Association of Psychobehavioral Variables With HOMA-IR and BMI Differs for Men and Women With Prediabetes in the PREVIEW Lifestyle Intervention

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Tanja C. Adam,[1] Mathijs Drummen,[1] Ian Macdonald,[2,3] Elli Jalo,[4] Pia Siig-Vestentoft,[5] J. Alfredo Martinez,[6–9] Teodora Handjiev-Darlenska,[10] Jennie Brand-Miller,[11] Sally Poppitt,[12] Gareth Stratton,[13] Mikael Fogelholm,[4] Kirsi H. Pietiläinen,[14,15] Moira Taylor,[2,3] Santiago Navas-Carretero,[6–8] Bjorn Winkens,[16] Svetoslav Handjiev,[10] Roslyn Muirhead,[11] Marta Silvestre,[12,17] Nils Swindell,[13] Maija Huttunen-Lenz,[18,19] Wolfgang Schlicht,[18] Tony Lam,[20] Jouko Sundvall,[21] Laura Råman,[21] Edith Feskens,[22] Thomas-Meinert Larssen,[5] Angelo Tremblay,[23] Anne Raben,[5,24] and Margriet Westerterp-Plantenga[1]

OBJECTIVE

Stress, sleep, eating behavior, and physical activity are associated with weight change and insulin resistance (IR). The aim of this analysis was the assessment of the overall and sex-specific associations of psychobehavioral variables throughout the 3-year PREVIEW intervention using the homeostatic model assessment of IR (HOMA-IR), BMI, and length of time in the study.

RESEARCH DESIGN AND METHODS

Associations of psychobehavioral variables, including stress, mood, eating behavior, physical activity (PA), and sleep, with BMI, HOMA-IR, and time spent in the study were assessed in 2,184 participants with prediabetes and overweight/obesity ($n = 706$ men; $n = 1{,}478$ women) during a 3-year lifestyle intervention using linear mixed modeling and general linear modeling. The study was a randomized multicenter trial using a 2 × 2 diet-by-PA design.

RESULTS

Overall, cognitive restraint and PA increased during the intervention compared with baseline, whereas BMI, HOMA-IR, disinhibition, hunger, and sleepiness decreased (all $P < 0.05$). Cognitive restraint and PA were negatively, whereas disinhibition, hunger, stress, and total mood disturbance were positively, associated with both BMI and HOMA-IR. Sleep duration, low sleep quality, total mood disturbance, disinhibition, and hunger scores were positively associated with HOMA-IR for men only. Participants who dropped out at 6 months had higher stress and total mood disturbance scores at baseline and throughout their time spent in the study compared with study completers.

CONCLUSIONS

Eating behavior and PA, control of stress, mood disturbance, and sleep characteristics were associated with BMI, HOMA-IR, and time spent in the study, with different effects in men and women during the PREVIEW lifestyle intervention study.

In adults, the occurrence of type 2 diabetes is associated with obesity, low levels of physical activity (PA), and poor diet. Despite substantial efforts to curtail the obesity

[1]*Department of Nutrition and Movement Sciences, NUTRIM School of Nutrition and Translational Research in Metabolism, Maastricht University, Maastricht, the Netherlands*
[2]*Medical Research Council/Arthritis Research UK (ARUK) Centre for Musculoskeletal Ageing Research, ARUK Centre for Sport, Exercise and Osteoarthritis, University of Nottingham, Nottingham, U.K.*
[3]*National Institute for Health Research Nottingham Biomedical Research Centre, Division of Physiology, Pharmacology and Neuroscience, School of Life Sciences, Queen's Medical Centre, Nottingham, U.K.*
[4]*Department of Food and Nutrition, University of Helsinki, Helsinki, Finland*
[5]*Department of Nutrition, Exercise and Sports, Faculty of Science, University of Copenhagen, Copenhagen, Denmark*
[6]*Centre for Nutrition Research, University of Navarra, Pamplona, Spain*
[7]*Centro de Investigacion Biomedica en Red Area de Fisiologia de la Obesidad y la Nutricion, Madrid, Spain*
[8]*IdisNA Instituto for Health Research, Pamplona, Spain*
[9]*Precision Nutrition and Cardiometabolic Health Program, IMDEA Food Institute, Madrid Institute for Advanced Studies, Campus of International Excellence Universidad Autonoma de Madrid and Spanish National Research Council, Madrid, Spain*
[10]*Department of Pharmacology and Toxicology, Medical University of Sofia, Sofia, Bulgaria*
[11]*School of Life and Environmental Sciences and Charles Perkins Centre, University of Sydney, Sydney, Australia*
[12]*Human Nutrition Unit, School of Biological Sciences, Department of Medicine, University of Auckland, Auckland, New Zealand*

