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## An Intensive Behavioral Weight Loss Intervention and Hot Flushes in Women

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*Drafting of the manuscript:* Huang and Macer. *Critical revision of the manuscript for important intellectual content:* Huang, Subak, Wing, West, Hernandez, and Grady. *Statistical analysis:* Hernandez. *Obtained funding:* Subak, Wing, West, and Grady.

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## Abstract

**Background**—Higher body mass index is associated with worse hot flushes during menopause but the effect of weight loss on flushing is unclear.

**Methods**—Self-administered questionnaires were used to assess bothersome hot flushes in a 6-month randomized controlled trial of an intensive behavioral weight loss program (intervention) vs a structured health education program (control) in 338 women who were overweight or obese and had urinary incontinence. Weight, body mass index, abdominal circumference, physical activity, calorie intake, blood pressure, and physical and mental functioning were assessed at baseline and at 6 months. Repeated-measures proportional odds models examined intervention effects on bothersome hot flushes and potential mediating factors.

**Results**—Approximately half of participants (n=154) were at least slightly bothered by hot flushes at baseline. Among these women, the intervention was associated with greater improvement in bothersome flushes vs control (odds ratio [OR] for improvement by 1 Likert category, 2.25; 95% confidence interval [CI], 1.20–4.21). Reductions in weight (OR, 1.32; 95% CI, 1.08–1.61; per 5-kg decrease), body mass index (1.17; 1.05–1.30; per 1-point decrease), and abdominal circumference (1.32; 1.07–1.64; per 5-cm decrease) were each associated with improvement in flushing, but changes in physical activity, calorie intake, blood pressure, and physical and mental functioning were not related. The effect of the intervention on flushing was modestly diminished after adjustment for multiple potential mediators (OR, 1.92; 95% CI, 0.95–3.89).

**Conclusion**—Among women who were overweight or obese and had bothersome hot flushes, an intensive behavioral weight loss intervention resulted in improvement in flushing relative to control.

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Hot flushes are among the most common concerns of women during menopause and persist for 5 or more years past menopause in as many as one-third of women.<sup>1</sup> These common symptoms can negatively affect women's quality of life by disrupting sleep, interfering with work and leisure activities, and exacerbating anxiety and depression.<sup>2</sup> The pathophysiology of hot flushes is poorly understood, although alterations in hypothalamic thermoregulation<sup>3</sup> or endothelial function<sup>4</sup> are hypothesized to play a role. With recent randomized trials documenting the adverse effects of long-term postmenopausal hormone therapy,<sup>5,6</sup> there has been growing interest in identifying alternate strategies to alleviate these symptoms.

In multiple observational studies,<sup>7–9</sup> women with a higher body mass index (BMI; calculated as weight in kilograms divided by height in meters squared) have reported more frequent or severe hot flushes compared with women with a lower BMI. It is currently unclear whether the observed relationship between a higher BMI and flushing is owing to greater insulation from peripheral fat, metabolic factors associated with visceral fat, or other clinical or lifestyle factors that exert independent effects on flushing. In addition, evidence of a beneficial effect of weight loss on hot flushes in women who were overweight is lacking, and some studies<sup>10–12</sup> have raised concerns that women who increase their physical activity in an effort to lose weight may experience worse flushing symptoms.

We conducted an ancillary study to the Program to Reduce Incontinence by Diet and Exercise (PRIDE) study, a randomized controlled trial of an intensive behavioral weight loss intervention vs a structured education program to promote weight loss in women who were overweight or obese and had urinary incontinence.<sup>13</sup> Our goal was to assess whether the intensive weight loss intervention was associated with significant improvement in bothersome hot flushes compared with the control program. We also examined whether changes in weight, BMI, abdominal circumference, physical activity, calorie intake, blood

pressure, and overall physical or mental functioning were associated with improvement in bothersome hot flushes in this population.

