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ORIGINAL ARTICLE

Does dieting make you fat? A twin study

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Objective: To investigate whether the paradoxical weight gain associated with dieting is better related to genetic propensity to weight gain than to the weight loss episodes themselves.
Subjects: Subjects included 4129 individual twins from the population-based FinnTwin16 study (90% of twins born in Finland 1975–1979). Weight and height were obtained from longitudinal surveys at 16, 17, 18 and 25 years, and number of lifetime intentional weight loss (IWL) episodes of more than 5 kg at 25 years.
Results: IWLs predicted accelerated weight gain and risk of overweight. The odds of becoming overweight (body mass index (BMI) $\geqslant 25\,kg\,m^{-2}$) by 25 years were significantly greater in subjects with one (OR 1.8, 95% CI 1.3–2.6, and OR 2.7, 1.7–4.3 in males and females, respectively), or two or more (OR 2.0, 1.3–3.3, and OR 5.2, 3.2–8.6, in males and females, respectively), IWLs compared with subjects with no IWL. In MZ pairs discordant for IWL, co-twins with at least one IWL were $0.4\,kg\,m^{-2}$ ($P=0.041$) heavier at 25 years than their non-dieting co-twins (no differences in baseline BMIs). In DZ pairs, co-twins with IWLs gained progressively more weight than non-dieting co-twins (BMI difference $1.7\,kg\,m^{-2}$ at 16 years and $2.2\,kg\,m^{-2}$ at 25 years, $P<0.001$).
Conclusion: Our results suggest that frequent IWLs reflect susceptibility to weight gain, rendering dieters prone to future weight gain. The results from the MZ pairs discordant for IWLs suggest that dieting itself may induce a small subsequent weight gain, independent of genetic factors.
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Keywords: weight loss; weight regain; longitudinal studies; genetic; twins

Introduction

'Dieting makes you fat' is the provocative title of a diet book published 25 years ago[1] and the subject of several articles thereafter.[2,3] Ample clinical data also confirm that most dieters rapidly re-gain any achieved weight loss or even more. In prospective studies, weight control efforts have predicted future weight gain[4–8] even after adjustment for potential confounders such as age, body mass index (BMI) at baseline, smoking, alcohol use and social class.[9] A 3-year follow-up study of adolescents[10] showed that baseline dieting behaviours predicted an increased risk for obesity, and that weight reduction efforts were likely to result in weight gain rather than weight loss. A 5-year follow-up study in adolescents found this to be partly due to the adoption of deleterious behavioural patterns (breakfast skipping, lower levels of fruit and vegetable consumption, and lower physical activity, and binging) that are counterproductive for weight management.[11] The long-term result of dieting thus may paradoxically be the opposite of the desired goal.

There are at least three possible explanations for the paradox. First, restrictive dieting may lead to preoccupation with food and trigger overeating.[12] Second, suppression of metabolic rate and loss of lean mass by the negative energy balance may facilitate post-dieting weight-rebound.[13] These 'defensive' reactions (psychological or physiological) to dieting work so as to restore any weight lost through dieting and could in theory persist beyond the point of weight restoration. In the worst case, net weight gain would be accompanied by undesirable changes in body composition, with a disproportionate replenishment of fat stores.[14] The third explanation, the so-called 'obesity paradox' reverses the direction of causality between dieting and weight gain that is, dieting is seen simply as a reaction to the propensity of weight gain rather than vice versa.[3]

Both BMI and the number of intentional weight loss (IWL) episodes have substantial genetic components, 75% and

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38–66%, respectively.[15] It is thus possible that subjects genetically most prone to obesity end up dieting the most and for that reason subsequently gain the most weight. However, it is difficult to distinguish the genetic effects from those of the lifestyle in free-living humans, and in previous weight loss studies genetic factors have not been controlled for. Experimental interventions of repeated dieting to verify whether weight loss itself causes weight gain would be impossible to perform in real life settings as after an individual has dieted, it is not possible to reverse the status to a never-dieted state. However, such a possibility exists in twin studies, where natural experiments of monozygotic (MZ) twins discordant for lifetime dieting can be used.

In the present study, we used this unique study design to investigate the association between dieting and weight gain independent of genetic effects in IWL-discordant MZ twins found from five birth cohorts of Finnish twins and followed up from age 16 to 25 years. Additionally, we studied the weight development of IWL-discordant dizygotic (DZ) twins and both MZ and DZ pairs concordant for dieting history, to examine whether genes (being similar in MZ co-twins and partly different in DZ co-twins) and dieting show any interactions.

