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Genetic predisposition to obesity, restrained eating and changes in body weight – a population-based prospective study

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ABSTRACT

Objectives: There is no consensus on whether cognitive control over food intake (i.e. restrained eating) is helpful, merely ineffective or actually harmful in weight management. We examined the interplay between genetic risk of obesity, restrained eating and changes in body weight and size. **Methods:** Participants were Finnish 25- to 74-year-olds who attended the DILGOM study at baseline in 2007 and follow-up in 2014. At baseline (n=5024), height, weight and waist circumference (WC) were measured in a health examination and participants self-reported their weight at age 20 years. At follow-up (n=3735), height, weight and WC were based on measured or self-reported information. We calculated 7-year change in body mass index (BMI) and WC, and annual weight change from age 20 to baseline. Three-Factor Eating Questionnaire-R18 was used to assess restrained eating. Genetic risk of obesity was assessed by calculating a polygenic risk score of 97 known BMI-related loci. **Results:** Cross-lagged autoregressive models indicated that baseline restrained eating was unrelated to 7-year change in BMI (β=0.00; 95%CI=-0.01, 0.02). Instead, higher baseline BMI predicted greater 7-year increases in restrained eating (β=0.08; 95%CI=0.05, 0.11). Similar results were obtained with WC. Polygenic risk score correlated positively with restrained eating and obesity indicators in both study phases, but it did not predict 7-year change in BMI or WC. However, individuals with higher genetic risk of obesity tended to gain more weight from age 20 years to baseline and this association was more pronounced in unrestrained eaters than in restrained eaters (P=0.038 for interaction). **Conclusions:** Our results suggest that restrained eating is a marker for previous weight gain rather than a factor that leads to future weight gain in middle-aged adults. Genetic influences on weight gain from early to middle adulthood may vary according to restrained eating, but this finding needs to be replicated in future studies.

INTRODUCTION

Many people living in high-income countries deliberately restrict their food intake to prevent weight gain or reduce weight. Despite considerable research efforts over several decades, there is still no consensus on whether restrained eating is helpful, merely ineffective, or actually harmful in weight management.[1,2] Several studies have reported positive cross-sectional correlations between restrained eating and indicators of obesity, though negative and non-significant associations have been observed as well.[3-5] In contrast, prospective cohort studies (for a review, see Lowe et al.[6]) have rather consistently found that restrained eating is unrelated to subsequent weight changes. Researchers have therefore proposed that restrained eating may be a marker for susceptibility to previous weight gain instead of being a factor that leads to future weight gain.[1,2] However, studies that have explicitly addressed this hypothesis by testing simultaneously the effect from restrained eating to weight change and that from weight to restrained eating change are scarce. Two family-based studies observed that higher initial level of body mass index (BMI) predicted 1- or 2-year increases in restrained eating in adolescents or their parents rather than the other way round.[4,7] It is unknown, however, whether these results can be generalized to a general adult population over a longer period of time.

Recent developments in the area of genetics might provide a novel avenue to further our understanding of the restrained eating – body weight relationship. Findings from adult twin studies imply that differences in restrained eating (26-63%) and even more in BMI (57-77%) are partly attributable to genetic differences between individuals.[8-10] Moreover, genome-wide association studies (GWAS) have increased knowledge of the common genetic variants associated with obesity. The most recent meta-analysis identified 97 genome-wide significant BMI-related single nucleotide polymorphisms (SNPs), while consideration of all

common variants accounted for nearly 20% of the variance in BMI.[11] This progress also provides an opportunity to examine the interplay between identified genetic variants and behavioral factors in the development of obesity. The common risk alleles for obesity are associated with increased appetite and reduced satiety,[12-15] but their relationships with cognitive control over food intake (i.e. restrained eating) have rarely been explored. Particularly, examining whether restrained eating modifies the impact of obesity-related genetic variants on weight change can provide insight into the extent to which restrained eating may be helpful in limiting or offsetting a genetic predisposition to obesity. There is consistent evidence that genetic risk of obesity is more pronounced in physically inactive individuals compared with active individuals,[16-20] but research on the gene – diet interactions has produced more mixed findings.[21-24]

We used a large population-based prospective study of Finnish adults to extend knowledge on the dynamics between genetic risk of obesity, cognitive control over food intake and changes in body weight and size. Our first aim was to examine whether restrained eating predicted changes in BMI and waist circumference (WC), or whether BMI and WC rather predicted changes in restrained eating during a 7-year follow-up period. Secondly, we investigated whether restrained eating modified the associations between 97 obesity-related genetic variants (using a polygenic risk score, PRS) and weight changes over adulthood.

MATERIALS AND METHODS

Study sample and design

Participants were 25- to 74-year-old Finnish men and women who took part in the DIetary, Lifestyle and Genetic determinants of Obesity and Metabolic syndrome (DILGOM) study at baseline (n=5024) in 2007 and at follow-up (n=3735) in 2014 (see Supplementary Figure 1

for a participant flow chart of the DILGOM study). The baseline phase was conducted as a part of the FINRISK 2007 study where a random sample of 10 000 people, stratified by 10-year age groups and gender, was drawn from the Finnish population register in five large study areas.[25] Altogether, 6258 (response rate=63%) participants took part in the FINRISK 2007 in January-March and they were all invited to the DILGOM 2007 study (n=5024, response rate=80%) conducted in April-June. The baseline phase contained a health examination at a study center and several self-administered questionnaires completed either during the visit or at home.[26] In the health examination, trained research nurses measured participants' height, weight and WC, and took blood samples from them. All baseline participants alive at the end of the year 2013 received an invitation to take part in the DILGOM follow-up phase, which was conducted 7 years later in April-June 2014 (n=3735, response rate=82%). The data collection was carried out in two groups: 1) participants who lived in the areas of Turku and Loimaa and in the cities of Helsinki and Vantaa were invited to a similar health examination to the one at baseline (n=1312); 2) participants who lived in the other three study areas (North Karelia, North Savo and Oulu) received a mail-back questionnaire and self-reported their current weight and height (n=2423). They also measured their WC themselves, with a measurement tape that was sent to them together with detailed instructions including a figure indicating measurement at a level midway between the lower rib margin and iliac crest.

