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The relationship between weight-related indicators and depressive symptoms during adolescence and adulthood: results from two twin studies

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Original Article

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Abstract

Background. The association between weight and depressive symptoms is well established, but the direction of effects remains unclear. Most studies rely on body mass index (BMI) as the sole weight indicator, with few examining the aetiology of the association between weight indicators and depressive symptoms.

Methods. We analysed data from the Twins Early Development Study (TEDS) and UK Adult Twin Registry (TwinsUK) (7658 and 2775 twin pairs, respectively). A phenotypic cross-lagged panel model assessed the directionality between BMI and depressive symptoms at ages 12, 16, and 21 years in TEDS. Bivariate correlations tested the phenotypic association between a range of weight indicators and depressive symptoms in TwinsUK. In both samples, structural equation modelling of twin data investigated genetic and environmental influences between weight indicators and depression. Sensitivity analyses included two-wave phenotypic cross-lagged panel models and the exclusion of those with a BMI <18.5.

Results. Within TEDS, the relationship between BMI and depression was bidirectional between ages 12 and 16 with a stronger influence of earlier BMI on later depression. The associations were unidirectional thereafter with depression at 16 influencing BMI at 21. Small genetic correlations were found between BMI and depression at ages 16 and 21, but not at 12. Within TwinsUK, depression was weakly correlated with weight indicators; therefore, it was not possible to generate precise estimates of genetic or environmental correlations.

Conclusions. The directionality of the relationship between BMI and depression appears to be developmentally sensitive. Further research with larger genetically informative samples is needed to estimate the aetiological influence on these associations.

Introduction

Obesity and depressive symptoms, including depression and anxiety, contribute significantly to the global disease burden, with an estimated global cost of trillions of dollars per annum (Chisholm et al., 2016; Tremmel, Gerdtham, Nilsson, & Saha, 2017; Whiteford et al., 2013). The prevalence rates for obesity are high among children and adults. For example, more than 1.3 billion adults worldwide are classified as overweight, defined by the World Health Organisation (WHO) as a body mass index (BMI) of $25 \leq 30\ kg/m^2$, and a further 600 million are classified as obese (BMI $\geqslant 30\ kg/m^2$) (Ng et al., 2014). Obesity and depressive symptoms both carry an increased risk for socio-economic hardship, cardiovascular disease, mortality, and disability-adjusted life-years (Ebbiling, Pawluk, & Ludwig, 2002; Firth et al., 2019; Kessler et al., 2005; Ng et al., 2014; Reilly & Kelly, 2011). They are also often comorbid, with an increase in risk of having obesity in around 40% of those reporting depressive symptoms (Firth et al., 2019). Cross-sectional studies provide evidence for moderate associations between obesity and depressive symptoms in childhood (Sutaria, Devakumar, Yasuda, Das, & Saxena, 2019), and adulthood (De Wit et al., 2010; Luppino et al., 2010). For example, higher BMI has been found to be associated with higher odds of depression (Onyike, Crum, Lee, Lyketsos, & Eaton, 2003; Scott, McGee, Wells, & Oakley Browne, 2008). These associations tend to be stronger in women than men, with a U-shaped relationship often observed, whereby a quadratic trend is found for the association between BMI and depression (De Wit, Van Straten, Van Herten, Penninx, & Cuijpers, 2009; McCrea, Berger, & King, 2012). Specifically, a BMI of less than

18.5 and more than 30 are associated with an increased level of depression, as compared to BMI ranging between 18.5 and 30.

A number of longitudinal studies have examined the direction of effects between BMI and depressive symptoms, with inconsistent findings demonstrating both unidirectional and bidirectional associations (Amiri, Behnezhad, & Nadinlui, 2018; Luppino et al., 2010). For example, increasing weight has been shown to precede the emergence of depressive symptoms (Konttinen et al., 2014; Luppino et al., 2010), but depressive symptoms have also been found to be associated with subsequent increases in weight (Luppino et al., 2010), suggesting a reciprocal relationship (Patalay, Moulton, Goodman, & Ploubidis, 2017). However, an important limitation of much previous research is failure to adjust for key confounding variables, which might artificially inflate estimates of the relationship between weight and depressive symptoms. For example, recent analyses using data from the Millennium Cohort study found that longitudinal associations between BMI and internalising symptoms were dramatically reduced, after adjustment for socio-economic status (Patalay et al., 2017).

Furthermore, little attention has been given to the aetiology of the relationship between weight and depressive symptoms. One possibility is that the association reflects environmental processes. For example, individuals with elevated depressive symptoms may experience increased appetite, leading to a rise in BMI (Maxwell & Cole, 2009). Similarly, elevated BMI may conflict with culturally imposed body shape ideals, increasing risk of weight discrimination and body shame, which in turn may raise vulnerability to depression (Jackson, Beeken, & Wardle, 2015). Alternatively, the association between weight and depressive symptoms could reflect common genetic risk factors. Twin studies have shown that genetic factors account for 30–50% of the variance in depression among adolescents and adults (Glowinski, Madden, Bucholz, Lynskey, & Heath, 2003; Rice, 2010; Sullivan, Michael Neale, & Kendler, 2000), and 0.31–90% of the variance in BMI (Elks et al., 2012; Min, Chiu, & Wang, 2013). Importantly, previous studies have also demonstrated overlap in the genetic influence on obesity and depression. For example, one study showed that 12% of phenotypic correlation between depression and obesity was explained by common genetic influences (Afari et al., 2010).

Further, a limitation of previous research in this field is an overreliance on BMI to assess weight. The validity of BMI to represent adiposity accurately had previously been criticised due to its failure to quantify body composition (Nevill, Stewart, Olds, & Holder, 2006). Thus, there is a need for research utilising alternative measures of adiposity including body fat percentage (BFP) and visceral fat percentage (VFP).