Subjects and methods

Subjects

The data are from FinnTwin16, a population-based study of five consecutive and complete birth cohorts of Finnish twins born in 1975–1979, identified from the Central Population Registry of Finland.[16] Baseline information was obtained by postal questionnaires at the age of 16 years, with follow-ups at 17, 18.5 (referred here as 18) and 22–27 (here, 25) years of age. The response rates were high (83–97%) on all occasions. Parents were sent their own questionnaire at the time of the first mailing. The twins were asked about height, weight, health habits, general health, social relationships at all ages and at 25 years the number of lifetime IWLs of at least 5 kg. This study is based on responses during the entire follow-up period. We excluded participants with known diseases (diabetes mellitus, systemic lupus erythematosus, inflammatory bowel disease, celiac disease, hyper- or hypothyroidism, malignancies, mobility disorders and eating disorder) and with medication affecting weight (for example, insulin, thyroxin and antipsychotic medication) ($n=302$).[17] We also excluded subjects with missing data on IWLs or on weight at baseline or at age 25 ($n=325$). Thus, our final study population comprised 4129 subjects, 1922 males and 2207 females. Twins' zygosity was determined b using the questions included in the baseline questionnaire as described previously.[18] The data included 542 MZ twin pairs, 516 same-sex DZ pairs, 554 opposite-sex DZ pairs and 48 pairs of unknown zygosity. The study protocol was approved by Indiana University's Institutional Review Board and the ethics committee of Helsinki University.

Measures

Lifetime IWL. IWL was assessed at 25 years by using the following question: 'How many times during your life have you intentionally lost $\geqslant$5 kg of weight?' The response alternatives were 'never, once, 2–4 times and 5 times or more'.[15]

Body mass index. Height and weight were self-reported at 16, 17, 18 and 25 years, and used to compute BMI (kg m^{-2}). The comparability of self-reported and measured data was ascertained in 566 twins on average 663 days after the completion of the 25-year questionnaire.[17] The intra-class correlation for BMI was 0.94 and κ-value for obesity was 0.66 (95% confidence interval (CI) 0.58–0.74).[17]

A BMI cut-off of 25 kg m^{-2} was used to categorize subjects into normal-weight and overweight at 25 years. BMI $\geqslant$30 kg m^{-2} was used to define obesity. Further, at 16 years, the baseline BMI was divided into three groups according to age-adjusted BMI *z*-scores[19] by using the zanthro-function of Stata:[20] low ($\leqslant$25th percentile, 19.0 kg m^{-2} in males; 18.7 kg m^{-2} in females), high ($\geqslant$75th percentile, 21.6 kg m^{-2} in males; 21.3 kg m^{-2} in females) and intermediate (the rest).

Confounding factors

Age at menarche was asked from females in the questionnaire at age 16 years.

Late physical maturity. Growth in height during late adolescence (16–18.8 years) was used as a proxy of delayed physical maturity.[21]

Physical activity. The frequency of leisure-time physical activity was assessed by a structured and validated questionnaire included in all four mailed questionnaires, with the following response alternatives: 'not at all, less than once a month, 1–2 times a month, about once a week, 2–3 times a week, 4–5 times a week and every day'.[22] Those who reported exercising 4–5 times per week or more at all three time points in adolescence (16–18 years) were 'active'; those exercising 1–2 times a month or less were 'passive'; and the remainder 'intermediate' at baseline.[22] The same categories were used at 25 years.

Smoking. Information on smoking was obtained at all ages and categorized into four groups: 'never smokers, former smokers, occasional smokers (current smokers other than daily smokers) and daily smokers'. As smoking status remained stable from 16 to 18 years,[17] baseline smoking was assessed based on information at 18 years and if this was missing, answers from 16 and 17 years were used.

Breakfast eating. Information on the frequency of eating breakfast (every morning, about 3–4 mornings a week and once a week or less often) was obtained at all ages, but used only at 16 years.[23]

Number of children. Information on the number of children (none, one, two or more) was obtained at age 25 years.

Parental BMI. Parents' BMI was calculated by using heights and weights recalled in the parental surveys filled out separately by both mother and father when the twins were 16 years.

Socio-economic status. Father's socio-economic status at twin age 16 years was determined based on questions concerning occupation, employment and education. Socio-economic status was classified into five categories (white collar, blue collar, manual worker, self-employed and farmer) by following the criteria of the Finnish Classification of Socio-economic Groups.[24]