The research protocols of the DILGOM baseline and follow-up studies were designed and conducted in accordance with the guidelines of the Declaration of Helsinki and have been approved by the Ethics Committee of Helsinki and Uusimaa Hospital District (decision numbers 229/E0/2006 and 332/13/03/00/2013, respectively). In addition, written informed consent was obtained from all participants.

Genotyping

Genome-wide genotyping data were available for 4719 DILGOM participants in the present analyses. The genotyping was done with Illumina arrays (Illumina, Inc., San Diego, CA, USA) within larger datasets in six batches: three batches with HumanCoreExome (N=3823), two batches with HumanOmniExpress (N=243), and one batch with Human 610-Quad BeadChip (N=653). Imputation was performed with IMPUTE2 v2.3.2 (ref. 27,28) separately within each genotyping batch, with the 1000 Genomes Project Phase 3 variant set (release 20130502) and Finnish SiSu sequencing data used as imputation reference panels. Prior to the imputation, individuals with call rate <98%, markers with call rate <95% and gender mismatches were excluded, and pre-phasing was performed with SHAPEIT v2 (ref. 29). All 97 BMI SNPs were in Hardy-Weinberg equilibrium and were imputed with very high certainty (information score >0.95). Closely related individuals were excluded by calculating the pairwise identity-by-descent for all pairs and excluding one sample from pairs with pi-hat values >0.2. Additionally, 93 DILGOM participants did not have genome-wide genotyping coverage and imputed genotypes, but had Illumina Cardio-MetaboChip genotyping data available for 89-90 of the 97 BMI SNPs. Genotyping quality was insured with thresholds of >95% call rate for each SNP and individual, and checking that the genotypes were in Hardy-Weinberg equilibrium. The missing 7-8 SNPs were imputed using the average coded allele frequency within the other DILGOM individuals.

Measures

Restrained eating was measured using the Cognitive Restraint scale of the 18-item Three-Factor Eating Questionnaire (TFEQ-R18)[30] at baseline and follow-up. The TFEQ-R18 was developed on the basis of a factor analysis of the original 51-item TFEQ in the Swedish Obese Subjects study[30] and it has been found to be valid in the general population.[5,31] The

Cognitive Restraint scale contains 6 items, such as "I deliberately take small helpings to control my weight". Respondents were asked to rate each item on a 4-point scale, except one item, which was rated on an 8-point scale (later transformed to the 4-point scale). Total scale scores (Cronbach's alpha was 0.72 at baseline and 0.73 at follow-up) were calculated as a mean of the rated items for respondents who had answered at least 3 of the 6 items (n=4865 at baseline and n=3297 at follow-up). The total scores ranged from 1 to 4 with higher scores reflecting greater tendency to restrained eating.

Changes in body weight and size. Height, weight and WC were measured using standardized international protocols[32] at baseline and follow-up. Participants' weight was measured to the nearest 0.1 kg, height to the nearest 0.1 cm and WC to the nearest 0.5 cm. All measurements were made in a standing position in light clothing and without shoes. WC was measured at a level midway between the lower rib margin and iliac crest. At baseline, weight and height measurements were available for 5017 (99.9%) participants to calculate BMI (kg/m^2), while WC measurement was available for 4994 (99.4%) participants. At follow-up, BMI and WC were based on measured (n=1310 and 1305, respectively) or self-reported (n=2352 and 2288, respectively) information. We computed *7-year change in BMI and WC* by subtracting the baseline value from the value at follow-up. In a recent validation study conducted in a subset of DILGOM participants, the mean differences between self-reported and nurse-measured height, weight and WC were small and the intra-class correlations were 0.95 or greater in both genders.[33] Respondents with measured and self-reported anthropometric data at follow-up were therefore included in the present study. Additionally, we calculated *annual weight change from 20 years of age to baseline* as in a recent article by Rukh and colleagues.[34] Participants reported twice at baseline (first in the FINRISK 2007 and then in the DILGOM 2007 study) how much they weighed (kg) at age 20 years. We calculated the mean of these two self-reports (r=0.94) to increase reliability of this

retrospective information. Annual weight change was then estimated by diving the difference between baseline weight and weight at age 20 years by the number of follow-up years (mean=32.2 years, SD=13.5).[34]

Genetic risk of obesity was assessed by calculating a PRS using 97 BMI SNPs identified in the most recent genome-wide meta-analysis.[11] The potential number of BMI-increasing alleles across the 97 SNPs ranged from 0 to 194 with higher scores indicating greater genetic predisposition to obesity. A weighted PRS (n=4812) was computed by multiplying the number of BMI-increasing alleles at each locus by its β coefficient with BMI in the European ancestry sex-combined analysis derived from the recent meta-analysis.[11]

Baseline age, gender, self-reported total years of education, leisure time physical activity and *smoking status* were used as covariates in the analyses. Leisure time physical activity was assessed using a single question with seven response options: "How often do you exercise at least 20 minutes in your leisure time so that you experience at least mild exhaustion and sweating?". Participants who were unable to exercise due to illness or injury (n=186) were excluded. Continuous scale (0=less than once a week, 1=once a week, 2=twice a week, 3=three times a week, 4=four times a week, 5=five times a week or more) was used in the analyses. Current smokers were defined as those who had smoked daily more than once a day during the preceding month and for at least one year, and were compared to former/occasional/never smokers.

