Obesity

Effects of a Mindfulness-Based Weight Loss Intervention in Adults with Obesity: A Randomized Clinical Trial

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Objective: To determine whether adding mindfulness-based eating and stress management practices to a diet-exercise program improves weight loss and metabolic syndrome components.

Methods: In this study 194 adults with obesity were randomized to a 5.5-month program with or without mindfulness training and identical diet-exercise guidelines. Intention-to-treat analyses with multiple imputation were used for missing data. The primary outcome was 18-month weight change.

Results: Estimated effects comparing the mindfulness to control arm favored the mindfulness arm in (a) weight loss at 12 months, −1.9 kg (95% CI: −4.5, 0.8; $P = 0.17$), and 18 months, −1.7 kg (95% CI: −4.7, 1.2; $P = 0.24$), though not statistically significant; (b) changes in fasting glucose at 12 months, −3.1 mg/dl (95% CI: −6.3, 0.1; $P = 0.06$), and 18 months, −4.1 mg/dl (95% CI: −7.3, −0.9; $P = 0.01$); and (c) changes in triglyceride/HDL ratio at 12 months, −0.57 (95% CI: −0.95, −0.18; $P = 0.004$), and 18 months, −0.36 (95% CI: −0.74, 0.03; $P = 0.07$). Estimates for other metabolic risk factors were not statistically significant, including waist circumference, blood pressure, and C-reactive protein.

Conclusions: Mindfulness enhancements to a diet-exercise program did not show substantial weight loss benefit but may promote long-term improvement in some aspects of metabolic health in obesity that requires further study.

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Introduction

Obesity and metabolic syndrome are among the most pressing public health issues in the United States today (1). Key features of metabolic syndrome include central obesity, impaired glucose metabolism, lipid abnormalities, and hypertension (2) with resultant increased risk of type 2 diabetes, cardiovascular disease, stroke, and mortality (3,4). Age-adjusted prevalence of metabolic syndrome in the United States was 34% from 1999 to 2006 (5).

Modest weight loss usually improves metabolic risk factors (6). However, weight loss maintenance is challenging. A meta-analysis of over 80 weight loss programs found weight loss of 5–9% after 6 months, yet half the weight was regained after 4 years (7). One factor that disrupts weight

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loss efforts and contributes to metabolic dysfunction is psychological stress. Over one in four Americans report overeating or eating unhealthy foods to manage stress (8). Animal, epidemiological, and mechanistic studies have linked stress to dysregulated eating, weight gain, impaired glucose metabolism, abdominal adiposity, and lipid abnormalities (9-11). Individuals also eat mindlessly in response to external cues and the rewarding value of food, overriding homeostatic hunger and satiety signals, which can be exacerbated by stress (12,13). However, stress management and techniques that promote increased responsiveness to homeostatic signals regulating food intake are not core components of most weight loss programs.

Meditation interventions, including mindfulness-based approaches, can be effective in reducing psychological stress (14). Mindfulness meditation, which cultivates awareness of present-moment experience with a nonjudging attitude, is theorized to promote adaptive self-regulation, which is thought to be key to maintaining long-term eating habits, particularly in the face of stress (15). Evidence suggests that mindfulness-based interventions improve eating behaviors, weight management, and metabolic health (16-22), but rigorous long-term randomized-controlled trials are limited (14). To address this gap, we performed a randomized-controlled trial to estimate the effects of adding mindfulness components to a diet-exercise program on weight loss and cardiometabolic risk factors in adults with obesity over a 5.5-month intervention period with a subsequent 1 year of follow-up. We hypothesized that the mindfulness intervention relative to the active control would show greater improvements in maintenance of weight loss and cardiometabolic risk factors up to 1 year after intervention termination.

Methods

Study design

We randomized adults with obesity in a 1:1 ratio to a 5.5-month diet-exercise intervention with or without mindfulness components. Participants were assessed at baseline and 3, 6, 12, and 18 months from intervention initiation. The primary outcome was 18-month weight change. The University of California, San Francisco (UCSF) Committee on Human Research approved study procedures and participants provided informed consent. The intervention was provided free of charge at UCSF; participants were compensated for assessment visits.

Participants

Eligibility criteria included body mass index (BMI) between 30 and 45.9, abdominal obesity (waist circumference > 102 cm for men; > 88 cm for women), and age 18 or older. Exclusion criteria included diabetes mellitus, fasting glucose ≥ 126 mg/dl, or hemoglobin A1c (HbA1c) between 6.0% and 6.5% with an abnormal oral glucose tolerance test and current weight loss diet or taking medications that may affect weight. See Supporting Information, Table S1 for further eligibility criteria.

Participant flow

We recruited participants for a weight loss study comparing two programs involving diet, exercise, and stress management from the community using fliers, newspaper advertisements, online postings, and referrals at UCSF clinics. Participants were enrolled in six rounds from July 2009 to February 2012. Assessments were completed in October 2013.

A computer-generated random allocation sequence using random block sizes of four to eight was programmed by a database manager not involved in enrollment. No other staff had access to the randomization sequence. The project director (PM) accessed the allocation sequence using a programmed database that could not be altered once randomized condition was revealed.

Intervention groups

Diet and exercise guidelines. Both interventions included identical diet-exercise guidelines presented in 45-min segments per session. The dietary component recommended healthy food choices that emphasized modest calorie reduction (typically 500 kcal/day), including decreasing calorie-dense nutrient-poor foods, decreasing simple carbohydrates and substituting whole grains, and increasing consumption of fresh fruits and vegetables, healthy oils, and proteins. The exercise component emphasized increasing daily activity and moderate-intensity exercise, primarily through walking, and strength training (see Supporting Information, Methods).

Mindfulness intervention. The mindfulness intervention added mindfulness training for stress management, eating, and exercise. Meditation practices, modeled on the mindfulness-based stress reduction program, included sitting meditation, loving kindness, and yoga postures (23). Mindful eating practices, modeled on the Mindfulness-Based Eating Awareness Training program, were designed to enhance awareness and self-regulation of physical hunger, stomach fullness, taste satisfaction, food cravings, emotions, and other eating triggers in the context of reduced caloric intake (16,17,24). Mindful walking included awareness of sensory experience, posture, and alignment (25). Home practice guidelines included meditation practice for up to 30 min a day/6 days a week, eating meals mindfully, and use of mini-meditations.

Active control intervention. To control for attention, social support, expectations of benefit, food provided during the mindful eating exercises, and home practice time in the mindfulness intervention, the control intervention included additional nutrition and physical activity information, strength training with exercise bands, discussion of societal issues concerning weight loss, snacks, and home activities. We controlled for a mindfulness approach to stress management by including progressive muscle relaxation and cognitive-behavioral training in the control group, although at a lower dose than in the mindfulness intervention (see Supporting Information, Methods and Figure S1 for more details of both intervention groups).

Both interventions included 16 sessions lasting 2 to 2.5 h (12 weekly, 3 biweekly, and 1 monthly) and one all-day session (6.5 and 5 h in the mindfulness and control interventions, respectively) over 5.5 months. Additional diet, exercise, and stress management content in the control intervention was shortened by 30 min in sessions 9–16 to increase participant acceptability with the primary goal to match groups on expectations of benefit. Based on pilot testing, we felt that longer sessions might decrease perceived benefit. The mindfulness intervention was led by one of three mindfulness meditation instructors and co-led by the same registered dietitian (except for one cohort). The control intervention was led by one of three registered dietitians masked to study hypotheses. Participants had three individual consultations with instructors.

Measurements

Participants were assessed between 8 and 10 A.M. (with occasional exceptions) under fasting conditions. Weight, height, blood pressure, and waist circumference were measured (see Supporting Information, Methods). Staff was not masked to group assignment; as feasible, staff either conducted assessments, or coordinated intervention sessions to minimize unmasking. A blood specimen was obtained for glucose, lipids, HbA1c, insulin, and C-reactive protein. Staff performing assays was masked to group assignment.

