

ORIGINAL ARTICLE

Trajectories of total and central adiposity throughout adolescence and cardiometabolic factors in early adulthood

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BACKGROUND/OBJECTIVES: Our aim was to identify trajectories of total and central adiposity from 13 to 21 years, and to investigate how adiposity changes at different phases of adolescence relate to adulthood cardiovascular risk factors.

SUBJECTS/METHODS: This study included participants from a population-based cohort (EPITeen), Portugal. Body mass index (BMI) and waist circumference (WC) were measured at 13, 17 and 21 years, and sex- and age-specific z-scores were calculated. Adiposity trajectories were identified using mixture growth models (BMI, $n = 2901$; WC, $n = 2898$). Cardiovascular risk factors were evaluated at 21 years ($n = 1763$): systolic (SBP) and diastolic blood pressure (DBP), insulin resistance (HOMA-IR), triglycerides and cholesterol. Association of trajectory, and changes in adiposity z-scores with each cardiovascular risk factor was estimated by linear regression models.

RESULTS: 'Normal', 'high, declining' and 'high, increasing' trajectories were identified in both sexes. 'High, increasing' BMI trajectory was associated with less favorable cardiovascular risk profile at 21 years in both sexes, whereas 'high, declining' presented a more favorable profile, similar to 'normal' trajectory in females. In addition, BMI increases between 13–17 years and 17–21 years were associated with increases in systolic and diastolic blood pressure, and insulin resistance, but more strongly for the later period. For every standard deviation (s.d.) increase in BMI between 17–21 years, mean SBP increased by 1.99 mmHg (95% confidence interval (CI): 1.01; 2.97) for females and 3.83 mmHg (2.67; 4.98) for males; the respective increase was 1.56 mmHg (0.72; 2.40) and 2.80 mmHg (1.97; 3.64) for DBP and 0.27 (0.21; 0.32) and 0.30 (0.24; 0.36) for HOMA-IR (log-transformed). Similar results were found for WC.

CONCLUSIONS: Increases in adiposity, particularly from late adolescence-to-young adulthood, were associated with unfavorable cardiovascular profile in early adulthood. A benefit on the cardiovascular risk profile for participants in the declining adiposity trajectory was observed.

International Journal of Obesity (2016) 40, 1899–1905; doi:10.1038/ijo.2016.170

INTRODUCTION

The prevalence of obesity has risen rapidly in the recent decades in most western populations.¹ High adiposity is one of main determinants of cardiovascular (CV) disease and its role as a CV risk factor starts early in life. It has also been implicated in the development of other CV risk factors.² Therefore, the study of how changes in adiposity across the life span influence the unfavorable progression of the CV risk factors is important to understand their impact on the disease development.

The study of growth trajectories in pediatric age is recognized to be of great relevance for surveillance, etiology and clinical practice,³ being useful for the identification of critical windows for intervention. A systematic review has shown a moderate tracking of childhood overweight status into adulthood.⁴ There is also evidence indicating substantial variations in individual growth trajectories.^{5–7} Some studies identified distinct groups of trajectories over the life course, which might impact differently on the risk of disease.^{5,8–11}

Although growth characteristics from birth to adolescence and its later association with CV risk factors are well documented,^{8,9,11,12} the impact of changes in adiposity from adolescence-to-young adulthood is less well described. Yet this

period is recognized as critical for weight gain^{13,14} and subject to important biological changes (for example, puberty).¹⁵

Research to estimate the relative contribution of fatness and fat gain at different life stages on adult CV risk factors tends to focus mainly on increases in adiposity in childhood^{16,17} and adulthood.¹⁸ Some studies have reported that changes in body mass index (BMI) early in life were of greater relevance for future atherosclerosis¹⁹ or metabolic disturbances.^{20,21} Also, changes in weight or BMI during adolescence or later in life are strongly associated to adult blood pressure and metabolic abnormalities.^{22–24} However, the periods assessed were different which may limit comparisons between studies, and limited evidence is available for the changes in other adiposity measures. Therefore, this study aims: (i) to identify distinct trajectories of total and central adiposity from adolescence (13 years) to early adulthood (21 years); (ii) to investigate how adiposity changes at particular age periods (13–17 or 17–21 years) are associated with CV risk factors at early adulthood.