Statistical methods

We used cross-lagged autoregressive models (part of the structural equation modeling framework) to determine the prospective relationships between restrained eating and the two indicators of obesity (BMI and WC). Maximum likelihood was used as an estimator and Figure 1 shows the model specifications in more detail. The models were initially adjusted for

baseline age and gender and thereafter baseline education, leisure time physical activity and smoking status were added as covariates. Linear regression analyses were used to test interactions between restrained eating and genetic risk of obesity in predicting 7-year change in BMI and WC, and annual weight change from age 20 years to baseline. An interaction term between restrained eating and weighted PRS was added after the main effects into the models. Linear regression analyses were similarly adjusted for several baseline variables including age, gender, BMI or WC (or weight at age 20 years), education, leisure time physical activity and smoking status. The annual weight change variable had non-normal distribution (skewness=2.1, kurtosis=14.2), which was normalized after excluding 83 outliers (>3 standard deviations from the mean). However, we present analyses based on all observations because removing these outliers did not affect the results. All statistical tests were two-sided and $P<0.05$ was considered significant.

Code availability

Mplus Versions 5 and 7 (Muthen & Muthen, Los Angeles, CA, USA) were utilized to perform cross-lagged autoregressive models, while all other analyses were conducted using IBM SPSS Statistics 23 (IBM Corp., Armonk, NY, USA). Relevant code are available from the corresponding author by request.

RESULTS

Table 1 displays descriptive characteristics for the study participants at baseline in 2007 and at follow-up in 2014 (see Supplementary Table 1 for the respective information by gender). The mean level of restrained eating remained the same during the 7-year follow-up period. Participants' weight and WC mostly increased with an average weight gain and WC increase

of 0.6 kg and 2.3 cm in men, and 0.9 kg and 2.1 cm in women. These changes varied by age as indicated by the following mean values in the three age groups (25-39-, 40-59- and 60-74-year-olds): 2.4 kg (SD=6.8), 1.5 kg (SD=5.3) and -1.1 kg (SD=5.6) for weight, and 3.6 cm (SD=7.6), 2.9 cm (SD=6.4) and 0.5 cm (SD=7.1) for WC (not shown in Table 1). A quarter of participants (26% in men and 25% in women) lost 3% or more of their initial weight, whereas around one third of them (33% and 39%, respectively) could be defined as weight gainers (gained 3% or more of their initial weight).[35] Annual weight gain from 20 years of age to baseline was 0.5 kg on average (Table 1). The number of BMI-increasing alleles ranged from 67 to 116, the mean number being 92.

Age-adjusted Pearson's correlation coefficients between the main study variables can be found in Supplementary Table 2. Weighted PRS correlated positively with obesity indicators at baseline ($r=0.17$ for BMI and $r=0.15$ for WC, both $P<0.001$) and follow-up ($r=0.15$ for BMI and $r=0.13$ for WC, both $P<0.001$). We also observed small positive associations between restrained eating and weighted PRS ($r=0.07$, $P<0.001$ at baseline and $r=0.06$, $P=0.001$ at follow-up). Participants in the lowest PRS quintile scored lower on restrained eating than those in higher PRS quintiles in both study phases (Figure 2).

Results from the age- and gender-adjusted and fully adjusted cross-lagged autoregressive models indicated that baseline restrained eating was unrelated to 7-year change in BMI and WC (Figure 1). Instead, higher baseline BMI and WC predicted greater 7-year increases in restrained eating. Multi-group analyses testing potential gender ($\Delta\chi^2=0.64$-6.31, $\Delta df=1$, $P=0.012$-0.424 with 3/4 P-values > 0.05) and age ($\Delta\chi^2=0.80$-2.60, $\Delta df=2$, $P=0.273$-0.672) differences in these cross-lagged associations implied that the effects did not vary across the three age groups. However, the effect from baseline BMI to restrained eating at follow-up was stronger in men (std. $\beta=0.12$; 95% CI=0.08, 0.16; $P<0.001$) than in women (std. $\beta=0.06$; 95% CI=0.02, 0.10; $P=0.002$) and similar gender difference was observed with

WC (Supplementary Figure 2). Finally, sensitivity analysis excluding participants with self-reported anthropometric data at follow-up produced comparable results: baseline restrained eating did not predict change in BMI (std. β=0.02; 95% CI=-0.01, 0.04; P=0.200) nor WC (std. β=0.02; 95% CI=0.00, 0.05; P=0.050), while higher BMI (std. β=0.10; 95% CI=0.05, 0.14; P<0.001) and WC (std. β=0.10; 95% CI=0.05, 0.15; P<0.001) at baseline were related to greater increases in restrained eating.