Statistical analysis

We performed intention-to-treat analyses on change in weight and cardiometabolic outcomes, using independent *t*-tests to compare means between arms using observed data. We compared these analyses of observed data to the primary analyses, mixed models that used multiple imputation to replace missing data, based on guidelines for reporting and interpreting results of multiple imputation analyses (26). Missing data were handled using SAS version 9.4 (SAS Institute Inc) procedures PROC MI and MIANALYZE. Imputation models for each outcome variable included values at other time points, attendance (counting the all-day session as two) and its interaction with arm, and an arm × round interaction term (ROUNDARM) to adjust for clustering effects. One thousand datasets were imputed for each outcome using the fully conditional specification method with predictive mean matching. We compared these results with nonimputed mixed models adjusting for ROUNDARM. For both types of models, arm, time, and their interaction were included as fixed effects, and person and ROUNDARM as random effects. Nonimputed models produced estimates similar to those of imputed models (Supporting Information, Table S2).

Power calculation. In our pilot study (16), we found a 2.0 kg between-group difference in weight change among participants with obesity post-intervention. We expected a smaller difference in the present trial due to an active comparison and a longer follow-up period. We planned for 200 participants based on pilot data and available resources. We estimated 85% power to find $P < 0.05$ if the true difference was 1.1 kg.

Secondary analyses of mindfulness instructors. Anonymous qualitative feedback from participants and qualitative supervisor assessments of session recordings during the trial raised some concerns that mindfulness teaching by one instructor (C) might be less effective than that of other mindfulness instructors (A and B). As a post-hoc analysis, we, therefore, categorized rounds by mindfulness instructor (A/B vs. C) and examined arm × categorized round interactions on outcomes, and also compared differences between mindfulness groups led by instructors A/B to all control groups and contemporaneous control groups We further compared instructor C to instructor A/B groups on instructor helpfulness ratings on a 1- to 4-point scale from anonymous questionnaires administered throughout the intervention (see Supporting Information, Methods).

Results

We randomized 194 participants to two arms (Figure 1) with similar baseline characteristics (see Table 1). Session attendance was similar for the mindfulness and control arms (74.7% vs. 71.2%, respectively; $P = 0.55$), as was 18-month retention (81% vs. 71%, respectively; $P = 0.13$). Mindfulness participants, on average, reported meditating 2.1 (SD = 1.2) hours/week (70% of recommendations) and eating 57% (SD = 29) of meals mindfully (see Supporting Information, Table S3 for additional adherence results). Participants with missing data at 18 months had lower attendance and baseline HbA1c levels; were younger, less educated, and more likely to be non-White (Supporting Information, Table S4). Mindfulness compared to control participants with missing 18-month data reported greater decreases in expectations of benefit from pre- to post-randomization, attended fewer sessions, tended to have better baseline lipid profiles, and, among those with post-randomization data, showed nonsignificant patterns of less improvement in metabolic risk factors (Supporting Information, Tables S5 and S6). No serious adverse events were observed in either intervention arm.

Weight loss

Between-group estimates of weight loss generally became larger over time with estimates favoring the mindfulness arm (see Table 2; Supporting Information, Table S7 for body mass index). At 12 months, group differences became most pronounced with a difference of −1.9 kg (95% CI: −4.5, 0.8; $P = 0.17$) in imputation analyses; observed data analyses estimated a slightly larger difference, −2.1 kg (95% CI: −4.3, 0.05; $P = 0.06$). At 18 months, the group difference was largely maintained in imputation analyses, −1.7 kg (95% CI: −4.7, 1.2 kg; $P = 0.24$): the mindfulness arm lost 4.2 kg (95% CI: −6.2, −2.2 kg), whereas the control arm lost 2.4 kg (95% CI: −4.5, −0.3 kg). Observed data analyses yielded similar results.

Cardiometabolic outcomes

At 12 months, group differences in fasting glucose levels favored the mindfulness arm, −3.1 mg/dl (95% CI: 26.3, 0.1; $P = 0.06$), and, at 18 months, differences were statistically significant, −4.1 mg/dl (95% CI: −7.3, −0.9; $P = 0.01$), in imputation analyses. At 18 months, glucose levels did not change substantially in the mindfulness arm, −0.31 mg/dl (95% CI: −2.5, 1.9), but increased in the control arm, 3.8 mg/dl (95% CI: 1.5, 6.1). Observed data analyses were consistent.

At 12 months, group differences in the triglyceride/HDL ratio favoring the mindfulness arm were statistically significant, −0.57 (95% CI: −0.95, −0.18; $P = 0.004$), in imputation analyses. The triglyceride/HDL ratio decreased in the mindfulness arm, −0.29 (95% CI: −0.54, −0.04), and tended to increase in the control arm, 0.28 (95% CI: −0.01, 0.57). At 18 months, the group difference was attenuated, −0.36 ($P = 0.07$), although the observed data analysis remained statistically significant (−0.41, $P = 0.04$).

Similarly, at 12 months, group differences in triglycerides favored the mindfulness arm, −17.6 mg/dl (95% CI: −33.6, −1.7; $P = 0.03$), in imputation analyses. Triglycerides decreased in the mindfulness arm, −14.3 mg/dl (95% CI: −24.8, −3.8), but did not change substantially in the control arm, 3.4 mg/dl (95% CI: −8.6, 15.3). At 18 months, group differences were attenuated in both imputation (−9.7 mg/dl, $P = 0.23$) and observed data analyses (−8.9 mg/dl, $P = 0.24$; Figure 2).

At 18 months, group differences in other metabolic and inflammatory outcomes did not approach statistical significance in imputation analyses (see Table 2 and Supporting Information, Table S7 for total cholesterol). However, observed data analyses indicated that the