Statistics
All statistical analyses were performed by using the Stata statistical software 9.0 (StataCorp. LP, College Station, TX, USA). Characteristics of subjects by never versus ever IWL groups were compared by using cross-tabulations and Pearson χ^2-test of independence. Differences in the rate of weight gain between IWL groups were tested by using linear regression models. First, a regression of BMI on age and IWL group was fitted as main effects for each sex and initial BMI group. Then, an additional term of the interaction of age with IWL group was added, and the change in fit between models was assessed by using a likelihood ratio test. A significant test would indicate that the slope of BMI with age differed by IWL category. The odds ratios (ORs) for having intentionally lost weight were assessed by using multinomial logistic regression models that controlled for BMI at baseline, physical activity, smoking, breakfast eating, number of children in females, mother's and father's overweight, and father's socioeconomic status. The ORs for having become overweight at 25 in previously non-overweight subjects by IWL categories was assessed by using logistic regression models that controlled for the same confounding factors as listed above. Analysis of variance was used to test whether the baseline BMI or mean BMI change differed by the number of weight losses in different baseline BMI groups. *t*-Tests were used to compare mothers' and fathers' BMIs in any of the IWL groups of the twin pairs (twins concordant for never IWL, twins concordant for IWL and twins discordant for IWL). The effect of the twin-sampling design on standard errors was taken into account in the individual-level analyses by computing robust standard errors by using the cluster option in Stata.[25] Differences in means between the co-twins were tested by using paired *t*-tests. In MZ twins, the differences within pairs are by definition independent of genetic factors. As DZ twins share half of their segregating genes, differences within pairs are partially but not fully adjusted for genetic factors. In both zygosities, the co-twins are matched for age and most environmental factors *in utero*, and in childhood and same-sex twins also for gender.

Results

Overweight and obesity
The prevalence of overweight was similar in females and in males at age 16 years, but after age 18, males were significantly more overweight than females (Table 1). At 25 years, 28% of males and 15% of females were overweight, and 4% of both genders obese.

Intentional weight loss
Thirty-eight percent of females and 24% of males reported an episode of IWL of 5 kg or more at least once during the lifetime (Table 1). Fifteen percent of females and 10% of males had a history of two or more IWLs.

In a multivariate analysis using BMI, physical activity, smoking, breakfast eating, parent's BMI and father's socio-economic status at baseline, growth in height from 16 to 18 years, age of menarche (in females) and number of children at 25 years as confounding factors, the odds for having at least one IWL was higher in males and females who had higher BMI at 16 years, smoked daily, skipped breakfast and were in the blue collar (in females also self-employed) socioeconomic group (Table 2).

IWL and weight development
Baseline BMI at age 16 was a highly significant determinant of future IWL episodes. Males (mean ± s.d. BMI $20.1 \pm 1.8\,kg\,m^{-2}$) and females ($19.5 \pm 2.0\,kg\,m^{-2}$) who had no IWL history, weighed significantly ($P<0.001$) less than either males ($21.3 \pm 2.5\,kg\,m^{-2}$) and females ($21.0 \pm 2.2\,kg\,m^{-2}$) with one IWL episode, or males ($22.2 \pm 2.8\,kg\,m^{-2}$) and females ($22.2 \pm 3.0\,kg\,m^{-2}$) who had at least two IWLs. The rate of weight gain differed significantly by IWL groups in both males and females for all three baseline BMI categories (low, intermediate and high) ($P<0.02$) (Figure 1). Subjects with no IWL gained the least, whereas those with five times or more IWLs had the largest weight gain in all BMI groups. The effects were especially large in those with the greatest BMI at baseline.

Figure 2 shows BMI change between 16 and 25 years by baseline BMI and the number of IWLs. Males gained much more weight than females, especially when the baseline BMI was low. Those who had the most IWL episodes had gained the most in all baseline BMI groups, in males particularly in the lowest BMI group (analysis of variance, $P<0.001$).

IWL and risk of becoming overweight
The risk of becoming overweight by 25 years in the initially non-overweight participants was proportional to the IWL frequency. Males with one (OR 1.8, 95% CI 1.3–2.6) or at least two (OR 2.0, 95% CI 1.3–3.3) IWLs were significantly more likely to become overweight than males with no IWLs (Table 3). Among females, the gradient by IWL was even