SUBJECTS AND METHODS

Study sample

This study included participants from the Epidemiological Health Investigation of Teenagers in Porto (EPITeen)—a population-based cohort

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Received 3 May 2016; revised 28 July 2016; accepted 9 September 2016; accepted article preview online 28 September 2016; advance online publication, 18 October 2016

that recruited 13-year-old adolescents.²⁵ Eligible participants were adolescents born in 1990, attending schools of Porto, Portugal, during 2003–2004. Second and third study waves took place when participants were on average 17 years (2007–2008) and 21 years of age (2011–2013).

We conducted our study in compliance with the principles of Declaration of Helsinki. The research protocol was approved by the Ethic Committee of Hospital S João and the Ethics Committee of the Institute of Public Health from the University of Porto. In the first and second study waves, a signed informed consent was required for adolescents and parents (or legal guardians), and only for participants in the third study wave.

At the recruitment, 2159 eligible adolescents agreed to participate (77.5% participation). In the second wave, we re-evaluated 1716 participants (79.5%), and a further 783 adolescents who moved to the schools in Porto joined the cohort. Sixty percent ($n = 1764$) of the entire cohort was re-evaluated in the third study wave.

Measures

Anthropometrics. Weight and height were measured with the subject in light indoor clothes and no shoes, according to standardized procedures. Waist circumference (to the nearest 0.1 cm) was measured midway between the lower limit of the rib cage and the iliac crest, at the end of gentle expiration, with a flexible and non-distensible tape.

BMI and waist circumference (WC) z-scores were calculated by sex and age for each study wave, using the mean and standard deviation of the study sample.

Cardiovascular risk factors. For this analysis we considered CV risk factors assessed at 21 years.

A blood sample was taken from an antecubital vein after an overnight fast. An Olympus AU5400 automated clinical chemistry analyzer (Beckman-Coulter, Brea, CA, USA) was used to measure glucose, total cholesterol, high-density lipoprotein cholesterol (HDL) and triglycerides. Insulin was measured by electro chemiluminescent immunoassay (Cobas e411 automated analyzer, Roche, Roche Diagnostics GmbH, Mannheim, Germany). All determinations took place in the Department of Clinical Pathology, Centro Hospitalar São João, Porto, Portugal.

The Friedewald equation²⁶ was used to estimate low-density lipoprotein cholesterol (LDL-C). The homeostatic model assessment (HOMA-IR) was used as a marker of insulin resistance, calculated through the formula: $\text{HOMA-IR} = \text{insulin } (\mu\text{U ml}^{-1}) \times \text{glucose } (\text{mg dl}^{-1}) / 405$.²⁷

Blood pressure was measured using the oscillometric method (OMRON Blood Pressure Monitor, M6 Comfort, OMRON Healthcare Co., Ltd., Kyoto, Japan), according to standard procedures.²⁸ A first reading was taken after 10 min of rest, and a second one after at least 5 min. When the difference between the first two readings was higher than 5 mmHg, a third one was taken. The average of the two closest measurements was used in this analysis.

Covariates. Perinatal information was obtained through questionnaires administered to the mothers at the baseline. When available, birth weight was extracted from child health book records ($n = 716$); otherwise was based on mother's report. Maternal smoking was classified as: non-smoker; smoker, but not during pregnancy; smoker during pregnancy.

Parental educational level was defined according to the parent presenting the highest education level. Parental occupational position was categorized as 'high' (professional and managerial occupations), 'medium' (non-manual and manual skilled occupations) and 'low' (semi-skilled and unskilled occupations). Self-reported weight and height of the parents was used to calculate BMI, then converted to z-scores separately for mother, father, and in each study wave. Parental BMI was defined using BMI z-score from the mother in study wave I, and if not available data from wave II (24.1%); or when mother's BMI was missing in both waves, from the father (2.9%).

Separately for the mother and the father, family history of diabetes, dyslipidemia and hypertension was collected, and for each of the diseases classified as: positive, when the diagnosis was present for at least one of the parents; negative, when none of the parents reported the diagnosis; or non-classifiable, when the available information showed no diagnosis for one of the parents, but missing regarding the other. The participant's practice of sports was defined as any planned, regular exercise, regardless of intensity and excluding obligatory curricular activities.