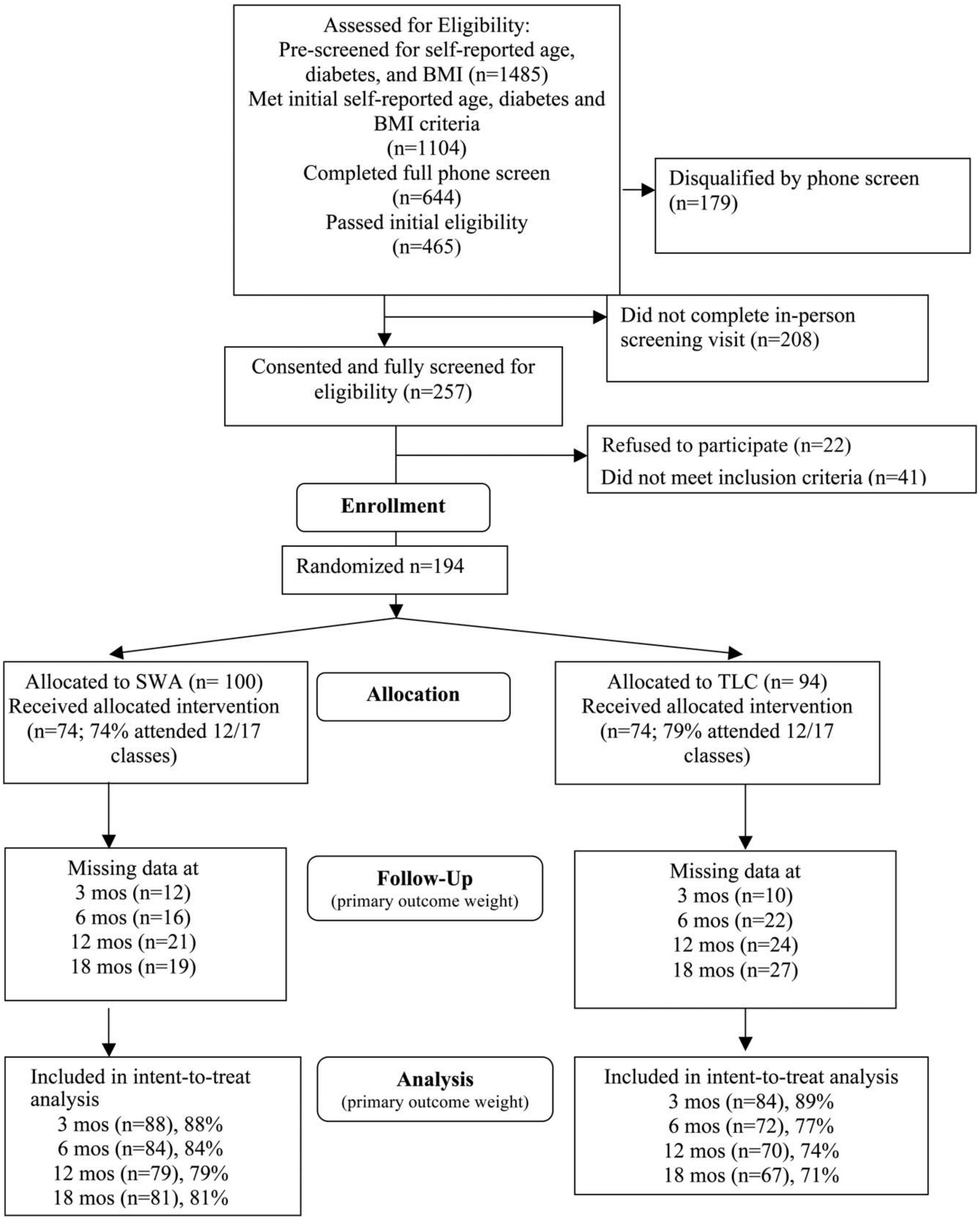

Figure 1 Participant flowchart. There were 1485 individuals who contacted us in response to advertisements for this trial, 216 individuals who were fully eligible, and 194 individuals who met eligibility criteria and elected to enroll in the trial.

mindfulness arm tended to show improvements over the control arm in HOMA ($P = 0.07$), HDL ($P = 0.05$), and C-reactive protein ($P = 0.09$).

Secondary analyses of mindfulness instructors

Mindfulness instructor C was rated as less helpful during the intervention (mean = 3.50; SD = 0.7) than instructors A/B (mean = 3.68; SD = 0.5; $P = 0.045$). Significant interactions ($P < 0.05$) were found between arm and rounds categorized by mindfulness instructor (A/B vs. C) on weight, BMI, fasting glucose, HOMA, and HbA1c, with a marginally significant effect for waist circumference ($P = 0.08$). Follow-up analyses indicated that at 18 months, instructor C participants lost less weight, −2.0 kg (95% CI: −4.7, 0.7), compared to instructor A/B participants, −6.3 kg (95% CI: −9.1, −3.6; $P = 0.02$; Table 3 and Figure 3). This difference persisted after adjusting for participant age, gender, education, and ethnicity (Supporting Information, Table S8). A comparison of mindfulness instructors A/B to the control arm indicated a difference of 3.9 kg favoring the mindfulness group (95% CI: −7.4, −0.4 kg; $P = 0.03$; Table 3). Mindfulness groups led by instructors A/B also had greater 18-month reductions in BMI (Supporting Information, Table S9) and waist circumference (Table 3) compared to Instructor C groups ($P = 0.02$ and $P = 0.05$, respectively) and the control arm ($P = 0.02$ and 0.03, respectively). Similar results were found if we restricted control groups to those enrolled in the same rounds as those led by instructors A/B, indicating that differences favoring mindfulness instructor A/B groups were unlikely to be due to temporal patterns of participant enrollment (Supporting Information, Table S10). Specifically, for weight, mindfulness instructor A/B groups lost 6.3 kg at 18 months and the control groups enrolled in the same round lost 0.9 kg, a difference of 5.4 kg (95% CI: −9.0, −1.8; $P = 0.004$).

Discussion

We examined the impact of adding mindfulness training to a diet-exercise weight loss program in adults with obesity. Participants receiving mindfulness training had a nonstatistically significant 1.7 kg greater weight loss at 18 months on average compared to control participants. Because this additional weight loss is not likely to confer clinical benefit, these results do not support adding mindfulness components to diet-exercise programs to enhance weight loss. Nevertheless, these results should not be viewed as conclusive evidence against the inclusion of mindfulness components in weight loss programs. The 95% confidence interval included weight loss advantages that may be clinically important.

Findings from secondary outcomes provide modest support for potential benefits of adding mindfulness components to diet-exercise programs for obesity. Overall, we assessed 11 outcomes related to weight, metabolic syndrome, or cardiovascular risk. Ten of these outcomes favored the mindfulness group at 12 months, and 9 at 18 months, some with statistically significant differences. We found a statistically significant 4.1 mg/dl difference in fasting glucose favoring the mindfulness arm at 18 months. The difference was primarily due to an increase of 2.5 mg/dl/year in the control arm and maintenance of glucose levels in the mindfulness arm. The increase in glucose levels among control participants is similar to increases observed in persons at risk of type 2 diabetes in other studies, such as the control group in the Diabetes Prevention Program (about 2 mg/dl/year), suggesting that an expected increase in fasting glucose over time was prevented among mindfulness participants (27). In population studies, each increase of 1 mg/dl in fasting glucose in the range typical of participants in this study corresponds to a 1–2%

TABLE 1 Baseline characteristics of study participants

Variable	Mindfulness ($n = 100$)	Control ($n = 94$)
Age, mean (SD) (years)	47.2 (13.0)	47.8 (12.4)
Sex, No. (%), female	79 (79)	81 (86)
Ethnic Origin, No. (%)		
European	65 (65.0)	50 (53.0)
African	13 (13.0)	12 (12.8)
Asian/Pacific Islander	8 (8.0)	11 (11.7)
Latina/Latino	7 (7.0)	16 (17.0)
Native American	0 (0.0)	2 (2.1)
Other	7 (7.0)	3 (3.2)
Education, No. (%), bachelor's degree[a]	69 (69.7)	56 (59.6)
Weight, mean (SD) (kg)	97.7 (14.1)	96.7 (14.8)
Body mass index, mean (SD)[b]	35.4 (3.5)	35.6 (3.8)
Waist circumference, mean (SD) (cm)	112.9 (9.7)	112.7 (10.6)
Glucose, mean (SD) (mg/dl)	86.6 (8.7)	85.5 (7.7)
HOMA, mean (SD)[c]	2.2 (1.4)	2.4 (1.8)
HbA1c, mean (SD) (%)	5.6 (0.4)	5.6 (0.3)
Lipids, mean (SD) (mg/dl)		
Total cholesterol	198.5 (37.5)	196.4 (34.8)
LDL cholesterol	117.2 (31.3)	117.3 (31.0)
HDL cholesterol	55.7 (15.0)	54.9 (13.0)
Triglycerides	128.0 (68.1)	121.0 (45.1)
Triglyceride/HDL ratio	2.6 (1.8)	2.4 (1.3)
Blood pressure, mean (SD) (mm Hg)		
Systolic	122.4 (16.6)	124.1 (16.8)
Diastolic	70.7 (10.7)	70.5 (9.5)
C-reactive protein, mean (SD) (mg/l)	5.4 (5.5)	4.7 (4.2)
Medications, No. (%)		
Lipid lowering	11 (11.0)	9 (9.6)
Blood pressure	16 (16.0)	21 (22.3)
Antidepressant	17 (17.0)	16 (17.0)
Metabolic syndrome, No. (%)[d]	28 (28.0)	27 (28.7)

No significant differences were observed between groups at baseline using independent samples t-tests ($P < 0.05$).
[a]One participant in the mindfulness arm was missing education data.
[b]Calculated as weight (kg) divided by height (m^2).
[c]HOMA is an abbreviation for homeostatic homeostasis model assessment of insulin resistance and is defined as (glucose × insulin/(40 × 33.25)).
[d]The criteria for metabolic syndrome were based on the guidelines developed by the National Cholesterol Program's Adult Treatment Panel III report. Metabolic syndrome was defined as the presence of three or more risk factors: increased waist circumference (88 cm for women; 102 cm for men); elevated triglycerides (≥150 mg/dl) or medication use; low HDL cholesterol (<50 mg/dl in women; <40 mg/dl in men) or medication use; hypertension (≥130/≥85 mm Hg) or medication use; and impaired fasting glucose (≥110 mg/dl).
HOMA, homeostatic model assessment (insulin resistance); HbA1c, hemoglobin A1c (glycosylated hemoglobin); LDL, low-density lipoprotein; HDL, high-density lipoprotein.
SI conversion factors: To convert HDL, LDL, and total cholesterol values to millimoles per liter, multiply by 0.0259; to convert triglycerides to millimoles per liter, multiply by 0.0113; to convert glucose values to millimoles per liter, multiply by 0.0555.