Table 1 Background characteristics of participants

	Males (n = 1922)	*Females (n = 2207)*
BMI (kg m^{-2}) at 16 years	20.4 (20.3–20.6)	20.2 (20.1–20.4)
BMI (kg m^{-2}) at 25 years	23.9 (23.7–24.0)	22.2 (22.0–22.3)
Prevalence of overweight (BMI ⩾ 25) (%)		
At 16 years	6.2	5.1
At 18 years	9.1	6.6
At 25 years	28.5	14.7
Intentional weight loss of 5 kg or more (%)		
Never	76.3	61.6
Once	13.4	23.4
2–4 times	8.6	13.2
⩾5 times	1.7	1.8
Physical activity at 16–18 years (%)		
Active	20.7	12.1
Intermediate	72.8	82.5
Passive	6.5	5.4
Physical activity at 25 years (%)		
Active	26.8	27.21
Intermediate	50.2	55.7
Passive	23.0	17.2
Smoking at 16–18 years (%)		
Never	48.9	51.4
Former	11.3	12.4
Occasional	12.3	15.0
Daily	27.5	21.2
Smoking at 25 years (%)		
Never	39.7	48.8
Former	13.6	14.1
Occasional	15.2	14.8
Daily	31.5	22.2
Breakfast eating at 16 years (%)		
Every morning	75.2	68.6
3–4 × week	12.9	16.5
Once a week or less	11.9	14.9
Age of menarche (years) in females		12.7 (12.7–12.8)
Late physical maturity (growth in height between 16 and 18 years) (cm)	3.6 (3.4–3.8)	0.8 (0.3–0.8)
Number of children at 25 years		
None	90.1	85.3
One	6.4	9.2
Two or more	3.5	5.4
Overweight mothers (%)	44.5	42.2
Overweight fathers (%)	60.3	60.9
Father's socioeconomic status		
White collar	25.7	23.5
Blue collar	17.0	16.7
Manual worker	37.8	38.9
Self-employed	9.3	11.1
Farmer	10.3	9.9

The values are the means and 95% confidence intervals or % of categories.

Table 2 The risk of having IWL of 5 kg or more by baseline characteristics in a multivariate model

	Males (n = 1396)	*Females (n = 1639)*
BMI at 16 years (kg m^{-2})	1.43 (1.33–1.53)***	1.51 (1.40–1.63)***
Late physical maturity (growth in height from 16 to 18 years) (cm)	0.95 (0.91–1.00)*	0.98 (0.90–1.63)
Physical activity at 16–18 years		
Active	1.00	1.00
Intermediate	0.98 (0.68–1.42)	1.19 (0.83–1.72)
Passive	0.67 (0.36–1.25)	0.59 (0.31–1.13)
Smoking at 16–18 years		
Never	1.00	1.00
Former	1.46 (0.92–2.30)	0.99 (0.68–1.45)
Occasional	1.52 (0.96–2.39)	1.25 (0.91–1.72)
Daily	1.81 (1.28–2.58)***	1.52 (1.11–2.08)**
Breakfast eating at 16 years		
Daily	1.00	1.00
3–4 times a week	1.65 (1.11–2.45)*	1.06 (0.77–1.45)
Once a week or less	1.56 (1.01–2.41)*	1.43 (1.02–2.01)*
Overweight mother	1.06 (0.78–1.44)	1.10 (0.86–1.40)
Overweight father	1.22 (0.91–1.65)	0.98 (0.77–1.25)
Father's socioeconomic status		
White collar	1.00	1.00
Blue collar	1.66 (1.08–2.56)*	1.54 (1.06–2.24)*
Manual worker	0.97 (0.67–1.40)	1.12 (0.82–1.54)
Self-employed	0.92 (0.51–1.64)	1.74 (1.12–2.71)*
Farmer	0.68 (0.37–1.23)	1.04 (0.66–1.66)

Abbreviation: IWL, intentional weight loss. Additionally adjusted for number of children at 25 years (NS) and age of menarche (in females) (NS). *P⩾0.05, **P⩾0.01, ***P⩾0.001.

steeper: OR 2.7 (95% CI 1.7–4.3) for those with one IWL and OR 5.2 (95% CI 3.2–8.6) for those with at least two IWLs. Adjusting for the possible confounders and baseline BMI did not change the result. Of the confounders, BMI at age 16 years highly significantly and independently predicted the risk of overweight at 25 years in the models in both genders. Further, in females, low physical activity at 25 years, low socio-economic status and father's overweight also predicted the risk of overweight (Table 3).

IWL and weight development in MZ and DZ twins

Next, we used the co-twin control approach to examine the effects of weight loss on later weight development adjusting fully (in MZ; Figure 3a) or partially (DZ twins; Figure 3b) for genetic effects. Further, in opposite-sex twins, we studied the effects of gender on weight loss and BMI development (Figure 3c).

The development of BMI from age 16 to 25 years was similar in co-twins who were concordant for never or ever IWL among both MZ and DZ twin pairs of the same sex (Figures 3a and b). Twins with a history of IWLs were heavier at all ages (for example, 2.7 and 3.0 kg m^{-2} for MZ and