crisis, rates have continued to increase in both adults and children (1). While precision medicine linked with physiological characteristics is a rapidly advancing field in health care, the potential significance of psychobehavioral characteristics and their ramifications for health outcomes, including the effectiveness of lifestyle interventions, are not well understood. Lifestyle intervention studies aiming to identify specific factors that predict success in weight loss and weight loss maintenance have demonstrated that patient compliance is a primary factor (2). Compliance behavior, however, is highly variable among individuals and depends on individual, cognitive, social, and environmental factors. A better understanding of factors facilitating compliance is a necessary step for avoiding failure in weight loss efforts to support long-term weight loss maintenance. Psychobehavioral variables previously associated with both weight change and insulin resistance (IR) include stress and mood disturbance (3,4), sleep duration (5), cognitive dietary restraint (6), and PA (7). For both weight gain and IR, all of these variables were previously associated with a sex-specific risk (8,9). Women face a unique risk for obesity because of hormonal fluctuations (i.e., during monthly cycles, menopause, and pregnancy), and they are also more likely to increase their food consumption and emotional eating habits under stress (10). Men, in contrast, seem to respond more favorably to an exercise-based approach to weight loss compared with women (11). Sex-related differences in the metabolic response to exercise as well as differences in volitional PA have been reported in the literature (12,13). Considering the evidence, the pursuit of a precision and tailored approach seems warranted to determine the psychobehavioral components conducive to the facilitation of long-term success for lifestyle intervention studies. The PREVIEW (Prevention of Diabetes Through Lifestyle Intervention and Population Studies in Europe and Around the World) study is a large multinational prevention project that is well suited to determine relevant psychobehavioral variables and their sex-specific associations with weight loss maintenance and insulin sensitivity (14). Here we present assessment of the associations of psychobehavioral variables and their change over time with the homeostatic model assessment of IR (HOMA-IR) and BMI. Sex-related differences and the length of time participants remained in the study were taken into account.

RESEARCH DESIGN AND METHODS

For the current report, data from the PREVIEW study, a 3-year multicenter randomized controlled trial, were analyzed. The study was designed to assess whether an ad libitum high-protein, low–glycemic index (GI) diet compared with a conventional diet of moderate protein, moderate GI in combination with either high-intensity or moderate PA was superior for weight loss maintenance. Data collection for the intervention took place in Denmark, Finland, the Netherlands, Spain, Hungary, Australia, New Zealand, and the U.K. in participants with prediabetes aged between 25 and 70 years.

Trial design and methods of the PREVIEW study have been published previously (15). BMI, HOMA-IR, and psychobehavioral variables for the present analysis were assessed at 5 of 7 clinical investigation day (CID) time points (at baseline [week 0], after 6 months [week 26], and after 1 year [week 52], 2 years [week 104], and 3 years [week 156]) and included the Perceived Stress Scale (16), the Three-Factor Eating Questionnaire (TFEQ) (17), the Profile of Moods Scale (18), the Pittsburgh Sleep Quality Index (19) (with higher scores indicating poor sleep quality), the Epsworth Sleepiness Scale (ESS) (20), and the Baecke questionnaire (21). PA and total sleeping time were assessed with ActiSleep$^+$ (ActiGraph LLC, Pensacola, FL), which was worn by participants for 24 h per day on 7 consecutive days before the CIDs. Based on validated algorithms, the principal output activity count and sleep duration (22) were assessed with ActiSleep$^+$.

Participants

Men and women (aged 25–70 years) with overweight or obesity (BMI $>$25 kg/m^2) and prediabetes were recruited via newspaper, radio, and television advertisements and by primary and occupational health care providers. Based on previously published inclusion and exclusion criteria, individuals were prescreened for eligibility. After providing informed consent, laboratory sessions started with a screening visit assessing prediabetes status according to the criteria of the American Diabetes Association (23). A total of 2,184 participants were included in the final analysis of the current study.

Intervention

All participants started with an 8-week low-energy diet (Cambridge weight plan) consisting of 3.4 MJ (800 kcal), 15–20 E% fat, 35–40 E% protein (84 g