TABLE 2 Intention-to-treat analyses of changes in cardiometabolic outcomes

	N	Observed				Multiple imputation			
		Mean (SE) change				Mean (SE) change			
Measure	M, C	Mindfulness	Control	Difference (M-C), mean (95% CI)	*P* value	Mindfulness	Control	Difference (M-C), mean (95% CI)	*P* value
Weight (kg)									
3m	88, 84	−3.9 (0.4)	−3.3 (0.4)	−0.6 (−1.8, 0.6)	0.34	−3.5 (0.8)	−3.1 (0.9)	−0.4 (−2.7, 2.0)	0.77
6m	84, 72	−5.2 (0.6)	−4.0 (0.7)	−1.2 (−3.0, 0.6)	0.19	−4.5 (0.9)	−3.3 (0.9)	−1.2 (−3.7, 1.3)	0.34
12m	79, 70	−5.1 (0.8)	−3.0 (0.8)	−2.1 (−4.3, 0.0)	0.06	−4.4 (0.9)	−2.5 (1.0)	−1.9 (−4.5, 0.8)	0.17
18m	81, 65	−5.0 (0.9)	−3.2 (1.0)	−1.7 (−4.4, 0.9)	0.20	−4.2 (1.0)	−2.4 (1.0)	−1.7 (−4.7, 1.2)	0.24
Waist circumference (cm)									
3m	88, 84	−3.0 (0.5)	−2.5 (0.5)	−0.5 (−2.0, 0.9)	0.50	−2.7 (0.9)	−2.2 (1.0)	−0.5 (−3.2, 2.1)	0.69
6m	84, 72	−4.8 (0.6)	−4.3 (0.7)	−0.5 (−2.3, 1.4)	0.63	−4.3 (1.0)	−3.7 (1.0)	−0.6 (−3.3, 2.2)	0.69
12m	79, 70	−4.5 (0.9)	−2.6 (1.2)	−1.9 (−4.3, 0.4)	0.11	−4.0 (1.0)	−2.0 (1.1)	−2.0 (−4.9, 0.9)	0.18
18m	81, 65	−4.8 (0.9)	−3.6 (1.0)	−1.2 (−3.9, 1.4)	0.37	−4.3 (1.1)	−2.7 (1.2)	−1.6 (−4.7, 1.6)	0.33
Glucose (mg/dl)									
3m	89, 84	−0.57 (0.7)	0.46 (0.7)	−1.04 (−3.07, 0.99)	0.32	−0.16 (1.0)	0.34 (1.1)	−0.50 (−3.42, 2.43)	0.74
6m	84, 72	−0.17 (0.8)	0.74 (0.9)	−0.90 (−3.29, 1.49)	0.46	0.03 (1.1)	0.98 (1.1)	−0.95 (−4.03, 2.13)	0.54
12m	79, 70	−0.06 (1.0)	3.26 (1.1)	−3.32 (−6.15, −0.49)	0.02	0.31 (1.1)	3.38 (1.2)	−3.07 (−6.27, 0.13)	0.06
18m	81, 66	−0.44 (1.0)	3.11 (1.1)	−3.55 (−6.35, −0.76)	0.01	−0.31 (1.1)	3.80 (1.2)	−4.10 (−7.32, −0.89)	0.01
HOMA									
3m	88, 84	−0.107 (0.2)	0.002 (0.2)	−0.11 (−0.63, 0.42)	0.68	0.023 (0.23)	−0.026 (0.23)	0.05 (−0.60, 0.70)	0.88
6m	83, 72	−0.276 (0.19)	0.002 (0.20)	−0.28 (−0.82, 0.27)	0.32	−0.115 (0.23)	−0.029 (0.25)	−0.09 (−0.76, 0.59)	0.80
12m	77, 69	−0.236 (0.22)	0.537 (0.23)	−0.77 (−1.39, −0.15)	0.02	−0.121 (0.25)	0.461 (0.28)	−0.58 (−1.32, 0.15)	0.12
18m	79, 66	−0.110 (0.23)	0.500 (0.25)	−0.61 (−1.26, 0.05)	0.07	−0.032 (0.23)	0.420 (0.27)	−0.45 (−1.16, 0.26)	0.21
HbA1c (%)									
3m	89, 84	−0.007 (0.03)	−0.022 (0.03)	0.02 (−0.06, 0.09)	0.67	−0.001 (0.05)	−0.006 (0.05)	0.01 (−0.12, 0.13)	0.94
6m	84, 72	−0.064 (0.03)	−0.028 (0.03)	−0.04 (−0.11, 0.04)	0.32	−0.042 (0.05)	0.001 (0.05)	−0.04 (−0.17, 0.09)	0.52
12m	79, 70	−0.078 (0.03)	−0.046 (0.03)	−0.03 (−0.11, 0.05)	0.43	−0.062 (0.05)	−0.023 (0.05)	−0.04 (−0.17, 0.09)	0.56
18m	81, 66	−0.085 (0.03)	−0.038 (0.03)	−0.05 (−0.13, 0.03)	0.24	−0.046 (0.05)	0.013 (0.05)	−0.06 (−0.19, 0.07)	0.38
LDL (mg/dl)									
3m	89, 84	−5.0 (2.0)	−6.7 (2.1)	1.7 (−3.9, 7.3)	0.56	−4.1 (2.3)	−5.1 (2.4)	1.1 (−5.6, 7.7)	0.75
6m	84, 72	−0.9 (2.1)	−3.7 (2.3)	2.8 (−3.3, 8.9)	0.36	−0.2 (2.4)	−3.7 (2.7)	3.6 (−3.5, 10.6)	0.32
12m	79, 70	1.6 (2.1)	−4.7 (2.2)	6.3 (0.4, 12.3)	0.04	0.1 (2.5)	−5.0 (2.7)	5.1 (−2.1, 12.2)	0.16
18m	81, 66	−1.5 (2.2)	−4.7 (2.4)	3.2 (−3.2, 9.6)	0.33	−1.4 (2.6)	−3.7 (2.8)	2.3 (−5.2, 9.9)	0.54
HDL (mg/dl)									
3m	89, 84	−1.8 (0.8)	−3.6 (0.9)	1.9 (−0.5, 4.2)	0.12	−1.7 (1.0)	−3.2 (1.0)	1.5 (−1.3, 4.3)	0.29
6m	84, 72	0.4 (0.9)	−1.0 (1.0)	1.4 (−1.4, 4.1)	0.32	−0.6 (1.1)	−0.3 (1.1)	−0.3 (−3.3, 2.8)	0.87
12m	79, 70	0.1 (1.0)	−1.6 (1.0)	1.7 (−1.1, 4.5)	0.24	−1.5 (1.1)	−2.1 (1.1)	0.6 (−2.5, 3.7)	0.72
18m	81, 66	0.4 (1.0)	−2.5 (1.1)	2.9 (0.0, 5.8)	0.05	−1.0 (1.1)	−2.4 (1.1)	1.4 (−1.8, 4.6)	0.39

TABLE 2. (continued).