Aims and hypotheses

In this study, we implemented genetically informed methods with two twin samples to investigate the nature of the relationship between different indicators of weight and depressive symptoms. First, using data from TEDS, we ran cross-lagged models to examine (i) the phenotypic bidirectional longitudinal association between BMI and depression, whilst adjusting for concurrent associations, and (ii) the influence of genes and the environment on BMI and depression during the period between pre-adolescence and young adulthood. Based on previous research, we hypothesised that there will be a stronger association between earlier BMI and subsequent depression across time (between ages 12 and 16, and 16 and 21 years). We also expected stability of BMI and depression symptoms over time (which would partly account for the longitudinal associations between the phenotypes). Second, using data from TwinsUK, we applied a genetically sensitive multivariate model to explore the magnitude of genetic and environmental influences on a wider array of adiposity (i.e. measures of fat) and anthropometric (i.e. measures of height and weight) indicators, depression, and their associations. If the relationship between weight indicators and depression is largely explained by common genetic influences, we would expect to see strong genetic correlations in both samples and a range of weight indicators. Alternatively, if depression symptoms are largely a functional consequence of elevated weight indicators, or vice versa, we would expect to see strong non-shared environmental correlations.

Methods

Participants

This study used data from two UK based twin studies, the Twins Early Development Study (TEDS) and the UK Adult Twin Registry (TwinsUK).

TEDS

The TEDS follows the lives of twin pairs born in England and Wales between January 1994 and December 1996, identified through birth records (Haworth, Davis, & Plomin, 2013; Oliver & Plomin, 2007). Although there has been some attrition, approximately 10 000 twin pairs are still engaged in the study. TEDS remains representative of the population in England and Wales in terms of ethnicity and family socio-economic factors, including data from the most recent data collection used in this study (Lockhart et al., 2023).

Three waves of assessment including data on BMI and depressive symptoms were analysed (ages 12, 16, and 21 years). General exclusion criteria were applied to remove twins with serious medical conditions or extreme adverse conditions that may have affected subsequent development or ability to take part (n = 466). The sample was further restricted to twin pairs with complete information on zygosity. The sample size by zygosity for each measure is presented in Table 1. The total sample (after exclusions) comprised of 7658 twin pairs (47.2% males), including 2729 monozygotic twin (MZ) pairs and 4929 dizygotic twin (DZ) pairs. For the phenotypic cross-lagged panel model, one twin from each pair (i.e. n of pairs = 7658) were selected for analysis. Of the individual twins selected the final analysis sample comprised of those with a rating of depressive symptoms and BMI from at least one assessment wave, as well as information on age, sex, and socio-economic position (n = 6992). Ethical approval was provided by the King's College London Research Ethics Committee (reference number: PNM/09/10–104) and informed written consent was received from all participants.

TwinsUK

The TwinsUK registry consists of a volunteer sample of twins born in the UK. Currently, the sample consists of 14 575 adult twins at present (55% monozygotic and 43% dizygotic) who are between 18 and 101 years of age. The registry was setup in 1992 via media campaigns which aimed to recruit middle-aged women to study osteoporosis and osteoarthritis. The success of these studies drove the growth of the registry, with the scope broadening to include both male, female, and mixed twins with

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Table 1. Longitudinal phenotypic and intraclass correlations between BMI (log transformed) and MFQ at ages 12, 16, and 21 (all TEDS twins)

			Phenotypic correlations and MZ/DZ intraclass correlations					
			Age 12		Age 16		Age 21	
	N twin pairs (% of total)	Mean (s.d.)	BMI	MFQ	BMI	MFQ	BMI	MFQ
Age 12								
BMI	4822 (57.03)	17.8 (3.14)	1.00 0.83/0.46					
MFQ	5833 (69.04)	2.32 (3.33)	0.06 0.11/−0.03	1.00 0.42/0.28				
Age 16								
BMI	2154 (25.47)	21.0 (3.24)	0.66 0.55/0.33	0.09 0.12/−0.02	1.00 0.73/0.40			
MFQ	5063 (60.08)	3.64 (4.44)	0.04 0.04/0.02	0.29 0.18/0.12	0.02 0.03/0.01	1.00 0.43/0.22		
Age 21								
BMI	4456 (53.03)	23.4 (4.62)	0.58 0.51/0.28	0.09 0.15/0.03	0.69 0.62/0.34	0.06 0.01/0.05	1.00 0.70/0.31	
MFQ	4727 (56.22)	4.47 (4.13)	0.06 0.05/0.01	0.18 0.18/0.10	0.01 0.05/0.03	0.37 0.26/0.16	0.09 0.13/0.03	1.00 0.33/0.16

Note. Total pairs $N = 7658$ (100%). Means and standard deviations (s.d.) are on raw (non-regressed) data. Phenotypic correlations are estimated on unrelated individuals ($n = 7658$) in the TEDS sample (by selecting 1 twin from each twin pair). MZ, monozygotic; DZ, dizygotic; BMI, body mass index; MFQ, Mood and Feelings Questionnaire.

a spectrum of clinical and behavioural phenotypes in addition to genotyping data. Most of the twins are female, with a mean age of 59 (Verdi et al., 2019). For these analyses, the TwinsUK sample was restricted to twin pairs with complete information on zygosity. Further exclusion criteria consisted of twins who were reared apart ($n = 29$) and who had a BMI <18.5 ($n = 78$). For the multivariate ACE analysis, the sample was also restricted to twins' pairs with complete information on at least one assessment of the Hospital Anxiety and Depression Scale, weight, height, body fat percentage, or visceral fat percentage in the largest region. Due to this, the sample size varied between measures. The analysis sample for TwinsUK comprised of 2775 twin pairs (12.1% males), including 1738 monozygotic twin (MZ) pairs and 1037 dizygotic twin (DZ) pairs. Sample size by zygosity is presented in online Supplementary Table S2 for TwinsUK. The mean age of twins included in the analytic sample was 62.3 (14.0) at the time the depression assessment was conducted (i.e. in 2017).

Measures

TEDS phenotypic measures

Depressive symptoms were self-reported by twins using the short moods and feelings questionnaire (SMFQ) at ages 12, 16, and 21 years. The SMFQ is a 13-item questionnaire widely used in adolescents that measures the presence of depressive symptoms in general (Messer et al., 1995). For this study, 11-item were asked at age 12 years, 13-item at age 16 years, and 8-item at age 21 years. Each item is scored between 0 and 2, with a summed total score ranging between 0 and 16–26 (depending on the number of items asked). The SMFQ correlates strongly with clinical depression (Thapar & McGuffin, 1998), and there was good internal consistency for the depressive symptoms scores used in this sample (age 12: $\alpha = 0.86$; age 16: $\alpha = 0.90$; and age 21: $\alpha = 0.87$). Descriptive information on the MFQ can be found in Table 1. Twins reported their own [BMI = weight (kg)/(height (m)^2)] by providing height (metre) and weight (kilogram) at ages 12, 16, and 21 years, respectively. Raw BMI values were converted to age- and sex-adjusted standardised deviation scores (SDS) using the LMS method [L (skewness), M (median), and S (coefficient of variation)] based on the British 1990 growth reference (Cole, 1990). Socio-economic status was assessed at first contact. This variable was based on a composite of five variables including mother and father employment levels, mother and father educational levels, and mother's age on birth of first child.