[13]Applied Sports Technology, Exercise and Medicine Research Centre, College of Engineering, Swansea University, Swansea, U.K.
[14]Obesity Research Unit, Research Program for Clinical and Molecular Metabolism, Faculty of Medicine, University of Helsinki, Helsinki, Finland
[15]Obesity Center, Abdominal Center, Helsinki University Hospital and University of Helsinki, Helsinki, Finland
[16]Department of Methodology and Statistics, Care and Public Health Research Institute, Maastricht University Medical Center, Maastricht, the Netherlands
[17]Centro de Investigação em Tecnologias e Serviços de Saúde, NOVA Medical School, NOVA University of Lisbon, Lisbon, Portugal
[18]Exercise and Health Sciences, University of Stuttgart, Stuttgart, Germany
[19]Institute of Nursing Science, University of Education Schwäbisch Gmünd, Schwäbisch Gmünd, Germany
[20]NetUnion, Lausanne, Switzerland
[21]Biochemistry Laboratory, Forensic Toxicology Unit, Department of Government Services, National Institute for Health and Welfare, Helsinki, Finland
[22]Division of Human Nutrition and Health, Wageningen University & Research, Wageningen, the Netherlands
[23]Department of Kinesiology, Laval University, Quebec City, Canada
[24]Steno Diabetes Center Copenhagen, Copenhagen, Denmark

Corresponding author: Tanja C. Adam, t.adam@maastrichtuniversity.nl.

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protein), and 45–50 E% carbohydrates), which was provided free of charge (14). Participants who reached the target weight reduction of ≥8% of baseline body weight after the low-energy diet period (24) were included in the 3-year weight maintenance phase and were randomly assigned to one of four intervention groups, stratified by age and sex. Stratification occurred sequentially, delivering six strata, in which the sequences (four intervention labels in random order) were created in blocks, with sizes of four to eight. Group allocation was not disclosed to the participants until they received information about the allocated intervention arm at week 8. All participants were supported in changing their behavior by using the PREVIEW Modification Intervention Tool (PREMIT) (25).

For the intervention, macronutrient composition of the diet, GI, and PA were combined into four different intervention arms. The two diets were a high-protein diet with 25 E% protein, 30 E% fat, and 45 E% carbohydrates, with a low GI (<50), and a moderate-protein diet with 15 E% protein, 30 E% fat, and 55 E% carbohydrates, with a moderate GI (>56). The two PA groups were defined as high-intensity PA for 75 min per week and moderate-intensity PA for 150 min per week. The intended diets and PA types were provided by instructors and recipes, and compliance was discussed during the regular group meetings (14).

Outcomes

The current paper addresses a secondary outcome analysis of the PREVIEW study, assessing associations of psychobehavioral variables as well as their change throughout the intervention period with HOMA-IR, BMI, and the time participants remained in the study in men and women (Supplementary Fig. 1). Results on primary outcome measures and participants have been published previously (14).

Power Analysis

Sample size estimation of the main study was based on expected type 2 diabetes incidence and has been described before (14). Based on the power calculation, at least 1,854 participants were required to start the weight maintenance phase. Using 80% power and α of 0.05, the estimated sample size for each treatment was 142. Allowing for a 30% drop-out rate, the sample size was 205 per intervention group.

Statistical Analysis

The present analysis included 2,184 participants (n = 706 men; n = 1,478 women). First, individual association of the psychobehavioral variables for BMI and HOMA-IR was tested with linear mixed modeling analysis. For HOMA-IR as well as BMI as a dependent variable, all mixed models included a participant-level random intercept, a repeated subject-by–study center component, and fixed effects for site, time, intervention group, age, and sex, as well as time-by-BMI, time-by–treatment group, time-by-sex, and time-by-age interactions. If applicable, nonsignificant interactions with time were omitted. Results from the mixed modeling analysis are presented as estimated means (EMs) and CIs.

Analysis regarding the length of time in the study was undertaken using general linear modeling including BMI, sex, and age as covariates. A time factor consisting of four groups (6 months, 1 year, 2 years, and 3 years) was created based on the length of participation in the study. Results are presented as means ± SDs. Post hoc analyses were Bonferroni corrected. $P < 0.05$ was considered significant for all analyses.

Ethical Approval

The study protocol and amendments were reviewed and approved by the local human ethics committee at each of the eight intervention centers (University of Helsinki, Finland; University of Copenhagen, Denmark; University of Maastricht, The Netherlands; University of Nottingham, United Kingdom; University of Navarra, Spain; University of Sofia, Bulgaria; University of Sydney, Australia; and University of Auckland, New Zealand). The work of PREVIEW was carried out in full compliance with the relevant requirements of the latest version of the Declaration of Helsinki (59th WMA General Assembly, Seoul, Korea, October 2008) and the International Conference on Harmonisation for Good Clinical Practice, to the extent possible and relevant. All participants provided written informed consent before any screening procedures. All information obtained during the trial was handled according to the local regulations and the European Directive 95/46/CE (directive on protection of individuals with regard to the processing of personal data and on the free movement of such data).

Data and Resource Availability

The technical appendix, statistical codes, and data sets are available from the corresponding author T.J.C. at t.adam@maastrichtuniversity.nl.