Tables 2 and 3 summarize results from the linear regression analyses. Restrained eating and weighted PRS were both unrelated to 7-year change in BMI and WC, and no statistically significant restrained eating × weighted PRS interactions were observed in relation to these changes. Age- and gender-adjusted and fully adjusted models produced comparable results. However, individuals with higher genetic risk of obesity tended to gain more weight from age 20 years to baseline and the interaction term between restrained eating and weighted PRS was nominally significant. Again, findings did not vary remarkably across age- and gender-adjusted (P=0.038 for the interaction) and fully adjusted (P=0.013 for the interaction) models. Similar estimates were also obtained from sensitivity analysis excluding participants (n=438, 11%) who had more than 5 kg difference in the two self-reports of their weight at 20 years (P=0.013 for the interaction). To interpret the interaction effect, participants were divided into three groups based on their score on the Cognitive Restraint scale and the weighted PRS - weight change association was modelled separately in these groups (Table 4). The positive association between the PRS and weight gain was more pronounced in participants with a low level of restrained eating (scores <2.0) compared to those with a high level of restrained eating (scores >3.0).

DISCUSSION

To our knowledge, this is the first study to examine the interplay between cognitive control over food intake and 97 obesity-related genetic variants in influencing weight changes during adulthood. We firstly showed that higher body weight and size predicted greater increases in restrained eating rather than the other way round during the 7-year follow-up period. Secondly, we found partial evidence for the gene – restrained eating interaction: the positive association between a 97-loci PRS and annual weight gain from age 20 years to middle age was somewhat stronger in unrestrained eaters than in restrained eaters.

Our findings from the cross-lagged models offer support for the suggestion that restrained eating is a marker for previous weight gain rather than a factor that leads to future weight gain. On the one hand, restrained eating was unrelated to changes in BMI as well as in WC during the 7-year study period indicating that the likelihood to gain or lose weight was similar between restrained and unrestrained eaters. On the other hand, participants with higher initial BMI and WC were more likely to increase their restrained eating over time. These observations are consistent with the results of the two earlier studies conducted in adolescents or their parents.[4,7] We additionally found that the effects from weight status to restrained eating were slightly stronger in men than in women. In a large population-based study of 18-39-year-old Finns, older men were more likely to agree with the claim "I am too fat" than younger ones, whereas the age trend was less clear in women.[36] Such gender differences in the effects of age on body image could play a role in explaining the detected difference across men and women in this middle-aged sample. Yet, it is worth noting that the associations were small in magnitude in both genders and restrained eating scores also showed moderate to high between-individual stability (r=0.57 between the two measurements) during the study period. Many authors[6,37] have argued that restrained eaters are best characterized as those who are concerned about their food intake, eat less than they desire (particularly energy-dense foods), and mainly aim to avoid weight gain. Accordingly, most restrained eaters are not currently on

a diet to lose weight and are not necessarily in a state of negative energy balance. Thus, it is reasonable that restrained eating did not predict weight changes over the 7 years, but a question that remains is whether restrained eaters would have gained (more) weight without their cognitive tendency and behavioral strategies to restrict food intake.

Further evidence for restrained eating being a proxy for susceptibility to previous weight gain was offered by its small positive correlations with the PRS: individuals with a higher polygenic risk of obesity were slightly more likely to restrict their food intake than those with a lower risk. Likewise, the BMI-increasing variant of the FTO gene was positively associated with restrained eating (assessed using the same scale as in our study) in two cohorts of older US adults, although a 32-loci PRS did not show a significant relationship.[14] A Finnish twin study demonstrated that the positive cross-sectional correlation between restrained eating and BMI was explained by shared genetic factors.[9] Together these results suggest that genetic predisposition to obesity is one factor underlying restrained eating. Individuals may recognize that they possess this predisposition (via its impact on increased appetite and body weight) and consequently engage in restrained eating as an attempt to counteract weight gain.

To date, rather few observational studies have explored whether GWAS identified BMI-loci influence weight changes with mixed evidence.[34,38] We found that the 97-loci PRS was unrelated to 7-year changes in BMI and WC regardless of the level of restrained eating. Results from twin studies have similarly implicated that genes affecting the level of BMI may differ from those affecting the change in BMI with age.[39-41] Interestingly, we detected a different pattern of associations with respect to longer-term weight changes over adulthood. Participants with higher PRS had gained more weight from 20 years of age to middle age supporting observations from a recent Swedish cohort study where the association between a 31-loci PRS and weight change from age 20 years to late middle age was

301 analyzed.[34] It could be that the PRS is more important in determining earlier than later weight
302 gain in adulthood, which is in line with twin studies of the heritability of BMI per se (not
303 change) showing that heritability increases steadily up to age 20, then plateaus before
304 declining around middle age.[10,42-44] A unique finding in our research was that the PRS had a
305 stronger effect on annual weight gain in unrestrained eaters than in restrained eaters,
306 potentially reflecting that restrained eating might be helpful in reducing genetic influences on
307 weight gain from early to middle adulthood. Nonetheless, since the TFEQ-R18 was
308 completed after the studied weight change period, it is possible that at least some individuals
309 started to restrain their eating after they had gained weight. In those cases, restrained eating as
310 assessed at baseline cannot be interpreted to causally limit the impact of genetic variants on
311 obesity. The causal ordering between restrained eating and weight changes across different
312 decades of the adult lifespan therefore remains to be determined in future prospective studies.
313 The strengths of the present study lie in using a large population-based cohort of
314 adults with information on obesity-related genetic variants as well as on long-term weight
315 changes to advance understanding on restrained eating and its helpfulness in weight control.
316 We utilized the most recent information on BMI SNPs[11] to construct the PRS and tested
317 reciprocity of the restrained eating – body weight associations over time by using structural
318 equation modeling. Several limitations need also to be acknowledged. Although the sample
319 was initially randomly derived from the Finnish population register, there were non-
320 participants as in all observational studies including the previous FINRISK studies.[45,46]
321 Supplementary Table 3 shows that drop-out during the 7-year study period was linked to
322 younger age, lower education (borderline significant), male gender, and higher BMI and WC,
323 while non-participants and participants at follow-up did not differ in terms of baseline
324 restrained eating and genetic risk of obesity. We utilized inverse probability weighting as an
325 attempt to evaluate whether such selective attrition biased the estimates.[47,48] These weighted