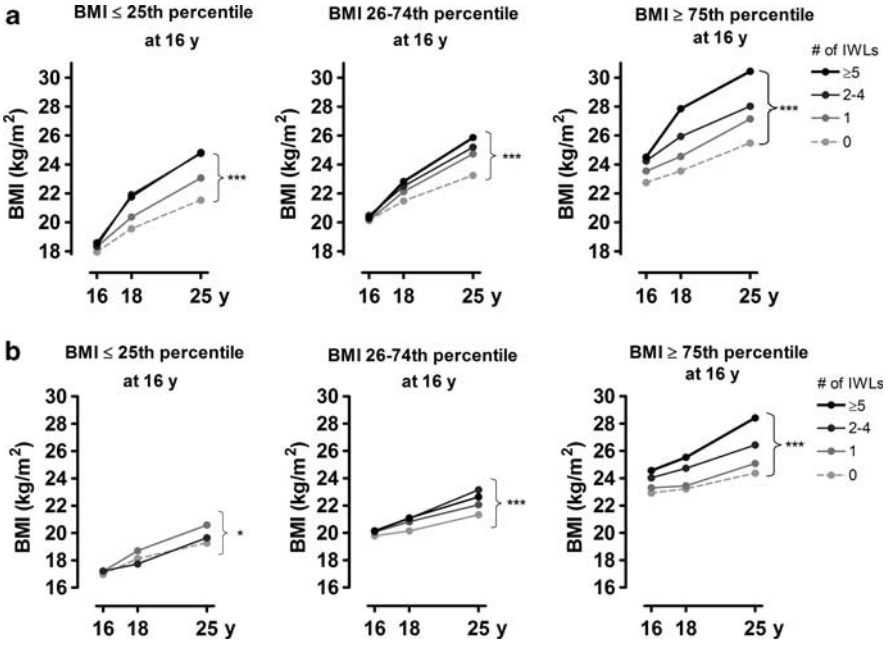

Figure 1 (**a**) BMI development from 16 to 25 years by lifetime IWL frequency and baseline BMI percentile at 16 years in males. For each group defined by sex and BMI baseline percentile, the regression slopes of BMI on age were significantly different by IWL frequency. *$P<0.05$, ***$P<0.001$ for interaction tests. (**b**) BMI development from 16 to 25 years by lifetime IWL frequency and baseline BMI percentile at 16 years in females. For each group defined by sex and BMI baseline percentile, the regression slopes of BMI on age were significantly different by IWL frequency. *$P<0.05$, ***$P<0.001$ for interaction tests.

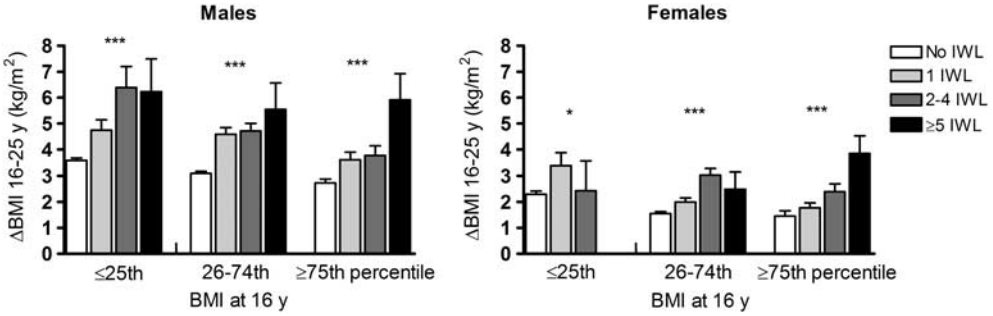

Figure 2 BMI change from 16 to 25 years by lifetime IWL frequency and baseline BMI percentile at 16 years. *$P<0.05$, ***$P<0.001$ (analysis of variance).

same-sex DZ pairs, respectively, at 16 years) and gained more weight (1.9 kg m^{-2} in MZ and 1.7 kg m^{-2} in same-sex DZ) than those with no such history ($P<0.001$ for all comparisons between pairs concordant for ever versus never weight loss).

A total of 145 MZ twin pairs were discordant for never versus ever IWL. At the age of 16 years, the weights of the co-twins of these pairs were similar. By age 25 years, co-twins with IWLs were slightly but significantly (0.4 kg m^{-2}, $P=0.041$) heavier than co-twins with no IWLs. In 179 DZ pairs discordant for IWL, co-twins with IWLs were constantly heavier (BMI difference at age 16 years 1.7 kg m^{-2}, $P<0.001$, and at 25 years 2.2 kg m^{-2}, $P<0.001$) than co-twins without IWLs.

In the opposite-sex DZ twins, males gained more weight than females in pairs where co-twins were concordant for IWL (Figure 3c). In IWL-discordant pairs, we examined the results separately by the gender of the dieting twin. Compared with their male co-twins, female twins with IWLs were 1.0 kg m^{-2} ($P<0.001$) heavier at 16, and as heavy at 25 years. In discordant pairs where the male had a history of IWLs, male twins were consistently much heavier than their twin sisters: 2.2 kg m^{-2} at 16 years and 4.3 kg m^{-2} at 25 years ($P<0.001$ for both).