## METHODS

### PRIDE PARTICIPANTS

PRIDE was a randomized controlled trial that evaluated the effect of a 6-month intensive lifestyle and behavioral change intervention vs a structured health education program to promote weight loss in 338 women who were overweight or obese and had urinary incontinence. Characteristics of the study sample, inclusion and exclusion criteria, sample size calculations, and interventions have been previously reported.<sup>13</sup> Briefly, women had to be at least 30 years of age, have a BMI of 25 to 50, and report in a voiding diary at least 10 episodes of incontinence per week to be eligible. Women were excluded if they reported any condition that would prevent them from safely participating in an intensive diet and exercise program without medical supervision and if they had undergone medical therapy for incontinence or weight loss in the previous month.

Participants were recruited from the local community at the Miriam Hospital in Providence, Rhode Island, and the University of Alabama at Birmingham and randomly allocated in a 2:1 ratio to the life style and behavior change program (intervention; n=226) or the structured education program (control; n=112). Although participants were aware of their treatment assignment, research personnel collecting outcomes data were masked to treatment. All participants gave informed consent to participate in the study, and the institutional review boards at both clinical sites and the coordinating center approved all study procedures.

### INTERVENTIONS

Participants in the intensive intervention group were assigned to a lifestyle and behavior change program modeled after the Diabetes Prevention Program and Look AHEAD (Action for Health in Diabetes) trials,<sup>14,15</sup> which were designed to produce an average loss of 7% to 9% of initial body weight by 6 months. This included weekly 1-hour group sessions led by experts in nutrition, exercise, and behavior change during which women were encouraged to increase physical activity to at least 200 minutes per week using brisk walking or activities of similar intensity and to record exercise time daily. In addition, women were instructed to follow a reduced-calorie diet (1200–1500 kcal/d), offered sample meal plans modeling appropriate food selections, and provided with vouchers for Slim-Fast (Unilever, Englewood Cliffs, New Jersey), a meal-replacement product.

Women randomized to the control group were assigned to participate in 1-hour group educational sessions at months 1, 2, 3, and 4 providing general information about weight loss, physical activity, healthy eating habits, and health promotion (the structured health education program). Participants in the intervention and control groups were also given pamphlets providing information about urinary incontinence but not about hot flushes or other menopausal symptoms.

### OUTCOME MEASURES

Bothersome hot flushes and other menopausal symptoms were assessed at baseline and at 6 months using questionnaire measures originally developed for the Breast Cancer Prevention Trial<sup>16</sup> and administered in subsequent prevention and hormone therapy trials involving middle-aged and older women.<sup>17</sup> Specifically, participants were asked to indicate how bothersome hot flashes or hot flushes had been in the past month, using a 5-point Likert scale with the response categories *not at all*, *slightly*, *moderately*, *quite a bit*, and *extremely*.

Other demographic and clinical characteristics were assessed using self-administered questionnaires at baseline and at 6 months. Physical activity was assessed using the validated Paffenbarger physical activity questionnaire,<sup>18</sup> which provides an estimate of the average kilocalories of energy expended per week based on participant self-report about walking, stair climbing, and medium-intensity and heavy-intensity physical activity. Dietary calorie intake was assessed using the validated Block food frequency questionnaire,<sup>19</sup> which estimates average daily diet and nutrient intake based on participant self-report of usual eating habits during the past 6 months. Overall physical and mental functioning was assessed using the physical and mental summary components of the 36-Item Short Form Health Survey (SF-36) functioning scales, scored from 0 to 100, with higher scores indicating better overall functioning.<sup>20</sup>

Participants were weighed at baseline and at 6 months using digital scales (Tanita BWB 800; Tanita Corporation of America Inc, Arlington Heights, Illinois), and height was measured using wall-mounted stadiometers. Abdominal circumference was measured after voiding using a tape measure (Gulick II Tape Measure model 67020; Creative Engineering Inc, Plymouth, Massachusetts). Heart rate and blood pressure were measured with the patient in the sitting position (Dinamap Monitor Pro 10; GE Healthcare, Buckinghamshire, England), following standardized protocols.<sup>14</sup>

## STATISTICAL ANALYSES

All analyses were restricted to participants who reported being at least slightly bothered by hot flushes at baseline and thus had the potential to show improvement during the trial. Among these participants, the baseline characteristics of women randomized to the intervention vs control group were compared by mixed linear regression for normally distributed continuous variables, ranked mixed linear regression for nonnormally distributed continuous variables, and proportional odds regression for categorical variables, using generalized estimating equations.<sup>21</sup> All models controlled for clinical site and accounted for clustering of outcomes among women participating in the same behavioral change or health education sessions.<sup>22</sup> Subsequent analyses of intervention effects were adjusted for any characteristics that were unequally distributed between the intervention vs control group at baseline.