analyses supported our conclusions: results from Figure 1 and Table 2 remained similar after incorporating the weights constructed using baseline age, gender, education and BMI (data not shown). Participants' weight at age 20 years was based on self-reported information (asked twice at baseline) and especially older participants may have experienced difficulties in recalling their weight correctly after several decades. But we were able to demonstrate that excluding those who had more than 5 kg difference in the two self-reports did not change the results. Finally, using the 6 items from the TFEQ-R18 to assess restrained eating did not allow us to determine whether different types of restraint would have produced divergent results. Particularly, it has been suggested that a form of restrained eating characterized by a flexible approach to controlling food intake is linked to successful weight management over time.[49] Nonetheless, the TFEQ-R18 is a purer measure of restrained eating than the widely used Concern for Dieting subscale of the Restraint Scale measuring preoccupation with food, concern about eating and overeating tendencies simultaneously.[50]

To conclude, our findings imply that higher level of restrained eating – as measured by the TFEQ-R18 – does not increase the probability of weight gain over the 7-year period in middle-aged adults. Instead, cognitive control over food intake appears to be a marker for susceptibility to previous weight gain – a predisposition that is partly inherited. There was also tentative evidence that genetic influences on weight gain from age 20 years to middle age may vary according to restrained eating. However, future long-term prospective studies with restrained eating measured in young adulthood should explore whether our results can be replicated and whether it is particularly flexible control that produces the positive effects.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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FIGURE LEGENDS

Figure 1. Prospective associations between restrained eating and obesity indicators in the Finnish DILGOM participants from 2007 to 2014. **(A)** Cross-lagged autoregressive model for restrained eating and BMI. **(B)** Cross-lagged autoregressive model for restrained eating and WC. Model 1 was adjusted for baseline age and gender. Model 2 was adjusted for baseline age, gender, education, leisure time physical activity and smoking status (covariates not shown in Figure). Standardized regression coefficients (95% confidence intervals) are shown on the arrows and correlation coefficients (95% confidence intervals) on the double arrows. ***P<0.001, **P<0.01, *P<0.05. BMI, body mass index; DILGOM, DIetary, Lifestyle and Genetic determinants of Obesity and Metabolic syndrome; WC, waist circumference.

Figure 2. Age-adjusted restrained eating mean scores and 95% confidence intervals by polygenic risk of obesity in the Finnish DILGOM participants. **(A)** Restrained eating mean scores by weighted PRS quintiles at baseline in 2007. **(B)** Restrained eating mean scores by weighted PRS quintiles at follow-up in 2014. ANCOVA was used to test the equality of the means between weighted PRS quintiles. Levene's test indicated that the variance was equal across the quintiles at baseline (P=0.200) and follow-up (P=0.950). DILGOM, DIetary, Lifestyle and Genetic determinants of Obesity and Metabolic syndrome; PRS, polygenic risk score.

Table 1. Descriptive characteristics of the Finnish DILGOM participants at baseline in 2007 and follow-up in 2014[1]

	All participants	Participants who attended baseline and follow-up phases	
Variables	Year 2007	Year 2007	Year 2014
Number of participants[2]	4681-5024	3236-3735	3236-3735
Age (yrs)	52.6 ± 13.5[3]	53.0 ± 13.0	60.0 ± 13.0
Men (%)	46.3	45.2	–
Education (yrs)	12.6 ± 4.0	12.7 ± 4.0	–
Restrained eating	2.4 ± 0.5	2.4 ± 0.5[4]	2.4 ± 0.6[4]
Change 2007-2014	–	–	0.0 ± 0.5
Weight (kg)	76.9 ± 15.5	76.2 ± 15.0[4]	76.9 ± 15.3[4]
Change 2007-2014	–	–	0.7 ± 5.9
BMI (kg/m^2)	27.0 ± 4.9	26.8 ± 4.7[4]	26.9 ± 4.7[4]
Change 2007-2014	–	–	0.1 ± 2.1
Overweight, BMI ≥ 25 kg/m^2 (%)	62.5	61.4[4]	62.3[4]
Obesity, BMI ≥ 30 kg/m^2 (%)	21.7	19.9[4]	20.6[4]
WC (cm)	91.4 ± 13.7	90.6 ± 13.1[4]	92.8 ± 13.3[4]
Change 2007-2014	–	–	2.2 ± 7.0
Annual weight change (kg) from age 20 years to baseline	0.5 ± 0.5	0.5 ± 0.5	–
97-loci PRS	91.8 ± 6.2	91.7 ± 6.2	–
Weighted 97-loci PRS	2.3 ± 0.2	2.3 ± 0.2	–
Leisure time PA ≥ 4 times/week (%)	28.3	28.7	–
Current smokers (%)	17.5	15.1	–

[1] BMI, body mass index; DILGOM, DIetary, Lifestyle and Genetic determinants of Obesity and Metabolic syndrome; PA, physical activity; PRS, polygenic risk score; WC, waist circumference. [2] Numbers are ranges as missing information varied between the study variables. [3] Mean ± SD (all such values). [4] Calculated for participants with information on the respective variable from both study phases.

