E to be only slightly better than placebo in reducing hot flashes.[42] No studies to date have shown any increased risk for hot flashes with multivitamin use.

Women who take supplements tend to have characteristics typically associated with healthful behavior. Whether multivitamin use is simply a marker for another behavior that contributes to hot flashes cannot be discerned from these data.[43,44] Given the likelihood that other confounding factors exist, our findings of a possible association between multivitamin use and hot flashes must be interpreted with caution.

We did not find a statistically significant association between exercise and hot flashes. In 1998, an analysis of postmenopausal women found that 5% of women reporting a high level of physical activity experienced hot flashes, compared to 14% to 16% of women with little or no weekly exercise (risk ratio [RR], 0.26; 95% CI, 0.10 to 0.71).[18] In 2000, an analysis of women in the SWAN study found that women rating themselves as less physically active were more likely to report hot flashes (OR, 1.24 to 2.33).[9] Other studies, including one randomized, controlled trial,[17] have not found a significant association between exercise and hot flashes.[45–47] Despite clinical guidelines supporting regular physical activity to reduce hot flashes,[48] the association between exercise and hot flashes remains unclear and is not supported by our findings.

Intake of at least 1 high-fat meal per day compared to intake of high-fat food weekly or less was associated with fewer hot flashes in the postmenopausal women in our analysis. Dietary fat did not influence hot flashes in the perimenopausal women. We found no interaction between high-fat intake and BMI, and thus the effect of dietary fat on hot flashes appears to be independent of BMI. As with multivitamin use, dietary fat may be confounded by variables that we were unable to control for, such as the health status of women who reported very low-fat diets.

To our knowledge, the association of dietary fat and hot flashes has not been reported previously. Additional evaluation, using prospectively gathered data and validated food frequency questionnaires, should be performed to assess the possible association between dietary fat and hot flashes.

Most[9,10,16,19,20] but not all[13–15] studies on correlates of hot flashes note an association between smoking and an increased risk of hot flashes. We found smoking to be significantly correlated with hot flashes in perimenopausal women with depression. Smoking was associated with 2-fold increased odds of reporting bothersome hot flashes (OR, 2.19; 95% CI, 1.06 to 4.54). We used interaction terms to assess effect modification between smoking and all other variables in the perimenopausal model. When the only statistically significant interaction term, between smoking and depression, was entered into the model for perimenopausal women, smoking alone was no longer an independent correlate (OR, 0.64; 95% CI, 0.19 to 2.14). This suggests that depression modifies the effect of smoking on hot flashes in perimenopausal women, such that perimenopausal women with a history of depression who smoked at the time of the study were more likely to have hot flashes than nonsmokers with depression. Smoking did not affect the hot flashes of women in the postmenopausal group.

Various mechanisms may contribute to the antiestrogenic effects of tobacco smoke.[49] Smoking is thought to have direct toxic effects on the ovary,[50] leading to menopause an average of 1.7 years earlier in women who smoke compared to nonsmokers.[51] Oral estrogen metabolism is affected by smoking via upregulation of liver metabolism[52] and estradiol clearance by hydroxylation.[53] Smoking has also been shown to alter serum androgen levels, with variable effects by menopausal stage.[54–56]

Given the small number of smokers in our sample and the apparent effect modification of smoking by depression, the role of smoking in the development of hot flashes by menopausal stage requires further investigation.

Limitations

One challenge of hot flash studies is the lack of universally accepted gold standards to define hot flashes and hot flash activity. Individual perceptions of what constitutes a hot flash may vary, making comparisons difficult. Our outcome measure evaluates bothersome hot flashes, rather than hot flash frequency. Because it is less likely for women who are not bothered by their hot flashes to seek medical attention, the degree to which hot flashes are bothersome may provide a more clinically useful measure. Small numbers of women reporting severe hot flashes limited our power to evaluate degree of hot flash bothersomeness as it relates to health behaviors. Ideally, prospective data, in the form of a hot flash diary, would make it possible to measure within-person change in hot flashes and would provide a more accurate measure of the relationship between health behaviors and hot flashes.

In addition, defining stages of menopause is problematic. Perimenopause is typically studied as a single stage of the menopause transition; however, physiologic differences have been shown to occur at early, middle, and late stages within perimenopause.[57] In this study we used a single definition of perimenopause. Using detailed menopausal staging may be a preferred method to evaluate variability in correlates of hot flashes.[5]

The results of this study may not be generalizable to all women due to the limited representation of minority women in the sample. Ethnicity and hot flash frequency were, however, representative of women in Massachusetts. Hot flashes have been reported to occur during the menopause transition in 70% of Massachusetts women, with 30% to 40% reporting bothersome hot flashes.[3] This is consistent with the distribution of bothersome hot flashes (34%) in our sample.

In summary, our findings suggest that modifiable characteristics such as overweight, smoking, alcohol consumption, and low dietary fat intake are associated with bothersome hot flashes. Moreover, the effect of these health characteristics appears to vary by menopausal stage. Observations of prior studies, as well as our own, emphasize the critical need for addressing menopausal status in studies evaluating correlates of hot flashes.

As public interest in identifying alternatives to HRT for hot flash management grows, understanding the contribution of behavior to the existence of hot flashes becomes a central issue. The modification of alcohol use, smoking, and weight in perimenopausal women, to the extent consistent with public health recommendations, may lead to an improvement in hot flashes and to health benefits beyond the management of menopausal symptoms.

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Dr. Riley was primarily responsible for the design and conduct of the data analysis and writing of the manuscript. Dr. Inui was the founding principal investigator of the randomized, controlled trial in which the baseline survey was conducted; he participated in the design and implementation of the trial, development of the survey instruments, and critical review of the manuscript. Dr. Kleinman provided substantial assistance with statistical analyses and critical review of the manuscript. Dr. Connelly provided assistance with all aspects of the study including conception, design, survey instrument development, data acquisition and analysis, and critical review of the manuscript.

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