RESULTS

Differences and Changes of Variables

BMI, HOMA-IR, and the psychobehavioral variables were not statistically different between the four intervention groups at baseline or at any other time point throughout the study.

In all participants, BMI and HOMA-IR remained lower compared with baseline at every time point ($P < 0.05$) (Table 1).

In all participants, cognitive dietary restraint and PA assessed by Baecke sport and leisure scores were increased compared with baseline at all time points (all $P < 0.05$) (Table 1). Stress, sleep duration, and accelerometer counts were increased at all time points in the whole group, with sex-specific differences (Supplementary Table 1*A* and *B*)

In all participants, disinhibition, hunger, and daytime sleepiness were decreased compared with baseline at all time points (all $P < 0.05$), with sex-specific differences (Supplementary Table 1*A* and *B*). While the Pittsburgh Sleep Quality Index was reduced at all time points for men, in women reductions were observed at weeks 26 and 52 only ($P < 0.05$). The Profile of Moods Scale total mood disturbance did not change significantly over time for the whole group, but sex-specific differences were seen (Table 1 and Supplementary Table 1*A* and *B*).

Associations of Psychobehavioral Variables With BMI

For the whole group, perceived stress, total mood disturbance, disinhibition, hunger perception, sleepiness, and poor sleep quality were consistently and positively associated with BMI over the 3-year time period (Table 2). Cognitive restraint and PA assessed by the accelerometer counts and by Baecke sport scores were negatively associated with BMI throughout the

Table 1—BMI, HOMA-IR, and PA of all participants throughout the PREVIEW lifestyle intervention study as determined by mixed modeling analysis

	Baseline (n = 2,184)		6 months (n = 1,857)		Year 1 (n = 1,381)		Year 2 (n = 1,093)		Year 3 (n = 962)	
	EM	95% CI	EM	95% CI	EM	95% CI	EM	95% CI	EM	95% CI
BMI, kg/m^2	35.26[a]	33.93–36.59	31.29[b]	29.96–32.61	32.28[c]	30.95–33.60	33.29[d]	31.97–34.62	33.8[e]	32.47–35.13
HOMA-IR	3.75[a]	3.58–3.92	2.32[b]	2.15–2.48	2.59[c]	2.42–2.75	2.85[d]	2.68–3.03	3.09[e]	2.92–3.27
Baecke sport	2.2[a]	2.04–2.36	2.6[b]	2.43–2.75	2.57[bc]	2.41–2.73	2.54[c]	2.38–2.70	2.54[c]	2.38–2.70
Baecke leisure	2.58[a]	2.47–2.69	2.9[b]	2.81–3.04	2.87[c]	2.76–2.98	2.86[c]	2.75–2.98	2.84[c]	2.73–2.95
Accelerometer count, cpm	294.3[a]	277.6–311.0	331.5[b]	314.7–348.4	321.7[c]	304.7–338.7	315.2[c]	298.2–332.2	301.2[a]	284.0–318.3
TFEQ-F1 (cognitive restraint)	8[a]	7.3–8.6	13.6[b]	13.0–14.29	12.98[c]	12.34–13.63	12.25[d]	11.61–12.90	12.02[d]	11.37–12.67
TFEQ-F2 (disinhibition)	9.06[a]	8.44–9.69	7.3[b]	6.6–7.9	7.7[c]	7.09–8.35	7.99[d]	7.36–8.63	7.97[d]	7.34–8.61
TFEQ-F3 (hunger)	6.97[a]	6.53–7.41	5.0[b]	4.54–5.42	5.37[c]	4.93–5.81	5.59[d]	5.15–6.04	5.62[d]	5.17–6.06
PSQI	6.49[a]	6.17–6.81	5.7[b]	5.42–6.06	6.11[c]	5.78–6.43	6.25[c]	5.92–6.58	6.19[c]	5.86–6.52
ESS	7.81[a]	7.07–8.56	7.1[b]	6.35–7.84	7.19[b]	6.45–7.94	7.2[b]	6.45–7.95	7.29[b]	6.54–8.04
Sleep duration, min	477.9[a]	470.0–484.9	473.9[a]	466.7–481.1	486.5[b]	478.5–494.6	516.6[c]	508.6–524.5	488.5[d]	480.4–496.7
PSS	14.01[a]	12.53–15.49	14.1[a]	12.57–15.53	14.75[b]	13.27–16.24	15.95[c]	14.46–17.44	15.26[d]	13.77–16.74
POMS (total mood disturbance)	18.13[a]	14.55–21.70	15.3[b]	11.69–18.90	16.37[ab]	12.73–20.01	15.68[b]	12.00–19.35	17.8[ab]	14.08–21.52

cpm, counts per minute of activity assessed with accelerometry; ESS, Epworth Sleepiness Scale; POMS, Profile of Mood Score; PSQI, Pittsburgh Sleep Quality Index; PSS, Perceived Stress Scale. Different letters indicate differences at $P < 0.05$.

intervention (Table 2). In terms of clinical relevance for BMI, increase in cognitive restraint, reduction in sleepiness, and increase in free-time PA were the most relevant variables. A 1-point increase on the cognitive restraint scale was associated with a −0.18 kg/m^2 decrease in BMI (Table 2). On average, participants increased their cognitive restraint from 8 to ∼13 points in the current study (Table 1), which would be associated with a −0.88 kg/m^2 decrease in BMI.