Table 2. Associations between restrained eating, polygenic risk of obesity and 7-year changes in BMI and WC in the Finnish DILGOM participants[1]

	BMI change 2007-2014 (n=3451)				WC change 2007-2014 (n=3368)			
Independent variables	β	95% CI for β	std. β	P-value	β	95% CI for β	std. β	P-value
Age- and gender-adjusted models								
Restrained eating 2007[2]	0.02	-0.13, 0.16	0.00	0.829	0.03	-0.44, 0.51	0.00	0.887
Weighted PRS[2]	-0.39	-0.82, 0.03	-0.03	0.069	-1.10	-2.54, 0.34	-0.03	0.133
Restrained eating × Weighted PRS[3]	-0.36	-1.20, 0.48	-0.22	0.406	-0.15	-2.99, 2.69	-0.03	0.917
Fully adjusted models								
Restrained eating 2007[4]	0.10	-0.04, 0.24	0.02	0.166	0.32	-0.16, 0.81	0.02	0.194
Weighted PRS[4]	0.04	-0.39, 0.47	0.00	0.846	0.46	-0.99, 1.92	0.01	0.531
Restrained eating × Weighted PRS[5]	-0.70	-1.54, 0.15	-0.42	0.106	-1.57	-4.43, 1.30	-0.29	0.284

[1] Linear regression models were used to calculate estimates. BMI, body mass index; DILGOM, DIetary, Lifestyle and Genetic determinants of Obesity and Metabolic syndrome; PRS, polygenic risk score; WC, waist circumference. [2] Independent variables: age, gender, restrained eating, and weighted PRS (model 1). [3] Independent variables: model 1 + restrained eating × weighted PRS interaction term. [4] Independent variables: age, gender, baseline BMI or WC, education, leisure time physical activity, smoking status, restrained eating, and weighted PRS (model 2). [5] Independent variables: model 2 + restrained eating × weighted PRS interaction term.

Table 3. Associations between restrained eating, polygenic risk of obesity and weight change from age 20 years to baseline in the Finnish DILGOM participants[1]

	Weight change from age 20 years to baseline (n=4460)			
Independent variables	β	95% CI for β	std. β	P-value
Age- and gender-adjusted models				
Restrained eating 2007[2]	0.03	0.00, 0.06	0.03	0.055
Weighted PRS[2]	0.24	0.15, 0.33	0.08	<0.001
Restrained eating × Weighted PRS[3]	-0.18	-0.36, -0.01	-0.46	0.038
Fully adjusted models				
Restrained eating 2007[4]	0.04	0.01, 0.07	0.04	0.007
Weighted PRS[4]	0.26	0.17, 0.35	0.08	<0.001
Restrained eating × Weighted PRS[5]	-0.23	-0.41, -0.05	-0.56	0.013

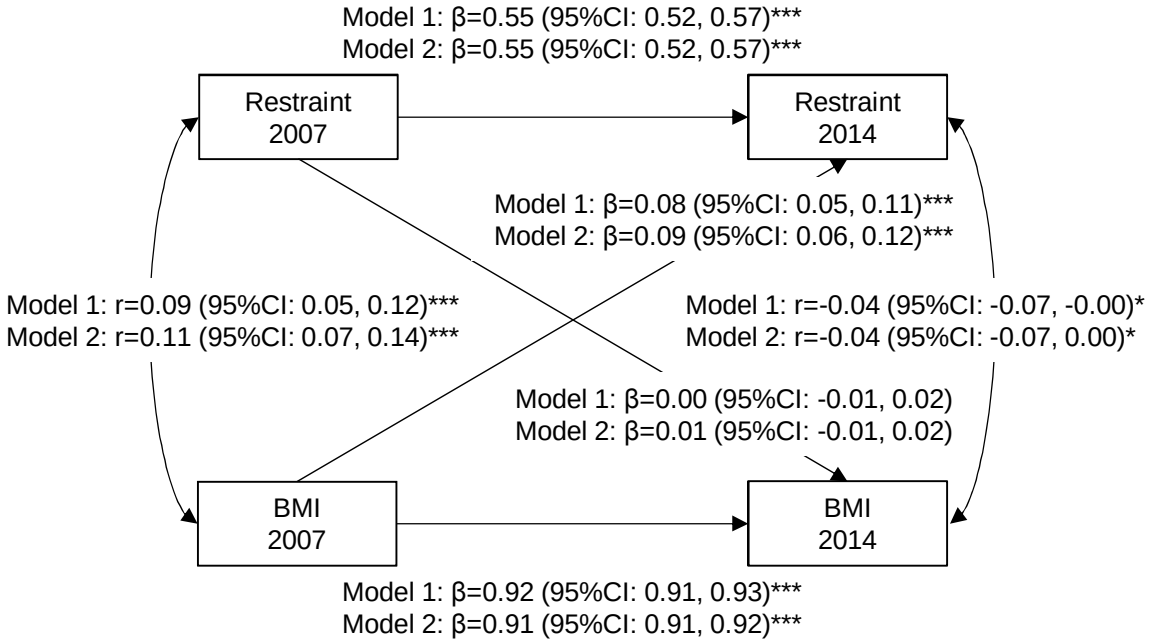
[1] Linear regression models were used to calculate estimates. DILGOM, DIetary, Lifestyle and Genetic determinants of Obesity and Metabolic syndrome; PRS, polygenic risk score. [2] Independent variables: age, gender, restrained eating, and weighted PRS (model 1). [3] Independent variables: model 1 + restrained eating × weighted PRS interaction term. [4] Independent variables: age, gender, weight at age 20 years, education, leisure time physical activity, smoking status, restrained eating, and weighted PRS (model 2). [5] Independent variables: model 2 + restrained eating × weighted PRS interaction term.