Statistical analysis

To identify trajectories of BMI and of WC from adolescence into adulthood (aim 1), we applied mixture growth models, using the PROC TRAJ procedure in SAS (v9.3, SAS Institute Inc., Cary, NC, USA).²⁹ The models were stratified by sex, and included a random intercept, a random linear and a quadratic age term. We tested models up to six trajectory groups, and the final number of trajectories was chosen based on the lowest Bayesian Information Criteria, and also by the interpretability of the results. For each individual, the mixture growth model generated the probability of belonging to each trajectory. Individuals were classified in the trajectory to which they had the highest probability of belonging.

Analysis of the growth trajectories was based on participants with adiposity measures at one or more ages ($n = 2901$ for BMI; $n = 2898$ for WC).

To investigate the association of adiposity levels and their changes at different ages with CV risk factors in early adulthood (aim 2), we used sex-specific z-scores of BMI and WC at each age so their associations with CV risk factors can be compared across ages. A logarithmic transformation was applied to triglycerides and HOMA-IR, as these variables were skewed.

First, we examined the associations of CV risk factors at 21 years with adiposity measures at each age separately. The regression coefficient represents the change in CV risk factor for a s.d. increase in the adiposity measure.

Second, the associations of changes in each adiposity measure (a change in the ranking of the individual in the sample) between two ages (13–17 and 17–21 years) with adult CV risk factors were examined. Each model was conditioned on the adiposity measure at the previous age. For example, to estimate the change in BMI z-score between 13 and 17 years of age on SBP at 21 years, we applied the regression model: $\text{SBP}_{21} = a + b \text{ BMI}_{13} + c \text{ BMI}_{17}$, which can be rewritten as $\text{SBP}_{21} = a + (b+c) \text{ BMI}_{13} + c (\text{BMI}_{17} - \text{BMI}_{13})$. The coefficient c can be interpreted as the estimated change in SBP associated with a s.d. increase in BMI between 13 and 17 years, given the BMI at 13 years.

All models were stratified by sex and further adjusted for birth weight, mother's smoking during pregnancy, parental education, household occupational position, family history of disease, parental BMI z-score and participant's practice of sports. Regarding practice of sports, for associations with changes in adiposity between 13 and 17 years, we used sports at 13 years; for changes between 17 and 21 years, sports at 17 years.

We applied multiple imputation to the total cohort to use the maximum information available. The imputation model included factors predicting non-response (that is, sex, maternal/paternal education and occupation), adiposity measures at all ages, CV risk factors at 21 years and all covariates in the analysis models. We created 30 imputed datasets assuming missing was at random given observed values of other variables. The regression models and multiple imputation by chained equations were conducted using SPSS (IBM Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY, USA: IBM). In the regression models, we used imputed covariates and adiposity measures, but not imputed outcomes, that is, we restricted our analysis to individuals with observed CV risk factors (1763 participants with valid information for at least one cardiovascular risk factor at 21 years). Parameters estimated were combined to obtain overall estimates using Rubin's rule.

RESULTS

Descriptive data on BMI and WC at each study wave and cardiovascular risk factors at 21 years is presented in Table 1.

Trajectories of BMI/WC from adolescence into adulthood

Three trajectory groups of BMI were identified for each sex (Figure 1): 'normal' (78.7% in females; 80.4% in males); 'high, increasing' (17 and 6.4%); and 'high, declining' (4.2 and 13.1%). 'Normal' trajectory presented the lowest mean BMI values and low prevalence of overweight at any of the three study waves (Supplementary Table S1). At 13 years, subjects in trajectory 'high, increasing' presented intermediate mean values of BMI, however they increased more rapidly with age, and were the highest at 21 years (29.3% in females; 65.2% in males), compared with the other trajectories. Trajectory 'high, declining' presented the highest mean values of BMI at 13 years, but they decreased with age, being the prevalence of obesity at 21 years 7.5 and 11.2% for females and males, respectively (Supplementary Table S1).

For waist circumference, three trajectories were also identified (Figure 2) and they were graphically and in prevalence similar to those identified for BMI. The agreement between the trajectories identified based on BMI and on WC was strong (observed agreement of 88 and 91.4%; kappa = 0.657 and 0.745, respectively, for females and males). 'Normal' WC trajectory was found in around 80% of the subjects in both sexes; 'high, increasing' in 17.9% of females and 8.4% of males; and trajectory 'high, declining' in 2 and 11.6% of females and males, respectively (Supplementary Table S2).