TwinsUK phenotypic measures

The hospital anxiety and depression scale (HADS) assessed depressive symptoms of twins and included in each of the three main comprehensive questionnaires ('TwinsUK Baseline Health,' 'Baseline Core,' and 'Longitudinal Core'). These data were collected between 2004 and 2018 (Verdi et al., 2019). The data used for this study were taken from the 2017 data collection wave. The HADS is a 14-item questionnaire that measures the presence of depressive and anxiety symptoms in the past week. HADS has previously been found to perform well in assessing the symptom severity and caseness of anxiety disorders and depression in general population-based samples (Bjelland, Dahl, Haug, & Neckelmann, 2002). To increase comparability with the TEDS results, the depression subscale of the HADS was used for the TwinsUK analyses. Internal consistency for the depression subscale of the HADS was also good for TwinsUK ($\alpha = 0.89$). The weight, height, and BFP of twins were measured using a whole-body dual-energy X-ray absorptiometry (DEXA) scan. The weight indicators derived for this analysis included

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total BFP and VFP. This was collected during a full-day clinical visit between the years May 2012 and May 2018.

Statistical analyses

All analyses were preregistered on the Open Science Framework (https://osf.io/s6hcq), prior to data access. All statistical analyses were conducted using R [version 4]. Structural equation modelling (SEM) was used to derive the following estimates in TEDS: (i) cross-lagged models to estimate the bidirectional phenotypic longitudinal effect between measures of depressive symptoms (MFQ) and BMI, while adjusting for observed confounds (sex, age, and socio-economic position); (ii) bivariate ACE models to estimate genetic and environmental influences of the covariation between BMI and MFQ (within each age). SEM was also used to construct a multivariate analysis to derive the following estimates for TwinsUK: (i) phenotypic correlations between body composition indicators including BFP, BMI, VFP (within the largest region), and measures of depression (derived from the HADS subscale), adjusted for observed confounds (sex, age); (ii) multivariate ACE model to estimate the genetic and environmental influences on the covariance between the three weight and adiposity measures and depression scores.

Cross-lagged model

Autoregressive cross-lagged panel models estimate longitudinal associations between variables while adjusting for the concurrent associations between all variables in the model. This model examines the stability and change in two or more variables across time and tests the extent to which each trait influences the other at later time points. In cross-lagged panel models (hereafter referred to as cross-lag), there are four central components: the autoregressive parameters that test the stability of each trait across time; the synchronous correlations that measure the within-time covariance between traits at each time point; the cross-lag components that estimate the extent to which variable 1 at time 1 influences variable 2 at time 2, and vice versa; and the innovations or residuals that represent time-specific factors influencing each trait, beyond the influences carried over from earlier time points. Using data from TEDS, the second-stage analysis of a genetically informed cross-lag model (https://osf.io/s6hcq) was not possible because the cross-lag paths were too small for models to converge (see Fig. 1). Due to this, within wave bivariate models, described below, were conducted. Using TEDS data, three separate cross-lag models were run. First, unadjusted (non-regressed) models were implemented. Second, adjustments were made for age, sex, and socio-economic position.

Missing data

As OpenMx uses full information maximum likelihood to handle missing data, data from twins with partially missing data (e.g. twins with data at ages 12 and 16, but not 21) were used in the analyses.

Sensitivity analyses

Sensitivity analyses were conducted to assess the bidirectional longitudinal associations between BMI and depression at ages 12 to 16 and 16 to 21, separately. Furthermore, the full cross-lag was re-run excluding those who had a BMI <18.5 ($n = 325$).

Model-fitting analyses

The twin design compares the degree of phenotypic similarity between monozygotic (MZ) twins, who share 100% of their genes, and dizygotic (DZ) twins who shared 50% of their segregating genes on average (Rijsdijk & Sham, 2002). Within-pair correlations for MZ twins are compared with those for DZ twins to estimate the effects of additive genetic factors (A), common or shared environment (C), and non-shared environment (E). Greater MZ compared to DZ phenotypic similarity is attributed to genetic effects. Within-pair similarity that is not accounted for by genetic factors is attributed to shared environmental effects. Non-shared environmental effects, which consist of environmental factors unique to each twin, are estimated from the within-pair differences between MZ twins and include measurement error.

The univariate twin design can be extended to bivariate and multivariate analyses to investigate the aetiology of covariance between multiple traits. The multivariate genetic method decomposes the covariance between traits into A, C, and E components by comparing the cross-trait cross-twin correlations between MZ and DZ twin pairs. This method also enables estimation of the genetic correlation (rG), indicating the extent to which the same genetic variants influence two traits or measures of the same trait. The shared environmental correlation (rC) and non-shared environmental correlation (rE) are estimated in a similar manner (Knopik, Neiderhiser, DeFries, & Plomin, 2017; Rijsdijk & Sham, 2002). All phenotypic and genetic modelling was conducted within R using OpenMx (Boker et al., 2011). Models were fitted using raw data full information maximum likelihood. Model fit was examined using Akaike information criterion (AIC), with lower values indicating a better balance between explanatory power and parsimony, and minus twice the log-likelihood (−2LL) of the observations, which provides a relative measure of fit, since differences in −2LL are Chi-square distributed.

Using TEDS data, we ran bivariate genetic analyses to calculate genetic, shared, and non-shared environmental correlations between BMI and depression at ages 12, 16, and 21 years, respectively. Variables were regressed for age and sex to avoid artificial inflation of MZ *v.* DZ correlations (McGue & Bouchard, 1984), as is standard practice for quantitative genetic model fitting.