Associations of Psychobehavioral Variables With HOMA-IR

For the whole group, perceived stress, total mood disturbance, sleep duration, disinhibition, and hunger perception were consistently and positively associated with HOMA-IR over the period of 3 years (Table 3). Cognitive restraint and PA, as measured by accelerometry and Baecke sport, work, and leisure scores, were negatively associated with HOMA-IR. Sleep variables assessed with questionnaires were not linked with HOMA-IR, considering the full intervention period (Table 3). Considering clinical relevance, decrease in stress and increase in free-time PA would be the most important variables for the improvement of HOMA-IR (Table 3). A 1-point increase in stress was associated with a 0.1 increase in HOMA-IR. In the current study, participants increased their stress report by almost 2 points from baseline to the end of the intervention, which would be associated with a 0.2 increase in HOMA-IR.

Table 2—Associations between psychobehavioral variables and BMI for all participants (N = 2,184)

	EM	95% CI	P
PSS	0.022	0.014–0.029	<0.001
TFEQ-F1(cognitive restraint)	−0.1750	−0.200 to −0.150	<0.001
TFEQ-F2 (disinhibition)	0.209	0.170–0.240	<0.001
TFEQ-F3 (hunger)	0.170	0.140–0.190	<0.001
POMS (total mood disturbance)	0.004	0.001–0.008	0.011
PSQI	0.0190	0.003–0.036	0.014
ESS	0.2510	0.019–0.038	<0.001
Baecke sport	−0.373	−0.514 to −0.232	<0.001
1) Baecke work	−0.080	−0.174 to −0.006	0.070
2) Baecke leisure	−0.525	−0.685 to −0.365	<0.001
Accelerometer count, cpm	−0.002	−0.003 to −0.001	<0.001
Sleep duration, min	0.006	−0.005 to 0.019	0.266

cpm, counts per minute of activity assessed with accelerometry; ESS, Epworth Sleepiness Scale; POMS, Profile of Mood Score; PSQI, Pittsburgh Sleep Quality Index; PSS, Perceived Stress Scale.

BMI, HOMA-IR, and Sex

Sex was a significant main effect in all analyses with regard to the relationship of psychobehavioral variables with HOMA-IR. Therefore, the mixed model analysis was repeated, including an interaction term considering the respective psychobehavioral variable × sex. Although sex was a significant variable for BMI overall, none of the relevant psychobehavioral variables differed by sex when men and women were compared separately.

For HOMA-IR, however, the impact of several psychobehavioral variables was different depending on sex. Poor sleep quality (EM 0.04; CI 0.02–0.06) and total mood disturbance (EM 0.006; CI 0.004–0.009), as well as disinhibition (EM 0.045; CI 0.027–0.063) and hunger (EM 0.056; CI 0.039–0.074), were

Table 3—Associations between psychobehavioral variables and HOMA-IR for all participants (*N* = 2,184)

	EM	95% CI	*P*
PSS	0.100	0.005–0.015	<0.001
TFEQ-F1(cognitive restraint)	−0.021	−0.030 to −0.011	<0.001
TFEQ-F2 (disinhibition)	0.014	0.003–0.026	0.010
TFEQ-F3 (hunger)	0.021	0.009–0.032	<0.001
POMS (total mood disturbance)	0.003	0.001–0.004	<0.001
PSQI	0.008	−0.002 to 0.020	0.132
ESS	0.000	−0.009 to 0.008	0.939
3) Baecke sport	−0.095	−0.148 to −0.042	<0.001
4) Baecke work	−0.053	−0.106 to 0.000	0.047
5) Baecke leisure	−0.100	−0.157 to −0.043	<0.001
Accelerometer count, cpm	−0.001	−0.001 to −0.001	<0.001
Sleep duration, min	0.015	0.005–0.025	<0.001

cpm, counts per minute of activity assessed with accelerometry; ESS, Epworth Sleepiness Scale; POMS, Profile of Mood Score; PSQI, Pittsburgh Sleep Quality Index; PSS, Perceived Stress Scale.

positively associated with HOMA-IR for men only (all $P < 0.001$). Baecke sport (EM −0.108; CI −0.168 to 0.049) and leisure (EM −0.14; CI −0.20 to 0.078) scores were negatively associated with HOMA-IR for women only ($P < 0.001$).