Measure	N	Observed				Multiple imputation			
		Mean (SE) change				Mean (SE) change			
	M, C	Mindfulness	Control	Difference (M-C), mean (95% CI)	*P* value	Mindfulness	Control	Difference (M-C), mean (95% CI)	*P* value
Triglycerides (mg/dl)									
3m	89, 84	−14.7 (4.3)	−8.0 (4.4)	−6.7 (−18.7, 5.3)	0.27	−11.6 (4.9)	−8.0 (5.1)	−3.6 (−17.6, 10.4)	0.61
6m	84, 72	−25.0 (4.8)	−9.7 (5.2)	−15.2 (−29.0, −1.4)	0.03	−19.9 (5.1)	−5.1 (5.6)	−14.8 (−29.6, 0.1)	0.05
12m	79, 70	−16.1 (5.5)	−1.1 (5.8)	−15.0 (−30.6, 0.6)	0.06	−14.3 (5.3)	3.4 (6.1)	−17.6 (−33.6, −1.7)	0.03
18m	81, 66	−11.9 (5.1)	−3.0 (5.7)	−8.9 (−23.8, 6.0)	0.24	−12.8 (5.2)	−3.1 (6.1)	−9.7 (−25.6, 6.2)	0.23
Triglyceride/HDL ratio									
3m	89, 84	−0.28 (0.1)	−0.02 (0.1)	−0.26 (−0.57, 0.04)	0.09	−0.24 (0.1)	−0.06 (0.1)	−0.18 (−0.53, 0.18)	0.32
6m	84, 72	−0.58 (0.1)	−0.16 (0.1)	−0.42 (−0.79, −0.06)	0.02	−0.46 (0.1)	−0.12 (0.1)	−0.33 (−0.70, 0.03)	0.07
12m	79, 70	−0.37 (0.2)	0.14 (0.2)	−0.52 (−0.97, −0.07)	0.03	−0.29 (0.1)	0.28 (0.1)	−0.57 (−0.95, −0.18)	0.004
18m	81, 66	−0.30 (0.1)	0.11 (0.1)	−0.41 (−0.81, −0.02)	0.04	−0.27 (0.1)	0.09 (0.1)	−0.36 (−0.74, 0.03)	0.07
C−reactive protein (mg/l)									
3m	88, 84	−1.3 (0.5)	−0.4 (0.5)	−0.9 (−2.2, 0.4)	0.17	−1.1 (0.5)	−0.2 (0.5)	−0.9 (−2.3, 0.5)	0.21
6m	84, 72	−1.3 (0.4)	−0.6 (0.4)	−0.8 (−1.9, 0.3)	0.18	−1.3 (0.5)	−0.8 (0.5)	−0.5 (−1.9, 0.9)	0.48
12m	78, 70	−0.9 (0.5)	−0.1 (0.5)	−0.8 (−2.2, 0.6)	0.28	−0.5 (0.6)	−0.1 (0.6)	−0.4 (−2.1, 1.2)	0.59
18m	81, 66	−1.1 (0.5)	0.2 (0.5)	−1.3 (−2.7, 0.2)	0.09	−0.9 (0.5)	0.4 (0.6)	−1.3 (−2.9, 0.3)	0.11
Systolic blood pressure (mm Hg)									
3m	86, 84	−7.5 (1.5)	−7.8 (1.5)	0.3 (−3.8, 4.4)	0.89	−8.2 (1.9)	−6.5 (1.9)	−1.8 (−7.1, 3.5)	0.51
6m	84, 72	−4.9 (1.5)	−6.7 (1.6)	1.7 (−2.6, 6.1)	0.43	−5.7 (1.9)	−4.6 (2.0)	−1.1 (−6.6, 4.4)	0.69
12m	79, 70	−2.7 (1.6)	−4.2 (1.7)	1.6 (−2.9, 6.1)	0.49	−2.8 (2.0)	−1.5 (2.1)	−1.3 (−7.0, 4.4)	0.65
18m	81, 66	−0.4 (1.4)	−2.0 (1.6)	1.6 (−2.5, 5.8)	0.44	−1.4 (1.9)	−1.2 (2.1)	−0.2 (−5.8, 5.5)	0.95
Diastolic blood pressure (mm Hg)									
3m	86, 84	−1.5 (0.9)	−1.8 (0.9)	0.3 (−2.2, 2.7)	0.83	−1.6 (1.0)	−1.2 (1.0)	−0.4 (−3.2, 2.5)	0.79
6m	84, 72	−1.5 (0.9)	−1.8 (1.0)	0.2 (−2.3, 2.8)	0.86	−1.8 (1.0)	−1.3 (1.1)	−0.5 (−3.5, 2.5)	0.73
12m	79, 70	0.7 (0.9)	0.8 (0.9)	−0.2 (−2.7, 2.4)	0.90	0.8 (1.1)	1.4 (1.1)	−0.6 (−3.7, 2.5)	0.71
18m	81, 66	2.8 (0.9)	1.4 (1.0)	1.4 (−1.2, 4.1)	0.28	1.9 (1.1)	1.5 (1.2)	0.4 (−2.9, 3.7)	0.81

Note: Independent *t*-tests were used to compare means between arms using observed data (left columns). These analyses were compared with mixed models using multiple imputation to replace missing data (right columns). Imputation models for each outcome variable included values at other time points, attendance (counting the all-day session as two) and its interaction with arm, and an arm x round interaction term (ROUND-ARM) to adjust for clustering effects. Two women had weight-related variables censored at 18 months due to pregnancy. Last observation carried forward at the time of medication initiation was implemented for fasting glucose, HOMA, and HbA1c values for three participants and for lipid values of 11 participants who initiated lipid lowering medications during the trial. CRP values over 30 mg/L were Winsorized to 30.

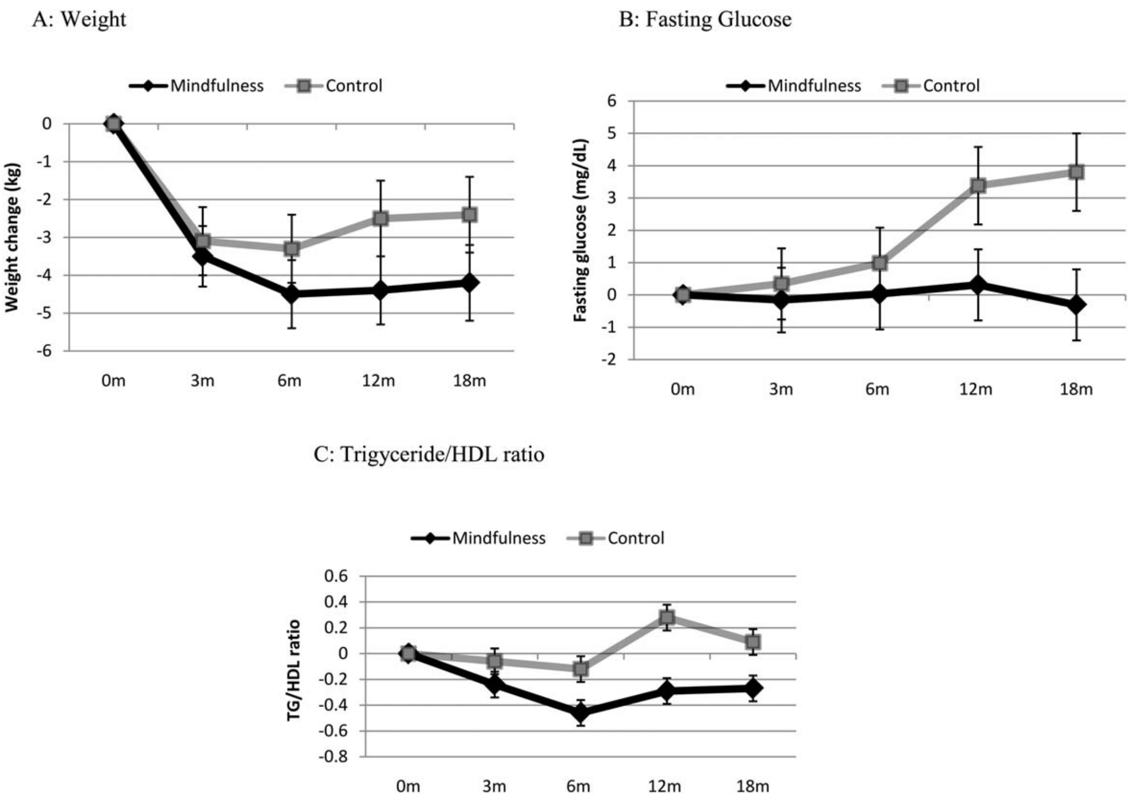

Figure 2 Changes in weight and metabolic risk factors over time. Each panel shows changes from trial initiation in metabolic risk factors, with the control group in gray lines and the mindfulness group in black lines. Standard error bars are shown. Panel A shows changes in weight, panel B shows changes in fasting glucose, and panel C shows changes in triglyceride/HDL ratio. See Table 2 for statistical tests at different time points. m = months; TG = triglycerides.