Among participants reporting bothersome hot flushes at baseline, the effects of the intervention vs control program on weight, BMI, abdominal circumference, physical activity, calorie intake, blood pressure, and overall physical and mental functioning during 6 months were examined using mixed linear regression for normally distributed continuous variables and ranked mixed linear regression for nonnormally distributed continuous variables,<sup>22</sup> again controlling for clinical site and accounting for clustering of outcomes among women participating in the same behavior change or health education sessions. Intervention effects on self-reported hot flushes during 6 months were then examined using repeated-measures proportional odds regression, using all available data from any study visit, after checking that there were no major violations of the proportional odds assumption. Repeated-measures regression was chosen to ensure efficient use of information about time-dependent covariates and to minimize loss of information resulting from loss to follow-up. Odds ratios (ORs) in these models were scaled to reflect improvement in hot-flush bothersomeness by 1 Likert category (eg, from *quite a bit* to *moderately* or *moderately* to *slightly* bothersome). To address possible bias introduced by the use of oral or transdermal estrogen use or selective serotonin reuptake inhibitor medication use, intervention effect models were run with and without adjustment for estrogen and selective serotonin reuptake inhibitor use at baseline and at 6 months.

Next, associations between change in weight, BMI, abdominal circumference, physical activity, calorie intake, blood pressure, and overall physical and mental functioning and change in hot flushes during 6 months were examined using repeated-measures proportional odds regression, combining data from the intervention and control groups. Finally, to assess for possible mediation of intervention effects by change in these variables, additional repeated-measures proportional odds models were developed to compare the effects of the intervention vs control program on hot flushes while adjusting for improvement in weight, BMI, abdominal circumference, physical activity, calorie intake, blood pressure, and overall functioning. All analyses were performed using SAS statistical software, version 9.2 (SAS Institute Inc, Cary, North Carolina).

## RESULTS

Of the 338 participants in PRIDE, 226 were randomized to the intensive weight loss intervention and 112 to the control group (Figure 1). Approximately half of participants in each group (99 in the intervention and 55 in the control group) reported being at least slightly bothered by flushing at baseline and were eligible for our analyses. Of these 154 participants, 141 (91.6%) provided data on hot flushes at 6 months. Self-reported hot-flush bothersomeness was not associated with frequency of urinary incontinence at baseline (OR, 0.99; 95% confidence interval [CI], 0.91–1.08).

The mean (SD) age of participants with baseline hot flushes was 53(8) years (Table 1). Eighty-nine of 147 participants (60.5%) reported no menstrual period in the past year, and 19 (12.3%) reported using oral or transdermal estrogen. Just more than half (n=79) indicated that they were at least moderately bothered and 13 (8.4%) indicated that they were extremely bothered by flushing at baseline. Compared with control individuals, women randomized to the intervention reported slightly greater physical activity at baseline but did not differ significantly with regard to other characteristics, including hot flushes (Table 1).

Among women reporting hot flushes at baseline, those randomized to the intervention group were significantly more likely to remain in the study and contribute hot-flush data at 6 months compared with controls (96 of 99 women [96.9%] in the intervention group vs 45 of 55 controls [81.8%];  $P=.001$ ). Women who were missing hot-flush data at 6 months reported being less physically active at baseline than women with complete data (mean [SD] kilocalories per week, 366[423] vs 79[1011];  $P=.08$ ) but did not differ significantly with respect to other characteristics, such as mean weight (98 vs 96 kg;  $P=.11$ ), BMI (38 vs 36;  $P=.25$ ), abdominal circumference (114 vs 108 cm;  $P=.25$ ), calorie intake (2226 vs 2013 kcal;  $P=.99$ ), systolic blood pressure (128 vs 129 mm Hg;  $P=.16$ ), diastolic blood pressure (73 vs 72 mm Hg;  $P=.98$ ), SF-36 physical functioning scores (49 vs 48;  $P=.81$ ) and mental functioning scores (49 vs 49;  $P=.52$ ), and self-reported hot flushes (49% vs 38% with at least moderately bothersome symptoms;  $P=.61$ ).