Psychobehavioral Variables and Time in Study

Of the 2,184 participants included in the analysis, 1,857 entered the 148-week weight maintenance phase after 8 weeks of weight loss; 1,529 remained in the study after 26 weeks, and 1,381 completed 52 weeks, which represented 74% of individuals eligible for the weight maintenance after weight loss; 1,093 participants completed 104 weeks (59%), and 962 completed the full 156-week study (52%), with no differences with regard to time spent in the study between the four intervention groups or between sexes (Table 1). Differences in the psychobehavioral variables according to the length of time in the study are given in Table 4. $P < 0.05$ for all results reported.

At baseline, mood disturbance (21.90 ± 28.84 vs. 14.52 ± 25.80; $P < 0.05$) and perceived stress (14.32 ± 6.36 vs. 12.07 ± 6.08; $P < 0.05$) were significantly higher in the individuals who dropped out of the intervention after 26 weeks compared with the individuals who completed the full 3-year intervention. Stress perception after weight loss and after 26 weeks was higher in those participants for whom the 26-week CID was the final visit, compared with participants who completed the entire 156 weeks.

With respect to time spent in the study, the 26-week visit seemed critical. Post hoc analysis showed that participants dropping out after the 26-week CID had a significantly higher increase in perceived stress during the preceding 18 weeks compared with individuals completing the entire 3-year intervention.

Changes in all aspects of the TFEQ during the 18 weeks after weight loss were different for the groups based on time spent in the study.

Post hoc analysis showed that specifically the patients who dropped out after 26 weeks were less able to increase their cognitive restraint compared with the individuals completing the intervention (1.58 ± 4.12 vs. 2.59 ± 3.96; $P < 0.01$). Those dropping out after 26 weeks were also less able to reduce their disinhibition compared with those completing the intervention (−0.19 ± 2.61 vs. −0.85 ± 2.68; $P < 0.01$). Similarly, they experienced less of a decrease in hunger perception compared with those completing the 3 years (−0.46 ± 2.63 vs. −1.08 ± 2.87; $P < 0.05$). Sleepiness was different for those dropping out compared with participants completing the study, with participants who dropped out reporting more sleepiness during the 18 weeks after 8 weeks of weight loss compared with those who completed the entire 3 years.

CONCLUSIONS

The current analysis underlines that the eating behavior variables, cognitive dietary restraint, disinhibition, and hunger perception, as well as PA were associated with changes in BMI and HOMA-IR throughout the intervention. Moreover, stress perception, total mood disturbance, and sleep duration were positively associated with BMI and HOMA-IR. For HOMA-IR, sex played a role, with poor sleep quality, mood disturbance, disinhibition, and hunger being positively associated in men only and Baecke scores of PA being negatively associated in women only. Most importantly, with respect to informing future lifestyle interventions, the analysis showed that psychobehavioral variables at baseline were associated with an individual's probability of completing the intervention and that the ability to change critical variables, such as lowering stress and increasing cognitive restraint, early on in the intervention was associated with the likelihood of completing the intervention.

Successful weight maintenance after weight loss has been elusive for many years, and although lifestyle interventions are quite successful during the weight loss period, approximately one-third of the weight lost is regained after 1 year, with most individuals back at their original weight after 3 to 5 years (26). The role of psychobehavioral variables herein, possibly in a sex-specific manner, has been previously discussed but has not been studied extensively to date (9,11). The National Weight Control Registry determined that after high levels of PA and a low-energy, low-fat diet, low levels of depression and disinhibition were important characteristics of long-term weight stability after weight loss (27), an observation that is supported in the current analysis.

The susceptibility and disposition to gain weight in an obesogenic environment has been estimated for many years through the assessment of cognitive restraint, disinhibition, and hunger by the TEFQ, among other psychometric measures (17). While cognitive restraint describes an individual's ability and

Table 4—Psychobehavioral variables at baseline, week 8 (after weight loss), and week 26 separated by last study visit of participant