Using TwinsUK data, we applied multivariate ACE model to calculate genetic, shared, and non-shared environmental between measures of body fat percentage, body mass index, visceral fat percentage (within the largest region), and depression scores (from the HADS). Owing to the high correlation between adiposity measures (see Table 2), gynoid and android regional fat percentage were excluded from the main analyses to avoid multicollinearity issues.

Results

Descriptive statistics (TEDS)

TEDS

Descriptive statistics for variables at each time point are presented in Table 1. BMI and depression data from 7658 (52.8% female) twin pairs at ages 12, 16, and 21 years were eligible.

Depression scores were found to increase at each age. Phenotypic concurrent and longitudinal correlations between BMI and depression are also presented in Table 1. Concurrent correlations between BMI and depression were low at ages 12 (e.g. $r = 0.06$), 16, and 21. BMI was highly correlated across ages

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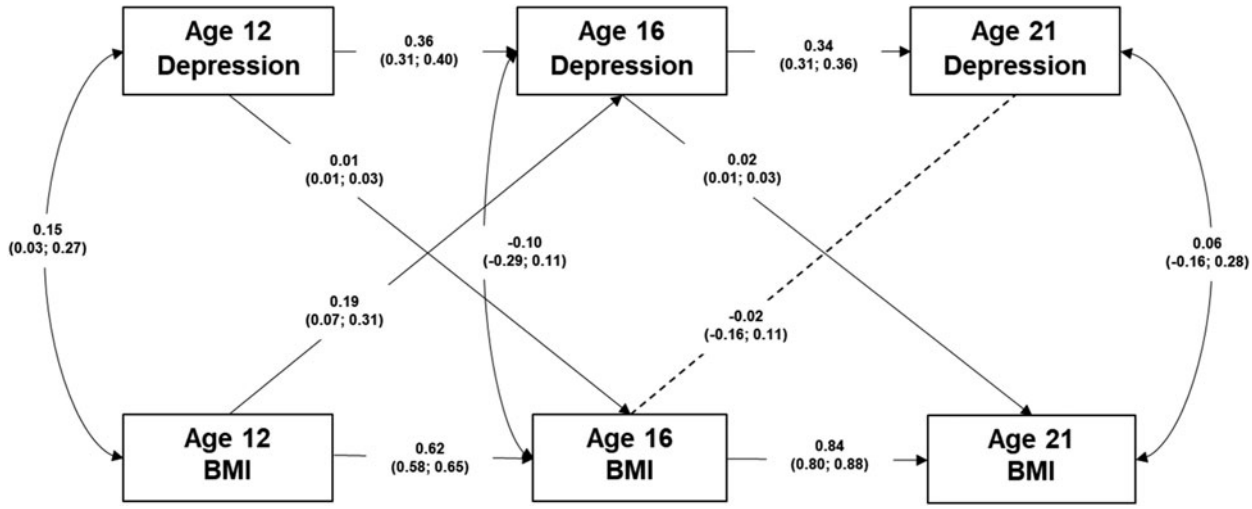

Figure 1. Path diagram presents the phenotypic longitudinal paths between BMI and depression (TEDS).
Note. $n = 6992$ unrelated individuals. Age, sex, and socio-economic regressed. Non-significant pathways are illustrated by dotted lines, and 95% CIs shown in parentheses. Model fit: comparative fit index (CFI), 0.97; Tucker–Lewis index (TLI), 0.89; standardised root mean square residual (SRMR), 0.030.

Table 2. Phenotypic and twin correlations between weight indicators and depression (TwinsUK)

		Phenotypic correlations and MZ/DZ intraclass correlations					
	Mean (s.d.)	BMI	Total body fat percentage	Android region fat percentage	Gynoid region fat percentage	Percentage of fat in the largest visceral fat region	Depression
BMI	26.3 (5.05)	1.00 0.78/0.49					
Total body fat percentage	39.0 (7.02)	0.68 0.52/0.32	1.00 0.83/0.54				
Android region fat percentage	40.2 (8.64)	0.75 0.58/0.32	0.87 0.68/0.39	1.00 0.72/0.37			
Gynoid region fat percentage	41.0 (6.68)	0.47 0.33/0.22	0.89 0.76/0.52	0.65 0.50/0.30	1.00 0.86/0.58		
Percentage of fat in the largest visceral fat region	35.9 (10.1)	0.74 0.86/0.58	0.85 0.86/0.58	0.97 0.72/0.41	0.63 0.51/0.31	1.00 0.86/0.58	
Depression	2.70 (2.95)	0.12 0.07/0.05	0.09 0.08/0.04	0.06 0.003/0.01	0.09 0.07/0.05	0.06 0.05/0.07	1.00 0.40/0.20

Note. Phenotypic correlation estimated on unrelated individuals ($n = 2786$) in the TwinsUK sample. MZ, monozygotic; DZ, dizygotic; BMI, body mass index.

12 and 16 (e.g. $r = 0.65$), ages 12 and 21, and between ages 16 and 21 years. Depression scores were also correlated across ages 12 and 16 (e.g. $r = 0.29$), ages 12 and 21, and ages 16 and 21 years.

Longitudinal associations (TEDS)

For the phenotypic cross-lag models, one twin from each pair was selected at random. Furthermore, those with a rating of depressive symptoms and BMI from at least one assessment wave, as well as information on age, sex, and socio-economic position were analysed ($n = 6992$). Bidirectionality of the longitudinal relationship between BMI and depression was estimated using a phenotypic cross-lagged panel model (Fig. 1). Presented results are adjusted for age, sex, and socio-economic position. Unadjusted results are presented in online Supplementary Table S3. Our results show stability of both BMI and depression between ages 12 and 16 [e.g. BMI: 0.62, 95% confidence interval (CI) 0.58–0.65] and 16 and 21 (BMI: 0.84, 95% CI 0.80–0.88). Furthermore, a bidirectional phenotypic association was found between BMI and depression between ages 12 and 16 (BMI ≥depression: 0.01, 95% CI 0.01–0.03; depression ≥BMI: 0.19, 95% CI 0.08–0.31), but not between ages 16 and 21 years. A small, unidirectional association was found between depression at age 16 and BMI at age 21. Notably, at ages 12–16 years, the strength of the association between earlier BMI and later depression was stronger than the association between earlier depression and later BMI (as indicated by the non-overlapping CIs).