increase in the likelihood of developing type 2 diabetes, suggesting that our observed difference may be clinically significant (28,29). Triglycerides and the triglyceride/HDL ratio showed moderate evidence of long-term improvement, as these decreased in the mindfulness compared to the control arm at 12 months, although differences were not statistically significant at 18 months. Elevated triglycerides and low HDL are both features of metabolic syndrome, and the ratio predicts cardiovascular mortality (30).

Improvements in fasting glucose and lipids may be related to greater improvements in mindfulness or stress management, greater weight loss in the mindfulness arm, or differences in food choices. In a separate analysis (31), participants in the mindfulness arm maintained reductions in sweet food intake from 6 to 12 months in comparison to participants in the control arm. Greater meditation and/or mindful eating practice during the intervention was related to greater weight loss, lower triglyceride/HDL ratio, and a trend for lower fasting glucose at 6 months, though not at 18 months (see Supporting Information, Table S11). Future analyses will examine to what extent mindfulness, stress reduction, or behavioral changes account for benefits observed in the mindfulness condition. We did not, however, find significant differences in insulin sensitivity (HOMA), a key secondary outcome, or HbA1c levels. This may be due, in part, to the fact that we excluded participants with HbA1c levels above 6.5%, which meant there was limited room for improvement among enrolled participants.

Although we believe that the total number of metabolic outcomes favoring the mindfulness arm suggests possible benefits of mindfulness components, we also note important cautions. Only the differences in fasting glucose were consistently statistically significant. We did not apply an adjustment for multiple-comparison testing because standard adjustments do not account for the expected direction of outcomes and coherence of the ensemble of findings. Yet, the multiplicity of outcomes assessed increases the risk that some statistically significant findings are due to chance. Future replication is needed to place greater confidence in these findings.

Most behavioral interventions show maximal weight loss at 6 months and gradual regain thereafter (7). This pattern was observed in our control group. In contrast, mindfulness participants maintained weight loss, regaining an average of only 0.3 kg from 6 to 18 months. The mindfulness intervention resulted in a mean of 4.2–5.0 kg (4.3–5.1%) 18-month weight loss, depending on analytic method. According to recent obesity guidelines, sustained weight loss of as little as 3–5% is likely to result in clinically meaningful reductions in levels of fasting glucose and triglycerides, as found in our study, and in the risk of developing type 2 diabetes (32).

We note that in interpreting these results our 5.5-month intervention dose was modest compared to many weight loss trials that provide continuous contact and current obesity intervention guidelines (32-34).

TABLE 3 Intention-to-treat multiple imputation estimates of cardiometabolic outcomes by mindfulness instructor groups

Variable	Mindfulness instructors A/B, mean (SE) change	Mindfulness instructor C, mean (SE) change	C–A/B difference, mean (95% CI)	*P* value	A/B–all control groups difference, mean (95% CI)	*P* value
Weight (kg)						
3m	−3.7 (1.2)	−3.2 (1.2)	0.5 (−2.9, 3.9)	0.76	−0.6 (−3.6, 2.4)	0.68
6m	−4.8 (1.2)	−4.1 (1.2)	0.7 (−2.7, 4.2)	0.67	−1.6 (−4.7, 1.5)	0.31
12m	−5.2 (1.3)	−3.6 (1.3)	1.6 (−1.9, 5.1)	0.37	−2.7 (−6.0, 0.7)	0.11
18m	−6.3 (1.4)	−2.0 (1.3)	4.3 (0.8, 7.9)	0.02	−3.9 (−7.4, −0.4)	0.03
Waist circumference (cm)						
3m	−3.4 (1.4)	−1.9 (1.4)	1.6 (−2.4, 5.6)	0.44	−1.2 (−3.9, 1.5)	0.37
6m	−5.0 (1.5)	−3.5 (1.5)	1.5 (−2.6, 5.5)	0.48	−1.2 (−4.0, 1.6)	0.41
12m	−5.6 (1.5)	−2.2 (1.5)	3.4 (−0.7, 7.5)	0.11	−3.6 (−6.6, −0.6)	0.02
18m	−6.3 (1.5)	−2.2 (1.6)	4.1 (−0.1, 8.3)	0.05	−3.5 (−6.7, −0.3)	0.03
Glucose (mg/dl)						
3m	−1.9 (1.2)	1.6 (1.2)	3.5 (0.3, 6.8)	0.03	−2.3 (−6.3, 1.8)	0.27
6m	0.8 (1.2)	−0.8 (1.2)	−1.6 (−4.9, 1.8)	0.35	−0.2 (−4.3, 4.0)	0.94
12m	−0.3 (1.3)	0.9 (1.3)	1.2 (−2.2, 4.6)	0.49	−3.7 (−7.9, 0.6)	0.09
18m	−0.9 (1.3)	0.3 (1.2)	1.3 (−2.1, 4.7)	0.45	−4.8 (−9.0, −0.5)	0.03
HOMA						
3m	−0.05 (0.33)	0.09 (0.32)	0.14 (−0.75, 1.04)	0.75	−0.02 (−0.91, 0.86)	0.96
6m	−0.05 (0.33)	−0.19 (0.32)	−0.14 (−1.03, 0.76)	0.76	−0.02 (−0.91, 0.87)	0.97
12m	−0.27 (0.35)	0.01 (0.33)	0.28 (−0.65, 1.20)	0.55	−0.72 (−1.68, 0.24)	0.14
18m	−0.19 (0.32)	0.11 (0.32)	0.30 (−0.59, 1.19)	0.51	−0.60 (−1.52, 0.32)	0.20
HbA1c (%)						
3m	−0.07 (0.08)	0.07 (0.07)	0.14 (−0.07, 0.35)	0.19	−0.06 (−0.22, 0.10)	0.43
6m	−0.11 (0.07)	0.02 (0.07)	0.13 (−0.08, 0.34)	0.23	−0.11 (−0.27, 0.05)	0.19
12m	−0.09 (0.08)	−0.04 (0.08)	0.05 (−0.16, 0.26)	0.62	−0.07 (−0.23, 0.10)	0.43
18m	−0.11 (0.08)	0.01 (0.08)	0.12 (−0.09, 0.33)	0.25	−0.12 (−0.28, 0.04)	0.15
LDL (mg/dl)						
3m	−2.8 (3.4)	−5.3 (3.2)	−2.5 (−11.6, 6.6)	0.59	2.3 (−5.9, 10.6)	0.58
6m	2.7 (3.4)	−3.0 (3.4)	−5.7 (−15.0, 3.5)	0.22	6.4 (−2.2, 15.0)	0.14
12m	0.7 (3.4)	−0.4 (3.4)	−1.1 (−10.4, 8.2)	0.81	5.7 (−3.0, 14.3)	0.20
18m	−1.6 (3.5)	−1.1 (3.5)	0.4 (−9.0, 9.8)	0.93	2.1 (−6.9, 11.1)	0.64
HDL (mg/dl)						
3m	−1.9 (1.5)	−1.4 (1.5)	0.5 (−3.8, 4.8)	0.82	1.3 (−2.1, 4.8)	0.45
6m	−0.6 (1.6)	−0.5 (1.6)	0.1 (−4.3, 4.5)	0.96	−0.2 (−3.9, 3.4)	0.89
12m	−1.8 (1.6)	−1.2 (1.6)	0.6 (−3.8, 5.0)	0.80	0.3 (−3.4, 4.1)	0.85
18m	−1.0 (1.6)	−0.8 (1.6)	0.2 (−4.2, 4.6)	0.93	1.4 (−2.4, 5.2)	0.48
Triglycerides (mg/dl)						
3m	−10.8 (7.4)	−12.5 (7.1)	−1.7 (−21.9, 18.5)	0.87	−2.7 (−20.6, 15.2)	0.76
6m	−20.4 (7.5)	−19.4 (7.4)	1.0 (−19.4, 21.4)	0.92	−15.3 (−33.9, 3.3)	0.11
12m	−19.3 (7.7)	−9.3 (7.6)	10.0 (−10.9, 30.9)	0.34	−22.7 (−42.2, −3.1)	0.02
18m	−14.0 (7.6)	−11.5 (7.6)	2.5 (−18.2, 23.1)	0.81	−10.9 (−30.3, 8.5)	0.27
Triglyceride/HDL ratio						
3m	−0.22 (0.18)	−0.25 (0.18)	−0.02 (−0.54, 0.49)	0.93	−0.17 (−0.61, 0.28)	0.46
6m	−0.52 (0.19)	−0.40 (0.18)	0.12 (−0.40, 0.64)	0.65	−0.39 (−0.85, 0.06)	0.09
12m	−0.40 (0.19)	−0.17 (0.19)	0.23 (−0.29, 0.76)	0.38	−0.68 (−1.16, −0.21)	**0.01**
18m	−0.33 (0.19)	−0.21 (0.19)	0.12 (−0.40, 0.64)	0.64	−0.42 (−0.89, 0.05)	0.08
C-reactive protein (mg/l)						
3m	−0.9 (0.8)	−1.4 (0.7)	−0.5 (−2.6, 1.5)	0.61	−0.6 (−2.3, 1.0)	0.45
6m	−1.2 (0.7)	−1.4 (0.7)	−0.2 (−2.3, 1.8)	0.82	−0.4 (−2.1, 1.3)	0.64