	6 months (n = 1529)	Year 1 (n = 1381)	Year 2 (n = 1093)	Year 3 (n = 962)
Baseline				
TFEQ-F1 (cognitive restraint)	7.58 ± 4.06	6.84 ± 3.97[a]	7.93 ± 4.25	8.26 ± 4.03
TFEQ-F2 (disinhibition)	9.62 ± 3.81	9.11 ± 3.25	9.25 ± 3.77	9.06 ± 3.52
TFEQ-F3 (hunger)	7.15 ± 3.53	6.45 ± 3.44	6.84 v 3.71	7.02 ± 3.51
PSS	14.32 ± 6.36[a]	13.72 ± 6.30	14.07 ± 5.96	12.07 ± 6.08
POMS (total mood disturbance)	21.90 ± 28.84[a]	20.63 ± 24.83	19.38 ± 28.71	14.52 ± 25.80
ESS	7.70 ± 4.45	7.69 ± 3.99	7.90 ± 4.41	7.55 ± 4.43
PSQI	6.24 ± 3.53	6.33 ± 3.04	6.64 ± 3.36	6.16 ± 3.16
Sleep duration, min	480.2 ± 78.5	451.1 ± 71.8[ab]	484.2 ± 68.4	474.0 ± 73.4
Baecke sport	2.10 ± 0.64	2.14 ± 0.63	2.08 ± 0.70	2.33 ± 0.71
Baecke leisure	2.60 ± 0.70	2.55 ± 0.72	2.53 ± 0.67	2.66 ± 0.68
Baecke work	2.38 ± 0.73	2.45 ± 0.74	2.43 ± 0.80	2.35 ± 0.74
Week 8				
TFEQ-F1 (cognitive restraint)	11.15 ± 4.50	10.80 ± 4.75	11.09 ± 4.55	11.29 ± 4.34
TFEQ-F2 (disinhibition)	8.16 ± 3.82	7.70 ± 3.52	8.06 ± 3.86	8.09 ± 3.61
TFEQ-F3 (hunger)	5.60 ± 3.72	5.92 ± 3.59	5.92 ± 3.72	5.96 ± 3.63
PSS	13.19 ± 6.43[a]	12.66 ± 6.04	12.46 ± 6.01	12.00 ± 5.72
POMS (total mood disturbance)	12.90 ± 28.19	13.03 ± 20.67	10.14 ± 26.64	9.62 ± 26.20
ESS	6.54 ± 4.26	6.45 ± 3.69	6.91 ± 4.02	6.61 ± 4.13
PSQI	4.91 ± 2.70	5.14 ± 2.86	5.60 ± 2.98	5.16 ± 2.89
6 months				
TFEQ-F1 (cognitive restraint)	12.85 ± 4.05	13.41 ± 3.89	13.16 ± 4.11	13.91 ± 3.55
TFEQ-F2 (disinhibition)	7.93 ± 4.01	7.22 ± 3.47	7.55 ± 3.66	7.24 ± 3.32
TFEQ-F3 (hunger)	5.15 ± 3.71	5.01 ± 3.29	5.15 ± 3.49	4.90 ± 3.46
PSS	15.10 ± 6.59[a]	13.54 ± 6.19	14.36 ± 6.76	12.91 ± 6.14
POMS (total mood disturbance)	21.46 ± 31.76[ab]	14.91 ± 22.06	14.28 ± 27.93	12.92 ± 26.78
ESS	7.18 ± 4.65	7.55 ± 4.47	7.40 ± 4.40	6.71 ± 4.19
PSQI	5.59 ± 3.23	5.39 ± 2.61	6.15 ± 3.26	5.47 ± 2.99
Sleep duration, min	483.9 ± 77.0[a]	473.0.1 ± 76.8	474.7 ± 71.5	467.6 ± 73.3
Baecke sport	2.44 ± 0.69	2.59 ± 0.76	2.53 ± 0.72	2.72 ± 0.71
Baecke leisure	2.93 ± 0.65	2.87 ± 0.62	2.93 ± 0.60	2.99 ± 0.66
Baecke work	2.41 ± 0.76	2.42 ± 0.78	2.46 ± 0.76	2.39 ± 0.75

Data are presented as mean ± SD. ESS, Epworth Sleepiness Scale; POMS, Profile of Mood Score; PSQI, Pittsburgh Sleep Quality Index; PSS, Perceived Stress Scale. [a]Significantly different from year 3 ($P < 0.05$). [b]Significantly different from year 2 ($P < 0.05$).

strategy to restrict food intake, disinhibition reflects the tendency to overeat in response to internally and externally challenging conditions, like stress experience and high palatability (28). In the present analysis, all three scales of the TFEQ showed an overall association with both BMI and HOMA-IR, and changes in these seemed critically associated with the ability to complete the intervention. Although aspects of eating behavior like cognitive restraint are often considered more of a personality trait, there is emerging literature on the importance of mindset pointing toward the possibility of adjusting personality traits to some extent with the manipulation of the individual state and supporting long-term weight management (29). Previous research from our laboratory and the current results point out that cognitive restraint is a changeable aspect of eating behavior, at least in healthy individuals. Particularly for men, a high level of disinhibition and hunger perception seemed important with regard to HOMA-IR. While there is a general conception of lower emotional susceptibility to disinhibition in men (30), it seems that, if present, disinhibition as well as hunger may have a more pronounced impact on metabolic health in men, based on the present analysis. In previous research, emotional susceptibility and high disinhibition have been linked to high perceived stress (31). Perceived stress was identified as critical for the time spent in the study and was one of the most relevant variables for HOMA-IR in the current analysis.