Among women who were at least slightly bothered by flushing at baseline, the intensive lifestyle intervention was associated with significantly greater decreases in weight, BMI, abdominal circumference, and systolic and diastolic blood pressure relative to the control group (Table 2). No statistically significant effect of the intervention on self-reported physical activity, total calorie intake, or overall physical or mental functioning was observed.

After 6 months, 65 of 141 participants (46.1%) with baseline hot flushes reported improvement in flushing by at least 1 category of bothersomeness, 53 (37.6%) reported no change, and 23 (16.3%) reported worsening by at least 1 category (Figure 2). In repeated-measures proportional odds regression, the intensive intervention was associated with more



than a 2-fold increased odds of improvement in flushing by 1 category of bothersomeness relative to the control group (OR, 2.23; 95% CI, 1.19–4.15;  $P=.01$ ). This effect was not diminished after adjustment for baseline differences in self-reported physical activity between intervention groups (adjusted OR, 2.25; 95% CI, 1.20–4.21;  $P=.01$ ), after adjustment for use of oral or transdermal estrogen at any visit (2.06; 1.09–3.89;  $P=.03$ ), or after adjustment for use of selective serotonin reuptake inhibitor medications at any visit (2.24; 1.19–4.23;  $P=.01$ ).

In aggregate analyses of all women reporting bothersome hot flushes at baseline, decrease in weight, decrease in BMI, and decrease in abdominal circumference were each associated with improvement in self-reported hot flushes during 6 months (Table 3). No significant associations between changes in physical activity, calorie intake, blood pressure, or overall self-reported physical and mental functioning and change in flushing bothersomeness were observed.

The effect of the intensive intervention on bothersome hot flushes was modestly decreased and no longer statistically significant after adjustment for improvement in weight (adjusted OR for improvement in flushing by 1 category of bothersomeness, 1.92; 95% CI, 0.94–3.92). Similarly modest decreases in intervention effects were noted after adjustment for BMI (adjusted OR, 1.88; 95% CI, 0.93–3.81) or abdominal circumference (1.88; 0.95–3.70). After cumulative adjustment for change in all potential mediating variables (ie, BMI, abdominal circumference, physical activity, calorie intake, blood pressure, and physical and mental functioning; weight was excluded because of collinearity with BMI), the effect of the intensive intervention on flushing remained modestly decreased and nonsignificant (OR, 1.92; 95% CI, 0.95–3.89).

## COMMENT

In this randomized controlled trial of an intensive behavioral weight loss intervention vs a structured health education program in women who were overweight or obese and had urinary incontinence, women with bothersome hot flushes who were randomized to the intensive intervention reported significantly greater improvement in flushing bothersomeness after 6 months compared with controls. Improvements in weight, BMI, and abdominal circumference (but not self-reported physical activity, calorie intake, overall physical and mental functioning, or measured blood pressure) were associated with improvement in bothersome hot flushes in this population. The effect of the intensive intervention on bothersome hot flushes was partly but not completely explained by improvements in weight, BMI, and abdominal circumference.

Multiple observational studies have documented that women with a higher BMI report more frequent or severe hot flushes during menopause, but the mechanisms underlying this association are poorly understood. Women who are overweight or obese are known to have higher circulating estrogen levels as a result of adipocyte-based aromatization of estrone and conversion of androstenedione to estrone, which might be expected to decrease rather than increase the severity of their menopausal symptoms. Recently proposed explanations for the observed association between BMI and hot flushes have included greater insulation against heat loss owing to increased peripheral fat,<sup>23</sup> abnormal sympathetic neural activity associated with increased visceral fat,<sup>24</sup> and alterations in leptin and other cytokines expressed by adipocytes that affect thermoregulatory function.<sup>25</sup> Alternatively, women who are overweight or obese may differ in psychological or social factors that affect their subjective experience of and willingness to report symptoms such as hot flushes.