TABLE 3. (continued).

Variable	Mindfulness instructors A/B, mean (SE) change	Mindfulness instructor C, mean (SE) change	C–A/B difference, mean (95% CI)	*P* value	A/B–all control groups difference, mean (95% CI)	*P* value
12m	−0.8 (0.8)	−0.3 (0.8)	0.5 (−1.7, 2.7)	0.64	−0.7 (−2.6, 1.2)	0.46
18m	−1.0 (0.8)	−0.8 (0.8)	0.1 (−2.0, 2.3)	0.92	−1.3 (−3.2, 0.5)	0.15
Systolic blood pressure (mm Hg)						
3m	−10.0 (3.0)	−6.5 (3.0)	3.5 (−4.9, 11.9)	0.41	−3.4 (−9.3, 2.4)	0.24
6m	−7.7 (3.0)	−3.7 (3.0)	3.9 (−4.4, 12.3)	0.35	−3.0 (−9.0, 2.9)	0.32
12m	−3.5 (3.1)	−2.2 (3.1)	1.3 (−7.1, 9.7)	0.76	−1.9 (−8.0, 4.2)	0.54
18m	−3.7 (3.0)	1.0 (3.0)	4.7 (−3.7, 13.1)	0.27	−2.5 (−8.5, 3.6)	0.42
Diastolic blood pressure (mm Hg)						
3m	−1.4 (1.6)	−1.9 (1.5)	−0.5 (−4.7, 3.8)	0.83	−0.2 (−3.8, 3.4)	0.92
6m	−2.3 (1.6)	−1.3 (1.6)	1.0 (−3.3, 5.2)	0.65	−1.1 (−4.7, 2.6)	0.57
12m	1.9 (1.6)	−0.2 (1.6)	−2.1 (−6.4, 2.2)	0.34	0.4 (−3.4, 4.2)	0.83
18m	0.9 (1.6)	2.8 (1.6)	1.9 (−2.5, 6.2)	0.39	−0.6 (−4.5, 3.3)	0.77

Note: Participants who had mindfulness instructors who were rated as more helpful (A/B) were compared to participants who had the mindfulness instructor who was rated as less helpful (C) in mixed models using multiple imputation to replace missing data. Imputation models for each outcome variable included values at other time points and attendance (counting the all-day session as two).

The 18-month time point, therefore, reflects 1-year maintenance effects after withdrawal of intervention support. We designed a rigorous control by controlling for attention, social support, expectations of benefit, diet-exercise guidelines, and elements of a mindfulness approach to stress management by providing limited progressive muscle relaxation and cognitive–behavioral training in the control condition. The dietary intervention used in both interventions was also modest in that we promoted sustainable, long-term caloric reduction with minimal use of food records (35). Interventions that integrate mindfulness training with more intensive dietary or exercise guidelines or other effective cognitive–behavioral therapies compatible with a mindfulness approach may achieve greater improvements. The cost of adding mindfulness components was modest, about $200 per participant.

In behavioral intervention trials, it is essentially impossible to mask participants to the intervention they receive. We made an effort, however, to mask participants to the fact that we were specifically testing effects of a mindfulness-enhanced intervention to prevent decreased expectations and drop out among participants assigned to the control arm. We assumed the majority of participants would have preferred to receive the mindfulness-enhanced intervention. The concealment of intervention content prior to randomization, however, may have led to the assignment of some participants to the mindfulness arm who had little interest in mindfulness. This approach may have resulted in treatment effects that are more conservative than those in trials or clinical settings in which potential participants choose to enroll in a mindfulness-based program. To assess this explanation, we compared participants missing 18-month data in the mindfulness arm ($n = 19$) to the active control ($n = 27$). Drop-outs in the mindfulness arm reported greater reductions in expectations of benefit after randomization (but prior to the first session), attended fewer classes, and showed trends of less improvement in metabolic outcomes. These findings support the notion that many drop-outs in the mindfulness arm may have had limited interest in the mindfulness components of the intervention. It may also explain why analyses using only observed data tended to show stronger effects of the mindfulness intervention on outcomes, including HOMA, HDL, and C-reactive protein, than the imputation analyses. These findings suggest that participant engagement is important and individuals with obesity who do not express interest in mindfulness approaches may respond less favorably to the inclusion of mindfulness training in weight loss programs.

Our results also suggest that efficacy of mindfulness training for weight loss may be instructor-dependent. Groups led by mindfulness instructors who were rated by participants as more helpful during the intervention lost an estimated 4.3 kg more at 18 months compared to groups led by an instructor rated as less helpful and 5.4 kg more than contemporaneous control groups, both statistically significant differences. These findings suggest that more effective

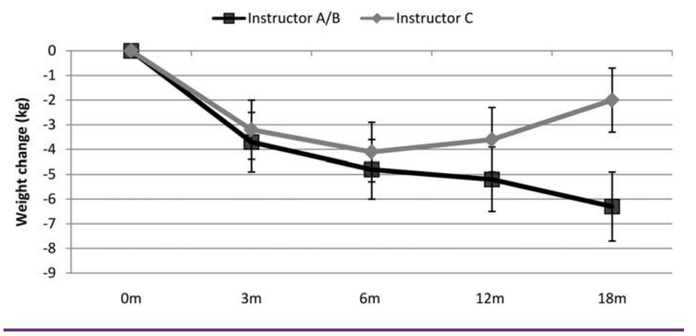

Figure 3 Changes in weight by mindfulness instructor groups. Changes from trial initiation in weight in the mindfulness arm by groups led by instructors A and B (black line) and groups led by instructor C (gray line). Instructors A and B were rated higher on helpfulness by participants compared to Instructor C. Standard error bars are shown. See Table 3 for statistical tests at different time points. m = months.

instructors may produce more weight loss benefit in mindfulness-enhanced interventions. We monitored adherence to a detailed intervention manual, yet instructor differences persisted in how the curriculum was delivered. Based on supervisor observations, closer adherence to the manual, at the possible cost of fuller personal engagement with group participants, could be a factor explaining instructor differences (36), consistent with findings in the psychotherapy literature (37). However, as we did not randomize instructors, findings could be due to chance, other explanations may be valid, and therefore, interpretation of these results requires caution. Further research is needed to investigate effects of instructor characteristics on outcomes of mindfulness-based interventions.