Table 4. Associations between polygenic risk of obesity and weight change from age 20 years to baseline according to the level of restrained eating in the Finnish DILGOM participants[1]

	Weight change from age 20 years to baseline			
	β	95% CI for β	std. β	P-value
Age- and gender-adjusted models				
Low restrained eating scores (< 2.0), n=719				
Weighted PRS[2]	0.31	0.07, 0.55	0.09	0.011
Restrained eating scores 2.0-3.0, n=3369				
Weighted PRS[2]	0.22	0.12, 0.32	0.07	<0.001
High restrained eating scores (> 3.0), n=372				
Weighted PRS[2]	0.15	-0.14, 0.43	0.05	0.321
Fully adjusted models				
Low restrained eating scores (< 2.0), n=671				
Weighted PRS[3]	0.41	0.16, 0.66	0.12	0.001
Restrained eating scores 2.0-3.0, n=3175				
Weighted PRS[3]	0.23	0.13, 0.33	0.07	<0.001
High restrained eating scores (> 3.0), n=336				
Weighted PRS[3]	0.26	-0.04, 0.57	0.09	0.087

[1] Linear regression models were used to calculate estimates. DILGOM, DIetary, Lifestyle and Genetic determinants of Obesity and Metabolic syndrome; PRS, polygenic risk score. [2] Independent variables: age, gender, and weighted PRS (model 1). [3] Independent variables: model 1 + weight at age 20 years, education, leisure time physical activity, and smoking status.

A


Model 1: β=0.55 (95%CI: 0.52, 0.57)***
Model 2: β=0.55 (95%CI: 0.52, 0.57)***
Restraint 2007
Restraint 2014
Model 1: β=0.08 (95%CI: 0.05, 0.11)***
Model 2: β=0.09 (95%CI: 0.06, 0.12)***
Model 1: r=0.09 (95%CI: 0.05, 0.12)***
Model 2: r=0.11 (95%CI: 0.07, 0.14)***
Model 1: r=-0.04 (95%CI: -0.07, -0.00)*
Model 2: r=-0.04 (95%CI: -0.07, 0.00)*
Model 1: β=0.00 (95%CI: -0.01, 0.02)
Model 2: β=0.01 (95%CI: -0.01, 0.02)
BMI 2007
BMI 2014
Model 1: β=0.92 (95%CI: 0.91, 0.93)***
Model 2: β=0.91 (95%CI: 0.91, 0.92)***

B

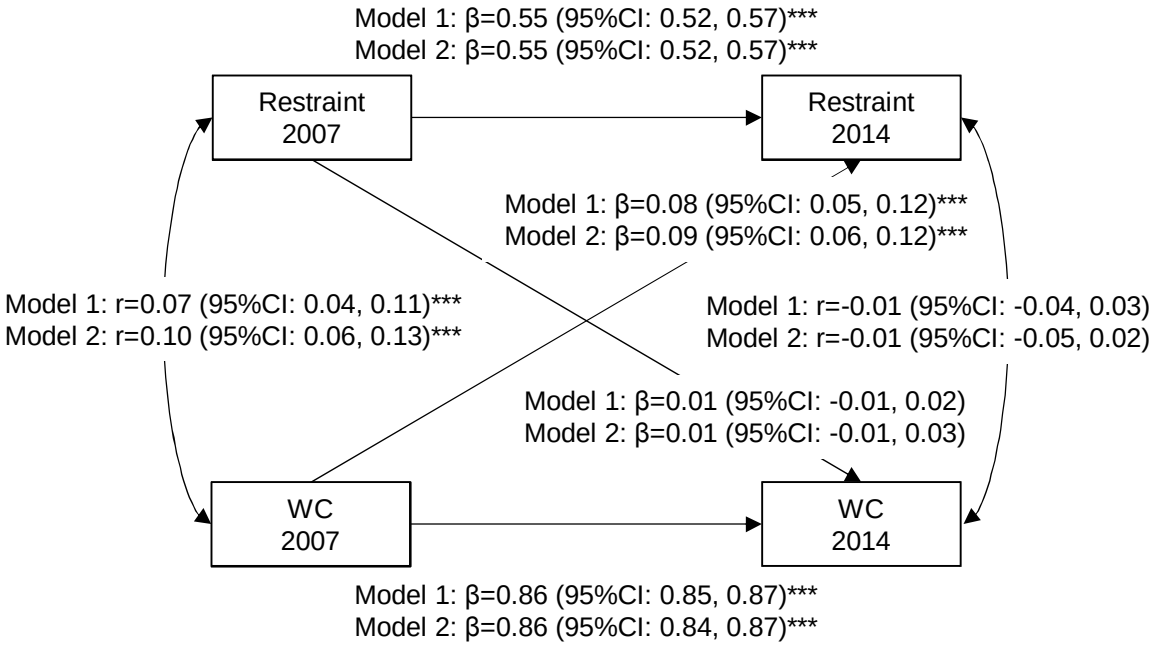
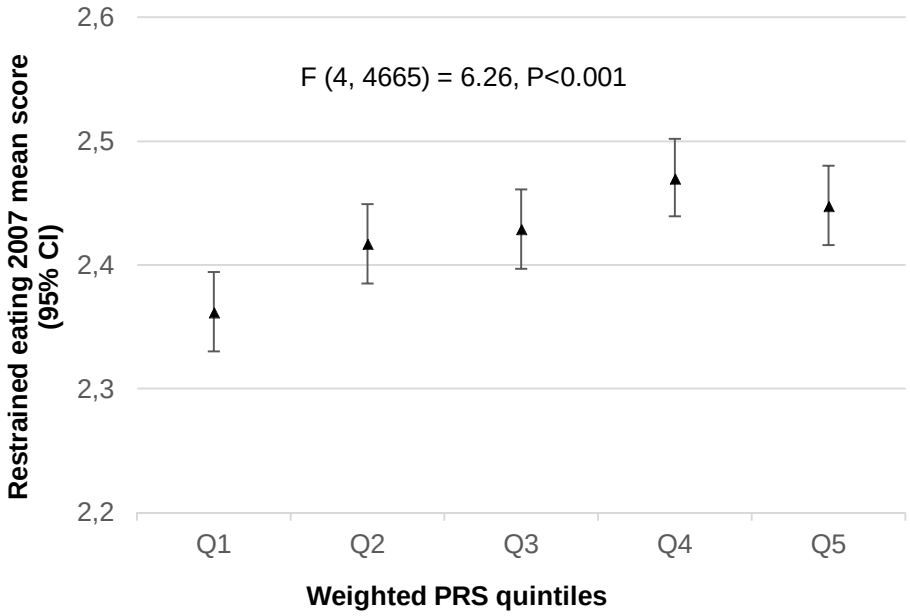