Table 2 relates CV risk factors at 21 years to the probability of belonging to each trajectory. Considering the 'normal' trajectory as the reference group, belonging to the 'high, increasing' trajectory was associated with higher SBP, HOMA-IR, triglycerides and LDL, and decreased HDL at 21y in both sexes, but stronger in males, except for HDL. For 'high, declining' trajectory, in females

there were no statistically significant differences in CV risk factors, compared with the 'normal' trajectory, except for HDL. In males, higher probability of belonging to the 'high, declining' trajectory was associated with higher mean SBP, DBP, HOMA-IR and triglycerides, and lower HDL at 21 years, but the magnitude was lower than for subjects belonging to the 'high, increasing' trajectory.

The associations for WC (Table 2) were in general similar to those for BMI, but weaker.

Associations between changes in BMI/WC and CV risk factors

Adjusted models using multiple imputation showed that BMI z-score at each age (13, 17 or 21 years) was positively associated with SBP, DBP, HOMA-IR, triglycerides and LDL, and inversely associated with HDL, in both sexes, and appeared to be stronger in males (Table 3). Associations generally strengthened with increasing age. Results for WC z-score were similar, but associations were slightly weaker (Table 3).

Changes in BMI z-score from 13 to 17 years and from 17 to 21 years were positively associated with SBP, DBP and HOMA-IR in both sexes (Table 4). For example, in females for every s.d. increase in BMI between 13 and 17 years, SBP increased on average by 1.79 mmHg (95% CI 0.48; 3.10), whereas for every s.d. increase between 17 and 21 years, SBP increased on average by 1.99 mmHg (1.01; 2.97); for males associations were stronger: 2.03 mmHg (0.47; 3.59) for BMI changes for 13–17 years, and 3.83 mmHg (2.67; 4.98) for 17–21 years. For triglycerides and LDL, the association was stronger for 17–21 years than 13–17 years. For HDL an inverse association was found for the period 13–17 years in both sexes, and for 17–21 years only in males.

Similar results were found for WC z-score (Table 4): positive associations between increases in WC and SBP, DBP, HOMA-IR, triglycerides and LDL and negative associations with HDL.

Either for BMI or WC, regression coefficients were in general stronger in males and for the period 17 to 21 years.

Analyses were repeated using complete cases and as conclusions were mostly unaltered, those results are presented only in Supplementary Tables S3 and S4.

DISCUSSION

Main findings

Using our longitudinal population-based study we identified three trajectories of total and central adiposity from adolescence-to-adulthood. Although the majority (>75%) of individuals were in the normal trajectory group, the 'high,

Table 1. Descriptive information on anthropometric measures and cardiovascular risk factors in the EPITeen cohort, Porto, Portugal					
	Females		Males		P-value ^a
	n	Mean (s.d.)	n	Mean (s.d.)	
Anthropometric variables					
BMI (kg m ⁻²)					
13 years	1053	21.1 (3.5)	984	20.7 (3.6)	0.003
17 years	1267	22.2 (3.4)	1202	22.5 (3.5)	0.048
21 years	903	22.6 (3.9)	854	23.6 (3.7)	< 0.001
Waist circumference (cm)					
13 years	1045	71.8 (8.2)	981	73.3 (9.5)	< 0.001
17 years	1274	74.6 (8.2)	1203	78.4 (8.8)	< 0.001
21 years	896	73.8 (9.3)	853	81.7 (9.4)	< 0.001
CV risk factors at 21 years					
SBP (mmHg)	903	102 (8.8)	853	115.9 (10.4)	< 0.001
DBP (mmHg)	903	68.1 (7.5)	853	69.6 (7.5)	< 0.001
HOMA-IR	864	1.86 (0.88)	806	1.74 (1)	0.014
Triglycerides (mg dl ⁻¹)	877	94.1 (42.9)	810	77.5 (33.9)	< 0.001
LDL (mg dl ⁻¹)	877	104.9 (27.8)	813	99.6 (25.9)	< 0.001
HDL (mg dl ⁻¹)	878	62.2 (12.4)	813	49.7 (9.4)	< 0.001

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; HDL, high-density lipoprotein cholesterol; HOMA-IR, homeostatic model assessment; LDL, low-density lipoprotein cholesterol; SBP, systolic blood pressure; s.d., standard deviation. ^aP-value from the Student *t*-test for the sex-differences comparison.