Our findings indicate that women who are overweight or obese and experience bothersome hot flashes may also experience improvement in these symptoms after pursuing behavioral weight loss strategies; however, improvements in weight or body composition may not be the only mediators of this effect. Given that the behavioral intervention in PRIDE could not be masked, 1 possible explanation for the apparent incomplete mediation of the intervention effect by weight loss is that participants' reporting of their symptoms at 6 months was influenced by knowledge of their treatment assignment. It is notable, however, that women randomized to the intensive intervention did not report greater improvement in other quality-of-life outcomes, such as physical or mental functioning as measured by the SF-36, compared with controls, even though these were also self-reported outcomes with the potential to be influenced by knowledge of treatment assignment. Furthermore, because the primary outcome of the PRIDE trial was change in frequency of urinary incontinence rather than improvement in menopausal symptoms, participants were given no special counseling about hot flashes and had no particular reason to expect that their flushing symptoms would be influenced by the study intervention.

Several previous studies of physical activity interventions have reported conflicting effects on menopausal symptoms, with one nonrandomized trial suggesting that physical activity is protective against hot flashes,<sup>26</sup> another randomized trial suggesting that physical activity may worsen hot flashes,<sup>10</sup> and other studies reporting no effect on flushing.<sup>27–29</sup> Prior interventional studies were not confined to women with hot flashes at baseline, however, and detection of intervention effects tended to be limited by the low prevalence of baseline symptoms. In our study, we did not find that increased self-reported physical activity was associated with either improvement or worsening in bothersome flushing among women who were symptomatic at baseline, and change in physical activity did not explain intervention effects. Physical activity may be overestimated when assessed by self-report,<sup>30</sup> however, and it is possible that more objective or precise quantification may have yielded a different pattern of associations with flushing symptoms.

Limited previous research has explored the role of calorie consumption and other dietary factors in influencing women's experience of hot flashes.<sup>31–33</sup> Although we did not find an association between total calorie intake and self-reported bothersome hot flashes in our study, it is possible that the effects of the PRIDE intervention on hot flashes may be mediated by changes in consumption of specific nutrient components or the timing of meals, and further research involving more detailed analysis of dietary habits may be helpful in addressing this issue.

Several other limitations of this research should be noted. First, participants in PRIDE had urinary incontinence at baseline, which may limit the generalizability of our findings to women without incontinence. Urinary incontinence is associated with decreased overall health and depression in women, which have the potential to influence the perceived bothersomeness of other health-related symptoms. To date, however, epidemiologic research has not supported an association between incontinence and menopause in women,<sup>34</sup> and in the PRIDE population itself, we found no evidence that women with more bothersome hot flashes had more severe or frequent incontinence at baseline.

Second, hot flashes were assessed by a single self-report measure emphasizing the bothersomeness of symptoms during the past month, which may be vulnerable to memory and reporting biases and which may reflect not only the frequency of symptoms but also the effect of symptoms on women's sense of well-being. Additional research using more detailed self-report measures of flushing frequency, such as hot-flush symptom diaries, may be helpful in confirming these findings and in assessing for possible differential effects on flushing frequency vs bothersomeness.

Finally, a greater proportion of women were lost to follow-up in the control than in the intervention group. If women who were lost to follow-up experienced greater improvement in hot flushes than those who remained in the study, this could result in overestimation of the main intervention effect on flushing in these analyses. Nevertheless, participants who drop out of weight management trials are often those who experience less improvement in weight or associated symptoms, and thus we might expect the greater loss to follow-up in the control group to bias our results toward the null.

From a clinical perspective, our findings suggest that women who are overweight or obese and have bothersome hot flushes may be counseled that behavioral weight loss efforts may decrease the burden of their symptoms. Further research is needed to assess for other biophysiologic factors associated with weight loss that may influence these symptoms in women who are overweight or obese. It should also evaluate whether women's perceptions of self-management success while attempting to change their lifestyle or lose weight may modify their experience of these symptoms.