Model 1: β=0.55 (95%CI: 0.52, 0.57)***
Model 2: β=0.55 (95%CI: 0.52, 0.57)***
Restraint 2007
Restraint 2014
Model 1: β=0.08 (95%CI: 0.05, 0.12)***
Model 2: β=0.09 (95%CI: 0.06, 0.12)***
Model 1: r=0.07 (95%CI: 0.04, 0.11)***
Model 2: r=0.10 (95%CI: 0.06, 0.13)***
Model 1: r=-0.01 (95%CI: -0.04, 0.03)
Model 2: r=-0.01 (95%CI: -0.05, 0.02)
Model 1: β=0.01 (95%CI: -0.01, 0.02)
Model 2: β=0.01 (95%CI: -0.01, 0.03)
WC 2007
WC 2014
Model 1: β=0.86 (95%CI: 0.85, 0.87)***
Model 2: β=0.86 (95%CI: 0.84, 0.87)***

Figure 1

A


2,6
2,5
2,4
2,3
2,2
F (4, 4665) = 6.26, P<0.001
Restrained eating 2007 mean score (95% CI)
Q1
Q2
Q3
Q4
Q5
Weighted PRS quintiles

B

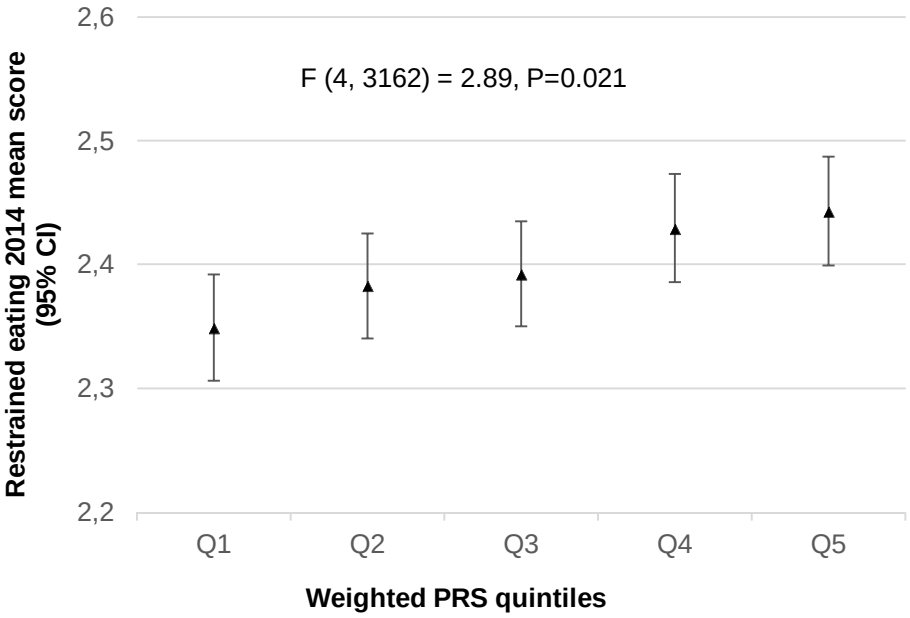

2,6
2,5
2,4
2,3
2,2
F (4, 3162) = 2.89, P=0.021
Restrained eating 2014 mean score (95% CI)
Q1
Q2
Q3
Q4
Q5
Weighted PRS quintiles

Figure 2