Sensitivity analyses (TEDS)

Two bivariate cross-lag models were conducted between BMI and depression at ages 12 to 16 and 16 to 21, respectively. Result from

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these models indicated a similar bidirectional phenotypic association between BMI and depression between ages 12 and 16 (see online Supplementary Fig. S1 and Supplementary Table S4). Furthermore, the full cross-lag was re-run excluding those who had a BMI <18.5 ($n = 312$). Results from this cross-lag model were consistent with the full model including those who have a BMI <18.5. Results are presented in online Supplementary Fig. S2.

Genetic and environmental influences (TEDS)

The aetiology of associations between BMI and depression was explored using bivariate correlated factors models at ages 12, 16, and 21 respectively. Table 3 presents the genetic, shared, and non-shared environmental influences between BMI and depression at each age. The models provided a good fit to the data (online Supplementary Table S5). Results from these separate bivariate models show BMI was highly heritable at ages 12, 16, and 21, with low shared environmental and moderate non-shared environmental influences. Depression was moderately heritable at ages 12, 16, and 21, with low shared environmental and high non-shared environmental influences (see Fig. 2). No genetic correlation was found between BMI and depression at age 12 (0.09, 95% CI −0.02 to 0.17), and small genetic correlations were found between BMI and depression at ages 16 (0.17, 95% CI 0.001–0.33), and 21 (0.19, 95% CI 0.09–0.33).

Descriptive statistics (TwinsUK)

TwinsUK

Descriptive statistics and correlations between depression and different indicators of weight distribution are presented in Table 2. The mean age of twins was 62.3 (14.0). Data from 5572 (87.9% female) twins were analysed using data from the three weight and adiposity measures and depression scores. Concurrent correlations of depression with BMI and each of the adiposity measures were low (e.g. $r = 0.09$ for depression and BFP). Weight and adiposity measures were highly correlated.

Genetic and environmental influences (TwinsUK)

The aetiology of the associations between the three weight and adiposity measures and depression scores was examined using a multivariate correlated factors model. Fit statistics are shown in online Supplementary Table S6. Although the AE model provided the best fit of the data, we may have been underpowered to estimate the C terms in the multivariate model. Due to this, we dropped the C terms from the model as this could have artificially inflated our estimates of A. Model estimates from the multivariate ACE model are shown in Fig. 3 and Table 4. Results show that all three adiposity measures were moderate to high heritable, with low shared environmental and moderate non-shared environmental influences. Depression (deprived from the subscale of the HADS) was found to be moderately heritable with low shared environmental and moderate non-shared environmental influences. Furthermore, no genetic correlations were found between any of the adiposity measures and depression (e.g. body fat with depression, 0.12, 95% CI −0.14 to 0.40). This indicates no or only very low genetic overlap in the genetic variants underlying these weight indicators and symptoms of depression. Furthermore, no non-shared environmental correlations were found (e.g. 0.23, 95% CI −1.00 to 1.00 for body fat percentage

Table 3. Genetic, shared, and non-shared environmental influences (with 95% CIs) on BMI and depression at ages 12, 16, and 21 years (TEDS)

	Depression			BMI			Correlations		
	A	C	E	A	C	E	A	C	E
Total genetic and environmental influences (from bivariate correlated factors model)									
Age 12	0.28 (0.20–0.37)	0.13 (0.06–0.19)	0.58 (0.55–0.61)	0.77 (0.71–0.82)	0.07 (0.02–0.13)	0.16 (0.15–0.17)	0.09 (−0.02 to 0.17)	−0.02 (−1.00 to −1.00)	0.03 (−0.015 to 0.08)
Age 16	0.40 (0.32–0.46)	0.02 (0.00–0.08)	0.57 (0.54–0.67)	0.68 (0.57–0.76)	0.06 (0.00–0.15)	0.26 (0.23–0.27)	0.17 (0.001–0.33)	−1.00 (−1.00 to −1.00)	−0.08 (−0.15 to −0.01)
Age 21	0.32 (0.22–0.36)	0.00 (−0.001 to −0.001)	0.67 (0.63–0.71)	0.73 (0.68–0.75)	0.00 (−0.001 to 0.001)	0.27 (0.25–0.29)	0.19 (0.09–0.33)	−0.02 (−1.00 to −1.00)	−0.08 (−0.15 to −0.01)

BMI, body mass index; A, additive genetic effects; C, shared environmental effects; and E, non-shared environmental effects.
Notes: 95% CIs shown in parentheses.