The results presented above show that twin pairs where both co-twins have IWL episodes are heavier throughout their adolescence and young adulthood than pairs where neither of the co-twins had IWLs. Such group differences may depend on an underlying genetic background, where the group, which later ends up experiencing IWLs, is in fact heavier and more susceptible to obesity in the first place.

Table 3 The risk of becoming overweight from 16 to 25 years by IWL of 5 kg or more and by other baseline characteristics in the same multivariate model

	Males (n = 1396)	*Females (n = 1639)*
Lifetime intentional weight loss of 5 kg or more		
Never	1.00	1.00
Once	1.82 (1.27–2.60)***	2.72 (1.72–4.30)***
Twice or more	2.04 (1.27–3.29)**	5.22 (3.17–8.60)***
BMI at 16 years	1.19 (1.10–1.28)***	1.13 (1.05–1.20)***
Growth in height from 16 to 18 years (cm)	0.95 (0.91–1.00)	1.02 (0.90–1.16)
Physical activity at 16–18 years		
Active	1.00	1.00
Intermediate	0.66 (0.47–0.92)*	2.04 (0.99–4.23)
Passive	0.78 (0.40–1.51)	3.43 (1.25–9.38)*
Smoking at 16–18 years		
Never	1.00	1.00
Former	1.41 (0.92–2.17)	0.92 (0.50–1.69)
Occasional	1.16 (0.76–1.43)	1.41 (0.86–2.33)
Daily	1.00 (0.71–1.43)	1.36 (0.85–2.18)
Breakfast eating at 16 years		
Daily	1.00	1.00
3–4 times a week	1.22 (0.81–1.84)	1.08 (0.68–1.73)
Once a week or less	1.29 (0.81–2.08)	0.83 (0.48–1.43)
Overweight mother	1.10 (0.81–1.48)	1.33 (0.91–1.94)
Overweight father	1.21 (0.89–1.65)	1.66 (1.10–2.50)*
Father's socioeconomic status		
White collar	1.00	1.00
Blue collar	0.82 (0.52–1.31)	1.93 (1.00–3.72)*
Manual worker	1.07 (0.75–1.53)	1.88 (1.04–3.37)*
Self-employed	0.89 (0.53–1.48)	0.86 (0.39–1.92)
Farmer	0.93 (0.54–1.61)	1.80 (0.82–3.95)

Abbreviation: IWL, intentional weight loss. Additionally adjusted for number of children at 25 years (NS) and age of menarche (in females) (NS). *$P \geqslant 0.05$, **$P \geqslant 0.01$, ***$P \geqslant 0.001$.

Further, the fact that in the DZ twins co-twins who had IWLs were clearly heavier already at age 16 than their non-IWL twin pair members would suggest that the need to diet only arises in co-twins who are more genetically predisposed to obesity.

Parental BMI in the IWL groups

To further elucidate the possible role of inherited predisposition, we analysed parental BMIs by the twin pair IWL groups (concordant for never IWL, concordant for IWL, discordant for IWL). In twin pairs concordant for never IWL, mothers' and father's mean ± s.d. BMIs ($24.6 \pm 3.9\,kg\,m^{-2}$ and $25.8 \pm 3.2\,kg\,m^{-2}$, respectively) were significantly ($P<0.001$) lower than in twin pairs concordant for IWL (mother's BMI $25.8 \pm 4.1\,kg\,m^{-2}$ and father's BMI $27.0 \pm 3.6\,kg\,m^{-2}$). In pairs discordant for IWL, mother's ($25.5 \pm 4.3\,kg\,m^{-2}$) and father's BMIs ($26.3 \pm 3.6\ kg\,m^{-2}$) were significantly higher than in pairs concordant for never IWL ($P<0.001$ for mother's and $P=0.0065$ for father's BMI). Father's BMI was also significantly lower than in pairs concordant for IWL ($P=0.021$). Such findings in concert would support the findings that subjects with a history of IWL are genetically predisposed to higher BMIs than subjects who do not have IWL.

Combined effects of IWL and exercise

The physical activity of subjects with and without IWLs differed only slightly at age16 and no differences were found at 25 years (data not shown). Among females with IWLs, those who were physically passive at age 16 gained more weight ($3.8\,kg\,m^{-2}$) than those who at baseline were active ($1.9\,kg\,m^{-2}$) or intermediately active ($2.2\,kg\,m^{-2}$) (analysis of variance, $P=0.0032$). Passive females also had an increased risk of becoming overweight (Table 3). This was not observed in males. Within twin pairs, physical activity did not explain the detected differences between dieting and non-dieting twins' weight development (data not shown).