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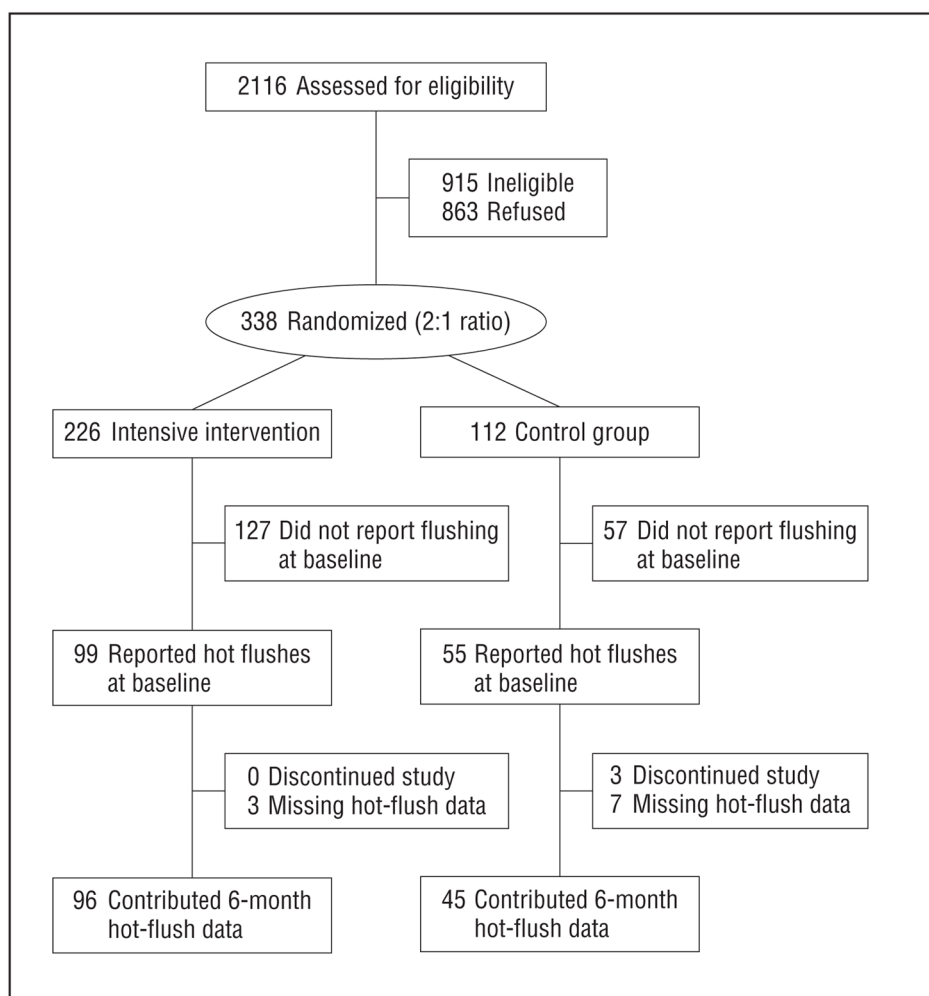
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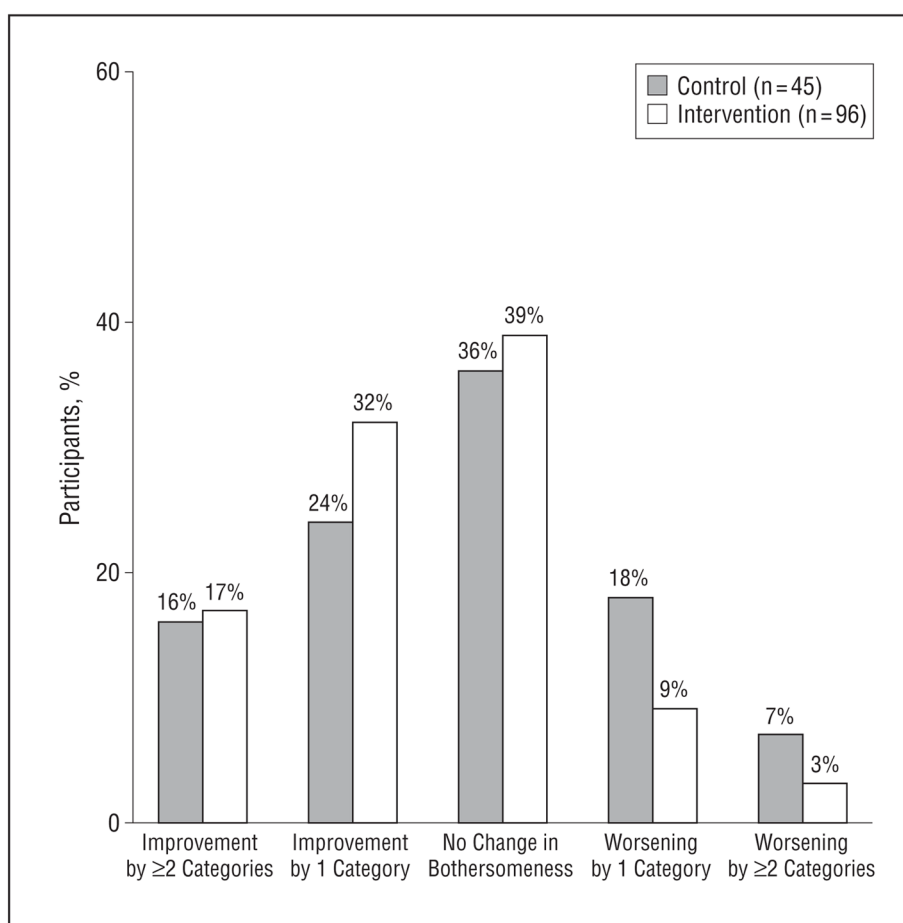