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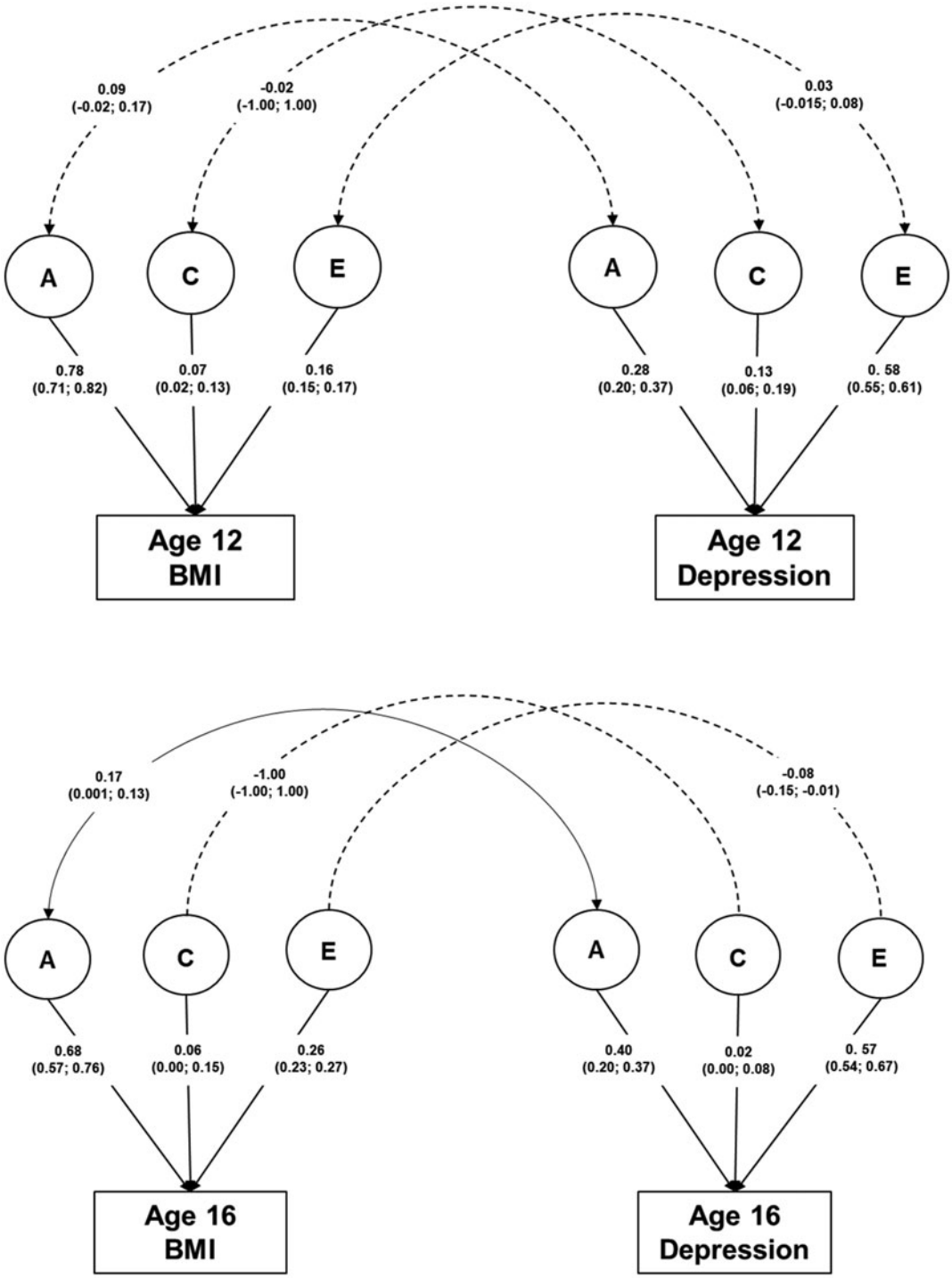

Figure 2. Bivariate ACE models (TEDS).
Notes. Non-significant pathways are illustrated by dotted lines. A, additive genetic effects; C, shared environmental effects; E, non-shared environmental effects. 95% CIs shown in parentheses.

and depression), suggesting distinct environmental risk factors for adiposity indicators and depression.

Furthermore, when assessing genetic and environmental influences on indicators of weight and adiposity and depression, a similar pattern of results emerged across TEDS and TwinsUK. Specifically, the genetic correlation between BMI and depression was very small in TEDS and zero in TwinsUK.

Discussion

In this study, first we investigated the longitudinal associations of BMI and depressive symptoms between ages 12-, 16-, and 21-year using data from the TEDS. Second, using data from both TEDS and TwinsUK, we assessed the aetiological relationship between different indicators of weight and adiposity and depression in childhood and adulthood.

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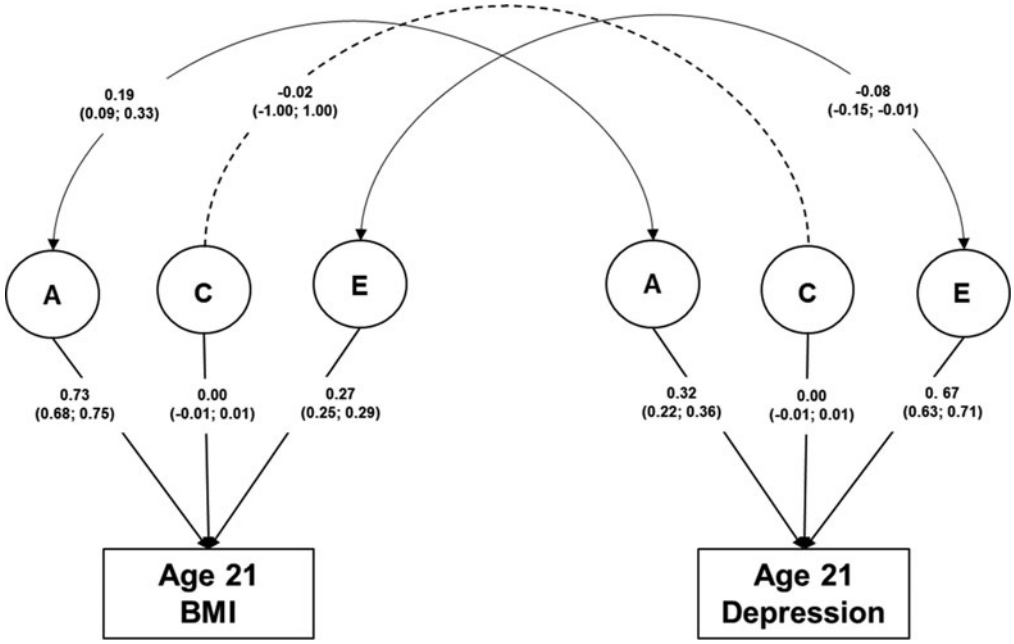

Figure 2. Continued

With respect to our first aim, the phenotypic cross-lag model indicated clear stability in BMI and symptoms of depression from ages 12 to 16 and 16 to 21 years. Furthermore, we found a bidirectional association between BMI and depression from ages 12 to 16, with a stronger association for earlier BMI and later depression, as compared to earlier depression and later BMI. A small unidirectional association between depression and BMI was also found from ages 16 to 21. Regarding our second aim, we found evidence of a genetic correlation between BMI and depression at ages 16 and 21 years, but not at age 12 years. However, these effects were small indicating modest genetic overlap in the genetic variants underlying BMI and symptoms of depression. Little evidence for shared environmental overlap between BMI and depression at each age was found, suggesting distinct environmental risk factors for BMI and depression. Furthermore, using data from TwinsUK, we found no genetic or non-shared environmental correlation between any of the weight or adiposity indicators and depression, suggesting distinct genetic and environmental risk for weight, assessed using different metrics, and depression.

When comparing across the two twin studies, similar aetiological estimates were found across the cohorts for depression and weight indicators, respectively. Specifically, moderate heritability and non-shared environmental influences for depressive symptoms were found for both TEDS and TwinsUK. Non-shared environmental factors previously theorised and found to be involved in the development of depression include peer victimisation and child neglect (Reijntjes, Kamphuis, Prinzie, & Telch, 2010). Moreover, moderate to high heritability, and low non-shared environmental influences for BMI were also consistent when comparing TEDS and TwinsUK.