Discussion

Our findings of a dose-dependent association between the number of lifetime weight losses, gain in BMI and risk of overweight in a large population-based twin cohort with a follow-up from adolescence to young adulthood confirm the results of several previous studies.[4–11] It is now well established that the more people engage in dieting, the more they gain weight in the long-term. The novelty of the present study was its ability to distinguish between genetic and environmental influences on the dieting-induced weight gain. In MZ co-twins who were discordant for IWLs, twin pair members with IWLs became $0.4\,kg\,m^{-2}$ heavier (approximately 1.2 kg in a person 170 cm tall) at 25 years than those who had never lost weight despite similar BMIs at 16–18 years. These results suggest a causal relationship, although clinically modest in magnitude, between IWL and subsequent weight gain.

The weight loss pattern of weight-discordant DZ twins suggests that dieting may be a response to predisposition to obesity. DZ twins who had tried to lose weight were significantly heavier already at age 16 and remained so at 25 years as compared with their co-twins who had no history of weight loss. Further evidence for the genetic underpinning of weight gain and subsequent efforts to control weight by dieting came from MZ and DZ pairs where both co-twins had frequent IWLs: These twins had identical weight development at a much higher level than those pairs in which neither co-twin had ever lost weight. Inherited predisposition to higher weight in the dieters was also confirmed by the fact that twins with a history of IWL had heavier parents than twins with no dieting history.

There are several possible non-genetic explanations for why short-term success in weight loss may turn into long-term failure. The psycho-physiological explanation suggests that restricted eating may lead to an increase in the sensation

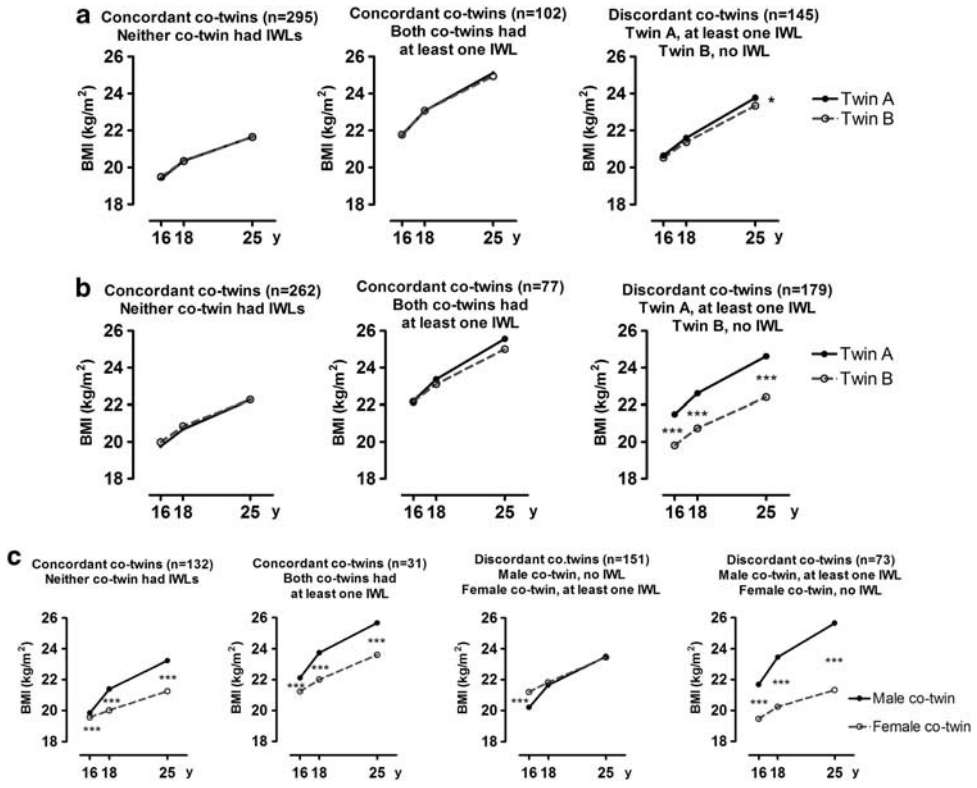

Figure 3 (**a**) BMI development from 16 to 25 years in MZ twin pairs concordant and discordant for lifetime IWL. (**b**) BMI development from 16 to 25 years in same-sex DZ concordant and discordant for lifetime IWL. (**c**) BMI development from 16 to 25 years in opposite-sex DZ concordant and discordant for lifetime IWL. *$P<0.05$, ***$P<0.001$.

of hunger and overeating as a physiological response to restore body energy stores. This phenomenon was first illustrated in 1945 in the classic Minnesota Starvation Study,[26] where 36 normal-weight men were given a restricted diet providing only half of their caloric needs for a 6-month semi-starvation period. With a 25% weight loss, the men became severely preoccupied with food. This pattern of behaviours with overeating continued in the rehabilitation phase with restoration of the energy needs, and have been observed also in later studies of adolescents[11] and adults.[27] Especially in too strict diets, weight loss maintenance is poor, and subjects describe uncontrolled appetites, overeating and food binges after the diet. It is typical that people in post-dieting situations eat automatically ('for no reason') but also for pleasure or control of tension.[28] The problem of repetitive contact with food and recurrent need to resist the temptation is a significant burden to many obese persons. Therefore, some patients choose to starve occasionally rather than follow an energy-deficient diet regularly—a fact that maintains the weight loss–regain cycle.