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**Figure 1.** Recruitment, randomization, retention, and hot-flush reporting in the Program to Reduce Incontinence by Diet and Exercise trial.



**Figure 2.** Change in bothersome hot flushes during 6 months among women reporting bothersome symptoms at baseline by treatment assignment.  $P=.01$  for difference in improvement in bothersome flushing by 1 Likert category between the intervention and control groups using repeated-measures proportional odds regression.

**Table 1**

Characteristics of Participants Who Were at Least Slightly Bothered by Hot Flushes at Baseline by Treatment Assignment<sup>a</sup>

Characteristic	Intervention (n=99)	Control (n=55)	P Value <sup>b</sup>
Demographics			
Age, mean (SD), y	53 (8)	53 (8)	.77
White, No. (%)	70 (71)	43 (78)	.27
Gynecologic variables, No. (%)			
No menses for >1 year	53 (58)	36 (65)	.34
Hysterectomy	36 (36)	17 (31)	.40
Bilateral oophorectomy	19 (20)	11 (20)	.99
Physical activity, No. (%) <sup>c</sup>			
<500 kcal/wk	53 (54)	35 (64)	.02
500–1000 kcal/wk	15 (15)	11 (20)	
1001–2000 kcal/wk	17 (17)	6 (11)	
>2000 kcal/wk	14 (14)	3 (5)	
Total calorie intake, mean (SD), kcal/d <sup>d</sup>	2193 (1038)	2235 (1055)	.99
Overall functioning, mean (SD)			
SF-36 physical component score <sup>e</sup>	47.8 (8.2)	47.5 (8.8)	.81
SF-36 mental component score <sup>e</sup>	49.8 (9.5)	47.0 (11.6)	.52
Current medications, No. (%)			
Systemic or transdermal estrogen	11 (11)	8 (14)	.44
Selective serotonin reuptake inhibitor	22 (22)	13 (24)	.83
Physical examination findings			
Weight, mean (SD), kg	99 (17)	92 (15)	.11
Body mass index, mean (SD)	37 (6)	36 (5)	.25
Abdominal circumference, mean (SD), cm	109 (13)	107 (13)	.25
Systolic blood pressure, mean (SD), mm Hg	129 (14)	127 (15)	.98
Diastolic blood pressure, mean (SD), mm Hg	72 (9)	72 (9)	.16
Hot flushes, No. (%)			
Slightly bothersome	48 (48)	27 (49)	.61
Moderately bothersome	30 (30)	11 (20)	
Quite a bit bothersome	13 (13)	12 (22)	
Extremely bothersome	8 (8)	5 (9)	

Abbreviation: SF-36, 36-Item Short Form Health Survey.