Our phenotypic findings add to the pre-existing literature, demonstrating mixed evidence for the bidirectional association between BMI and depression in children (Sutaria et al., 2019), adults (Luppino et al., 2010). Notably, our pattern of results differs from recent evidence which indicates a unidirectional association between internalising symptoms at age 11 and BMI at age 14 (i.e. not from earlier BMI to later internalising symptoms) (Patalay & Hardman, 2019). Our findings are also supported by evidence that utilises molecular genetic techniques, such as Mendelian randomisation (MR), to explore the causal relationship between higher BMI and depression (Hartwig et al., 2016; Hung et al., 2014). For example, a recent study that applied MR to data from the UK Biobank found higher BMI leads to higher odds of depression (Tyrrell et al., 2019). More specifically, they highlight potential sex differences in the causal relationship between BMI and depressive symptoms, with stronger associations in women.

It is notable that, path coefficients observed were small. However, when applied to longitudinal data, cross-lagged panel models often yield small effect sizes, owing to large intervals between data collections and adjustment for stability effects in autoregressive models (Adachi & Willoughby, 2015; Funder & Ozer, 2019). Our phenotypic findings extend the current literature through demonstrating that, after accounting for the bidirectional associations from early- and mid-adolescence, the association from BMI and depression is lost from mid-adolescence to early adulthood. However, the lack of genetic covariation was also consistent when assessing the genetic and environmental influences between different weight and adiposity indicators and depression in adults using data from TwinsUK. Overall, these findings contribute to the current mixed evidence of the common aetiology between weight and depressive symptoms. Improving our understanding of the direction of the association between BMI and depression, is important for identifying targeted intervention and prevention strategies. For example, this analysis indicated the age at which individuals may particularly benefit from support.

Our current findings do not provide insight into the mechanisms involved in the bidirectional association between BMI and depression. Theoretical explanations, including biological, psychological, and behavioural pathways have been previously hypothesised for adolescents [see Maxwell and Cole (2009)], and adults [see Milaneschi, Simmons, van Rossum, and

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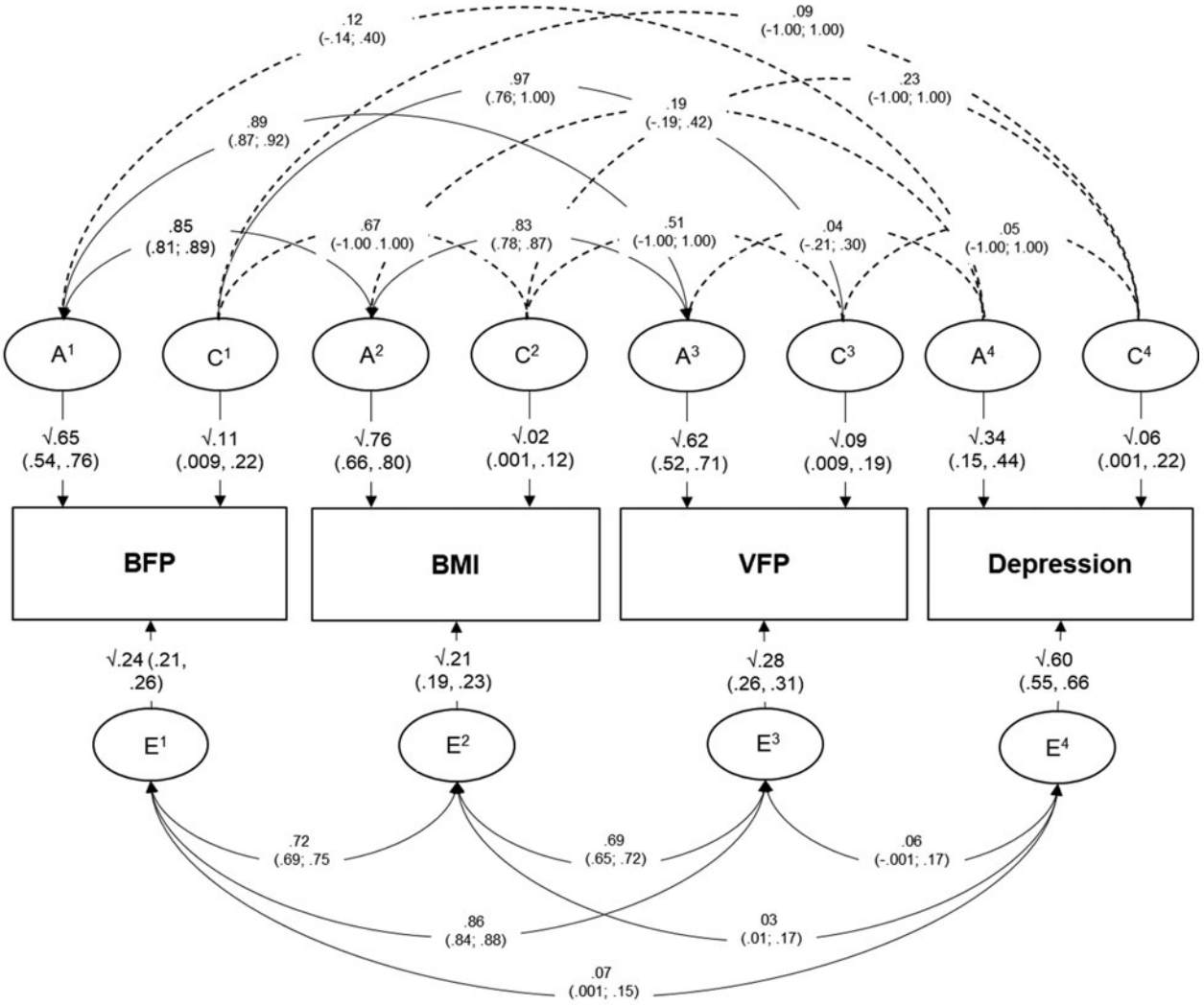

Figure 3. Multivariate ACE model (TwinsUK).
Notes. $n = 2775$. Age and sex-regressed models. BFP, body fat percentage; BMI, body mass index; VFP, visceral fat percentage; A, additive genetic effects; C, shared environmental effect; E, non-shared environmental effect.