In conclusion, the effect of adding mindfulness components to diet-exercise programs on weight loss in individuals with obesity was not statistically significant. We found some evidence that the mindfulness intervention may lead to long-term maintenance of fasting glucose levels and improved atherogenic lipid profiles. Further research is needed to determine whether potential benefits can be confirmed or strengthened. O

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References

1. Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of obesity among adults: United States, 2011-2012. *NCHS Data Brief* 2013;1-8.
2. Alberti KG, Eckel RH, Grundy SM, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation* 2009;120:1640-1645.
3. Shin JA, Lee JH, Lim SY, et al. Metabolic syndrome as a predictor of type 2 diabetes, and its clinical interpretations and usefulness. *J Diabetes Investig* 2013;4:334-343.
4. Malik S, Wong ND, Franklin SS, et al. Impact of the metabolic syndrome on mortality from coronary heart disease, cardiovascular disease, and all causes in United States adults. *Circulation* 2004;110:1245-1250.
5. Mozumdar A, Liguori G. Persistent increase of prevalence of metabolic syndrome among U.S. adults: NHANES III to NHANES 1999-2006. *Diabetes Care* 2011;34: 216-219.
6. Papadaki A, Linardakis M, Plada M, et al. Impact of weight loss and maintenance with ad libitum diets varying in protein and glycemic index content on metabolic syndrome. *Nutrition* 2014; 30:410–417.
7. Franz MJ, VanWormer JJ, Crain AL, et al. Weight-loss outcomes: a systematic review and meta-analysis of weight-loss clinical trials with a minimum 1-year follow-up. *J Am Dietetic Assoc* 2007;107:1755-1767.
8. Stress a major health problem in the U.S., warns APA. American Psychological Association Web Site. Available at: http://www.apa.org/news/press/releases/2007/10/stress.aspx. Accessed May 20, 2015.
9. Rosmond R. Role of stress in the pathogenesis of the metabolic syndrome. *Psychoneuroendocrinology* 2005;30:1-10.
10. Li L, Li X, Zhou W, Messina JL. Acute psychological stress results in the rapid development of insulin resistance. *J Endocrinol* 2013;217:175-184.
11. Wardle J, Chida Y, Gibson EL, Whitaker KL, Steptoe A. Stress and adiposity: a meta-analysis of longitudinal studies. *Obesity* 2011;19:771-778.
12. Wansink B. From mindless eating to mindlessly eating better. *Physiol Behav* 2010; 100:454-463.
13. Murray S, Tulloch A, Gold MS, Avena NM. Hormonal and neural mechanisms of food reward, eating behaviour and obesity. *Nat Rev Endocrinol* 2014;
14. Goyal M, Singh S, Sibinga EM, et al. Meditation programs for psychological stress and well-being: a systematic review and meta-analysis. *JAMA Intern Med* 2014;
15. Brown KW, Ryan RM, Creswell JD. Mindfulness: theoretical foundations and evidence for its salutary effects. *Psychol Inquiry* 2007;18:211-237.
16. Daubenmier J, Kristeller J, Hecht FM, et al. Mindfulness intervention for stress eating to reduce cortisol and abdominal fat among overweight and obese women: an exploratory randomized controlled study. *J Obes* 2011;2011:651936
17. Kristeller J, Wolever RQ, Sheets V. Mindfulness-based eating awareness training (MB-EAT) for binge eating: a randomized clinical trial. *Mindfulness* 2014;5:282-297.
18. Kristeller JL, Hallett CB. An exploratory study of a meditation-based intervention for binge eating disorder. *J Health Psychol* 1999;4:357-363.
19. Katterman SN, Kleinman BM, Hood MM, Nackers LM, Corsica JA. Mindfulness meditation as an intervention for binge eating, emotional eating, and weight loss: a systematic review. *Eat Behav* 2014;15:197-204.
20. O'Reilly GA, Cook L, Spruijt-Metz D, Black DS. Mindfulness-based interventions for obesity-related eating behaviours: a literature review. *Obes Rev* 2014;15:453-461.
21. Miller CK, Kristeller JL, Headings A, Nagaraja H, Miser WF. Comparative effectiveness of a mindful eating intervention to a diabetes self-management intervention among adults with type 2 diabetes: a pilot study. *J Acad Nutr Diet* 2012;112:1835-1842.
22. Kiernan M, Brown SD, Schoffman DE, et al. Promoting healthy weight with "Stability Skills First": a randomized trial. *J Consult Clin Psychol* 2013;81:336-346.
23. Kabat-Zinn J. *Full Catastrophe Living*. New York: Dell Publishing; 1990.
24. Kristeller JL, Wolever RQ. Mindfulness-based eating awareness training for treating binge eating disorder: the conceptual foundation. *Eat Disord* 2011;19:49-61.
25. Dreyer D, Dreyer K. *Chi Walking: The Five Mindful Steps for Lifelong Health and Energy*. New York: Simon and Schuster; 2006.
26. Sterne JA, White IR, Carlin JB, et al. Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. *BMJ* 2009;338:b2393
27. Knowler W, Barrett-Connor E, Fowler S, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med* 2002;346: 393-403.
28. Schmidt MI, Duncan BB, Bang H, et al. Identifying individuals at high risk for diabetes: the atherosclerosis risk in communities study. *Diabetes Care* 2005;28: 2013-2018.
29. Barr EL, Zimmet PZ, Welborn TA, et al. Risk of cardiovascular and all-cause mortality in individuals with diabetes mellitus, impaired fasting glucose, and impaired glucose tolerance: the Australian Diabetes, Obesity, and Lifestyle Study (AusDiab). *Circulation* 2007;116:151-157.
30. Vega GL, Barlow CE, Grundy SM, Leonard D, DeFina LF. Triglyceride-to-high-density-lipoprotein-cholesterol ratio is an index of heart disease mortality and of incidence of type 2 diabetes mellitus in men. *J Investig Med* 2014;62:345-349.
31. Mason AE, Elepl EE, Kristeller J, et al. Effects of a mindfulness-based intervention on mindful eating, sweets consumption, and fasting glucose levels in obese adults: data from the SHINE randomized clinical trial. *J Behav Med* in press.
32. Jensen MD, Ryan DH. New obesity guidelines: promise and potential. *JAMA* 2014; 311:23-24.
33. Jensen MD, Ryan DH, Donato KA, et al. Guidelines (2013) for managing overweight and obesity in adults. *Obesity* 2014;22(S2):S1–S410.
34. Jakicic JM, Tate DF, Lang W, et al. Effect of a stepped-care intervention approach on weight loss in adults: a randomized clinical trial. *JAMA* 2012;307:2617-2626.
35. Burke LE, Wang J, Sevick MA. Self-monitoring in weight loss: a systematic review of the literature. *J Am Diet Assoc* 2011;111:92-102.
36. Crane RS, Eames C, Kuyken W, et al. Development and validation of the mindfulness-based interventions - teaching assessment criteria (MBI:TAC). *Assessment* 2013;20:681-688.
37. Kim D, Wampold BE, Bolt DM. Therapist effects in psychotherapy: a random-effects modeling of the National Institute of Mental Health Treatment of Depression Collaborative Research Program data. *Psychother Res* 2006;16:161-172.