<sup>a</sup>Data were missing or incomplete for 2 participants for oophorectomy and 7 participants for last menstrual period in the intervention group.

<sup>b</sup>P values were derived from mixed linear regression for normally distributed continuous variables, ranked mixed linear regression for nonnormally distributed continuous variables, and proportional odds regression for categorical variables, controlling for clinical site and correlation of outcomes within treatment groups.

<sup>c</sup>Assessed via the Paffenbarger activity questionnaire,<sup>18</sup> which provides an estimate of the kilocalories of energy expended per week.

<sup>d</sup>Assessed via the Block food frequency questionnaire<sup>19</sup> based on participant self-report of eating habits.



<sup>e</sup> Scores on the physical and mental components of the SF-36 functioning questionnaires<sup>20</sup> are scaled from 0 to 100, with higher scores indicating better overall functioning.

**Table 2**

Change in Weight, Body Composition, Physical Activity, Dietary Intake, Blood Pressure, and Overall Functioning During 6 Months Among Women With Baseline Bothersome Hot Flushes by Treatment Assignment<sup>a</sup>

Characteristic	Change Between Baseline and 6 Months		
	Intervention (n=99)	Control (n=55)	P Value <sup>b</sup>
Weight, kg	−7.5 (6.2)	−2.0 (3.7)	<.001
Body mass index	−2.8 (2.3)	−0.8 (1.4)	<.001
Abdominal circumference, cm	−5.6 (7.3)	−2.3 (5.6)	.01
Physical activity, kcal/wk	735 (1358)	562 (1051)	.43
Total dietary calorie intake, kcal/d	−717 (937)	−488 (980)	.09
Systolic blood pressure, mm Hg	−6.1 (12.5)	−0.2 (13.9)	.01
Diastolic blood pressure, mm Hg	−1.8 (8.6)	1.9 (8.3)	.03
SF-36 physical component score	2.1 (10.4)	−0.2 (8.5)	.09
SF-36 mental component score	1.7 (10.2)	2.0 (11.0)	.87

Abbreviation: SF-36, 36-Item Short Form Health Survey.

<sup>a</sup>Data are presented as mean (SD) unless otherwise indicated.

<sup>b</sup>P values obtained from mixed linear regression for normally distributed continuous variables and from ranked mixed linear regression for nonnormally distributed continuous variables, controlling for clinical site and accounting for clustering of outcomes within treatment groups.

**Table 3**

Relationship of Change in Weight, Body Composition, Physical Activity, Blood Pressure, and Overall Functioning to Change in Self-reported Bothersome Hot Flashes During 6 Months

Change in Variable	OR (95% CI) for Improvement in Flushing by 1 Likert Category <sup>a</sup>
Decrease in weight, per 5 kg	1.32 (1.08–1.61) <sup>b</sup>
Decrease in body mass index, per 1 point	1.17 (1.05–1.30) <sup>b</sup>
Decrease in abdominal circumference, per 5 cm	1.32 (1.07–1.64) <sup>b</sup>
Increase in physical activity, per 100 kcal/wk	1.07 (0.92–1.24)
Decrease in total dietary calorie intake, per 100 kcal/d	1.00 (0.99–1.00)
Decrease in systolic blood pressure, per 10 mm Hg	1.00 (0.98–1.03)
Decrease in diastolic blood pressure, per 10 mm Hg	1.02 (0.98–1.06)
Increase in SF-36 physical component score, per 10 U	0.97 (0.59–1.60)
Increase in SF-36 mental component score, per 10 U	0.95 (0.72–1.26)

Abbreviations: CI, confidence interval; OR, odds ratio; SF-36, 36-Item Short Form Health Survey.

<sup>a</sup>The ORs were derived from repeated-measures proportional odds regression and adjusted for clinical site and the baseline value of each variable (ie, weight, body mass index, abdominal circumference, physical activity, dietary calorie intake, blood pressure, or SF-36 physical or mental component summary score), controlling for correlation from repeated measures on study participants.

<sup>b</sup> $P < .05$ .