Recurrent weight losses and weight cycling have been proposed to exacerbate obesity by increasing metabolic efficiency both in animals[29] and in humans.[13] A small experiment on five normal-weight female subjects showed that two consecutive weight cycles of 4 kg lead to significant decreases in lean body mass, serum tri-iodothyronine and thyroxine concentrations, and in resting energy expenditure.[30] Similarly, in the re-analyses of the Minnesota Starvation Study of normal-weight subjects, post-starvation overshoot in body fat and delayed protein repletion was considered to result from the suppression of thermogenesis specifically favouring the replenishment of the fat stores.[31] However, in obese subjects, one[32] or three[33] consecutive cycles of dieting have not been observed to affect resting energy expenditure or body composition. Thus, the detrimental effects of weight loss seem to be most significant in initially normal-weight subjects.[34] This seemed to be the case at least in the males of the present study.

Studies to date do not unequivocally support the theory that energy expenditure is permanently depressed by dieting,[35,36] nor do they provide a biological explanation for why recurrent weight loss attempts paradoxically seem to lead to subsequent weight gain. One important factor not addressed in previous studies is genetics. It is well known that susceptibility to obesity is partly determined by genes, as are body weight and composition changes.[37] The seminal overfeeding[38] and energy restriction[39] studies on MZ twins showed that subjects sharing the same genotype respond to interventions in a similar way with large between-pair variation. In earlier quantitative genetic analyses of the

present cohort, both BMI (75%) and IWL (38–66%) were heritable, but this was only partially attributable to the same genetic factors.[15] In the current study, we found several pieces of evidence for the hypothesis that genetic factors may explain why those most frequently engaging in dieting gain most weight: (1) In both MZ and DZ twins, pairs where both co-twins had a history of IWL were heavier at all ages; (2) had a higher rate of weight gain and (3) had heavier parents than pairs in which neither co-twin had ever lost weight. (4) In discordant DZ pairs, co-twins who had lost weight were constantly and considerably heavier than co-twins with no (need for) weight loss attempts.

We also found evidence that dieting may promote weight gain independent of genetic effects in weight loss-discordant MZ pairs, although such effects are probably very small. However, given the well-documented high failure rate in weight maintenance and the observed potential of excessive regain, special efforts are clearly warranted to ensure improved and sustainable outcomes. This could reduce the pressure for excessive repeated dieting and counteract the obsession with weight loss that may in part be responsible for the current obesity epidemic.

Weight cycling has been shown to predict subsequent weight gain and the risk of obesity even in the athletes.[40] In a national cohort of 1838 male elite athletes who had represented Finland in international sport competitions in 1920–1965, men performing sports where weight cycling is common (boxers, weight lifters and wrestlers), gained $5.2\,kg\,m^{-2}$ from age 20 to age 60, whereas control men without an athletic background gained only $4.2\,kg\,m^{-2}$. However, the group best protected from long-term excess weight gain was athletes without weight cycling ($3.3\,kg\,m^{-2}$).[40] In the present study, physical activity was significantly related to enhanced weight control especially in females. Thus, weight loss strategies, which combine physical activity, may prevent subsequent weight re-gain. The advantages of physical activity were shown in a recent study, where none of the dietary approaches alone predicted weight change; however, in combination with frequent exercise, limiting portion sizes proved to be the most successful strategy for weight gain prevention.[41] Li *et al*.[42] have shown that an obesity gene risk score, based on 12 obesity-related genes, is associated with prospectively assessed weight change, the direction of which is dependent on physical activity levels. Among sedentary subjects, risk alleles are associated with weight gain, but among physical activity subjects, the same risk alleles predict weight loss. Thus, there is a complex interaction of genetic predisposition and physical activity in the trajectory of weight over time.

In summary, our results suggest that one important explanation for the poor long-term success in dieting is genetic susceptibility to weight gain. The findings in MZ twins suggesting that dieting *per se* is associated with later weight gain even independent of genetic effects merit further studies.

Conflict of interest

The authors declare no conflict of interest.

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