Penninx (2019)] For example, those with higher BMI have been found to experience weight-related discrimination, which has been associated with increased depressive problems (Jackson et al., 2015; Robinson, Hunger, & Daly, 2015; Stunkard, Faith, & Allison, 2003). Further, higher BMI is also associated with elevated rates of body dissatisfaction and negative body image (Unlu, Aykut, Borlu, & Kaner, 2019), which have also been found to predict subsequent depressive symptoms around the transition to adolescence (Maxwell & Cole, 2009). Depression symptoms and weight increase may also be associated with behavioural pathways. For example, children and adults experiencing depressive symptoms are more likely to experience increased appetite, or have difficulties with sleeping, which have been associated with a susceptibility to weight gain. Furthermore, evidence from community-based studies has shown that depressive symptoms are associated with less healthy dietary intake, a higher tendency for emotional eating, and a decline in physical activity.

Notably, mechanistic pathways involved in the bidirectional associations between weight and depression for adolescents and older adults may differ. For example, several mechanistic factors aiming to explain the link between depression of weight increase are factors that tend to be in flux during puberty (Maxwell & Cole, 2009).

Strengths and limitations

This study draws on data from two large genetically sensitive twin studies. Our first set of analyses utilised prospectively collected longitudinal BMI and depressive symptom data from TEDS. Strengths include our ability to adjust for potential confounding, including socio-economic position. Due to the size and population-based nature of TEDS, BMI was based on self-reported height and weight. Previous studies have shown that while self-reported estimates of height and weight are correlated with objective measurements, individuals on average overestimate height and underestimate weight compared with measured values (Gorber, Tremblay, Moher, & Gorber, 2007; Maukonen, Männistö, & Tolonen, 2018; Pérez, Gabriel, Nehme, Mandell, &

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Table 4. Genetic, shared, and non-shared environmental influences (with 95% CIs) on BFP, BMI, VFP, and depression (TwinsUK)

	A	C	E	rA	rC	rE	rPh
BFP	0.65 (0.54–0.76)	0.11 (0.009–0.22)	0.24 (0.21–0.26)	0.12 (−0.14 to 0.40)	0.23 (−1.00 to 0.1.00)	0.07 (0.001–0.15)	0.10 (0.06–0.12)
Depression	0.34 (0.15–0.44)	0.06 (0.001–0.22)	0.60 (0.55–0.66)				
BMI	0.76 (0.66–0.80)	0.02 (0.001–0.12)	0.21 (0.19–0.23)	0.19 (−0.19 to 0.42)	−0.08 (−1.00 to 0.1.00)	0.09 (0.02–0.17)	0.13 (0.08–0.17)
Depression	–	–	–				
VFP	0.62 (0.52–0.71)	0.09 (0.009–0.19)	0.28 (0.26–0.31)	0.04 (−0.21 to 0.30)	0.45 (−1.00 to 0.1.00)	0.06 (0.001–0.83)	0.07 (0.03–0.11)
Depression	–	–	–				

Notes. Age and sex-regressed models; 95% CIs in parentheses. BFP, body fat percentage; BMI, body mass index; VFP, visceral fat percentage; A, additive genetic effects; E, non-shared environmental effect; rA, genetic correlation; rE: non-shared environmental correlation; rPh, phenotypic correlation.

Hoelscher, 2015). Moreover, evidence suggests that self-reported BMI values tend to overestimate measured BMI values at the low end of the BMI scale (<22) and underestimate BMI values at the high end, particularly at values >28 (Stommel & Schoenborn, 2009). Due to the mode of measures available, we were not able to directly test this. It is possible that the average BMI score in the sample would be lower than if height and weight were measured objectively. However, this would not have impacted the direction of effects observed in this study. Further, clinical assessments of depression were not used to assess depressive symptoms, however, this allowed us to assess symptoms across a continuous scale, capturing individuals who may not have otherwise been included if binary cut-offs were used. Our second set of analyses utilised TwinsUK data which included prospectively collected anthropometric, adiposity, and depressive symptom data. Study strengths include the diverse set of objectively collected adiposity and anthropometric indicators. Further, although attrition is common in longitudinal cohorts, our models were able to account for missingness, using well-established methods.

Limitations in the study include the lack of power to run the genetically sensitive cross-lag models, initially proposed in the preregistration (https://osf.io/s6hcq). This was due to the intraclass correlations being too small to decompose within the longitudinal cross-lag model. Further limitations in the current study are mostly related to the classical twin design assumptions. One of them is the generalisability of twin research findings to the general population which are mostly singletons. However, the prevalence of both BMI (%) and depressive problems (%) in the current study is comparable with the rates we see in population-based data of comparable age groups. Another assumption in the classical twin design is the absence of gene-environment interaction and correlation, which may have led to the bias of estimates in the current study.

In conclusion, the current study demonstrated a bidirectional association between BMI and depression from ages 12 to 16 with stronger directional effect from BMI to depression. Due to the lack of statistical power and the small phenotypic correlations between indicators of weight and depression, we were unable to detect significant genetic correlations in TwinsUK. Replication in larger twin cohorts would add to the current evidence base. Future studies should further aim to use different methods to triangulate the evidence between BMI and depression to elucidate potential associations. Furthermore, known common risk factors should be explored, such as health behaviours including unhealthy dietary preferences and physical activity (Luppino et al., 2010). Identification of these genetic and environmental factors could highlight new opportunities for intervention among high-risk individuals.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S0033291723002155.

Data. Twin Early Development Study: Data for this study came from the Twins Early Development Study (TEDS). Researchers can apply for access to the data: https://www.teds.ac.uk/researchers/teds-data-access-policy.

TwinsUK: Data for this study came from the UK Adult Twin Registry. Researchers can apply for access to the data: https://twinsuk.ac.uk/resources-for-researchers/our-data/

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Authors' contributions. EJT, TE, and CJS conceptualised the study with input from all authors. EJT led on data preparation and analysis. EJT drafted the manuscript and all authors contributed to drafting. All authors approved the final version for submission.

Competing interest. All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work, no financial relationships with any organisations that might have an interest in the submitted work in the previous three years, no other relationships or activities that could appear to have influenced the submitted work.

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