Several clinical and population-based studies have established positive associations between chronic stress, elevated glucocorticoid exposure, adiposity, and weight gain (32), potentially catalyzed by an insulin mediated route (3,33). Chronic glucocorticoid exposure is associated directly, as well as indirectly, with whole-body IR through stimulation of gluconeogenesis, interference with the insulin receptor pathway, and stimulation of lipolysis (34). Similar to stress, general mood disturbance and negative mood states were identified as obstructing weight loss efforts in intervention studies and promoting early dropout (35). Individualized pretreatment preparation of individuals in terms of coping strategies and stress reduction may be useful to secure long-term success of weight management efforts.

An additional factor that was shown to be associated with HOMA-IR was poor sleep quality, specifically for men (36). In several cross-sectional studies, sleep deprivation was associated with increased

systemic concentrations of ghrelin, an appetite stimulating hormone (37), which in turn is associated with peripheral IR (38), and therefore has been discussed as a potential mechanistic link between sleep, weight gain, and IR. There is support for the relationship between poor sleep quality and IR, particularly in men (36); however, reports are inconsistent (39) and may have been influenced by the increased prevalence of issues relating to obstructed breathing during sleep, including obstructive sleep apnea, in men (40). However, in an obstructive sleep apnea population including both men and women, the risk of disordered sleep posed a higher risk of metabolic complications for men specifically because of increased IR to maintain glucose homeostasis, and had a more pronounced impact on the functionality of β-cells (41).

In the current analysis, the increase in PA was not only relevant for all participants, but specifically relevant for women with regard to a reduction in HOMA-IR. There are several studies demonstrating that PA as a weight loss approach may be less effective in women, possibly because of less energy spent per given activity or a different compensatory behavior in response to increased energy expenditure (13,42).

Together with the increasing knowledge about the complexity of weight regulation, it has become evident that the simple advice of eat less, exercise more, is of limited success and may mostly work in individuals who may not necessarily be in need of intensive weight management support in the first place. Here, lifestyle-induced changes in psychobehavioral scores were differentially associated with changes in BMI and HOMA-IR; for HOMA-IR, differences between men and women are relevant independent of bodyweight, thus supporting more individualized, as well as sex-specific, approaches to weight loss and weight maintenance.

While this perspective has already gained attention in the medical treatment of disease, lifestyle intervention may need individual and sex-specific preparatory assessments to be successful for the long-term improvement of metabolic health. The current analysis covers many psychobehavioral aspects relevant to IR and weight maintenance, but it is by no means exhaustive. To get a more complete assessment, the impact of other variables, including cognition, depression, and anxiety, for example, should be added. While objective assessment like the use of accelerometry for activity and sleep has been used as much as possible, other physiological underpinnings would strengthen the analysis (i.e., cortisol measurements to underscore stress perception). Another potential limitation of the current analysis is the condition of weight loss before entering the intervention. Because only successful participants were considered for the current analysis, we cannot fully exclude selection bias.

Besides the general parameters of eating behavior and physical activity, control of stress, mood disturbance, and sleep characteristics were associated with changes in BMI, HOMA-IR, and the length of time spent in the PREVIEW study and may pose useful targets in the preparation for successful weight loss maintenance on an individual basis.

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oversees a glycemic index testing service at the University of Sydney, and is a co-author of books about diet and diabetes. S.P. was the Fonterra Chair in Human Nutrition and principal investigator for NZ National Science Challenge High Value Nutrition during the PREVIEW intervention. T.-M.L. is an advisor for the Sense diet program. No other potential conflicts of interest relevant to this article were reported.

Author Contributions. T.C.A. attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted. T.C.A., M.D., and M.W.-P. designed the part of the PREVIEW intervention study presented. T.C.A., M.D., and B.W. were responsible for the statistical analyses. T.C.A. and M.W.-P. drafted the manuscript. J.B.-M., M.F., W.S., E.F., A.R., and M.W.-P. designed the main PREVIEW project. All authors contributed to the implementation of the experimental trial and the analysis and interpretation of the data. All authors contributed to the critical revision of the manuscript for important intellectual content. All authors agreed that the accuracy and integrity of the work were appropriately investigated and resolved, and all authors approved the final version of the manuscript. T.C.A. and M.W.-P. are the guarantors of this work and, as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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