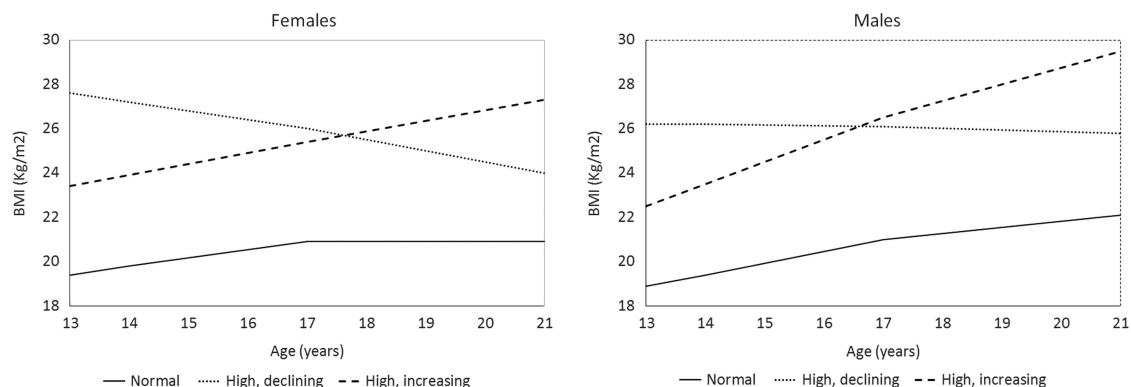


Figure 1. Trajectories of body mass index from 13 to 21 years of age in females (left) and in males (right), in the EPITeen cohort, Porto, Portugal.

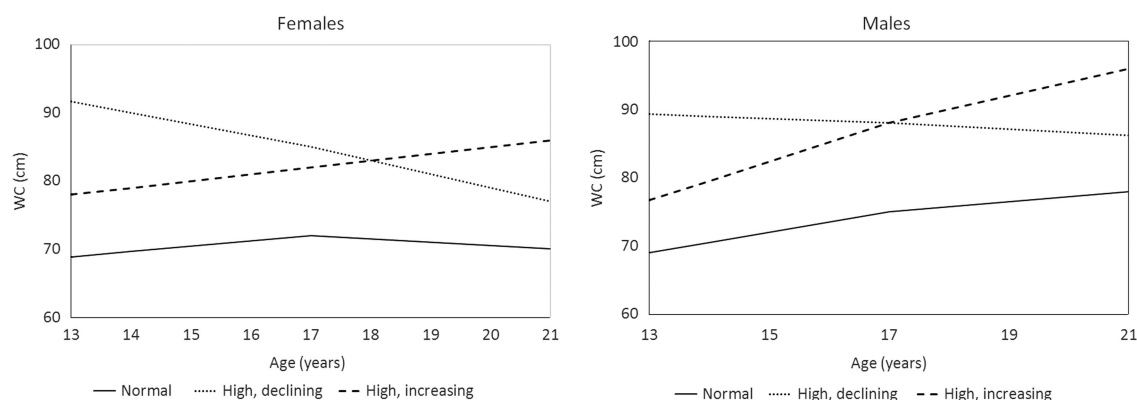


Figure 2. Trajectories of waist circumference from 13 to 21 years of age in females (left) and in males (right), in the EPITeen cohort, Porto, Portugal.

Table 2. Crude regression coefficients for the association between probability of trajectory membership and cardiovascular risk factors at 21 years of age in the EPITeen cohort, Porto, Portugal

Outcome 21 years	Probability of BMI trajectory membership in females ^a		Probability of BMI trajectory membership in males ^a	
	High, increasing	High, declining	High, increasing	High, declining
SBP	6.14 (4.34, 7.94)	−0.05 (−3.13, 3.03)	10.37 (7.46, 13.29)	2.48 (0.12, 4.84)
DBP	5.64 (4.10, 7.17)	−0.08 (−2.70, 2.54)	10.30 (8.25, 12.36)	2.34 (0.68, 4.00)
HOMA-IR ^b	0.58 (0.48, 0.68)	−0.06 (−0.23, 0.11)	0.94 (0.79, 1.08)	0.18 (0.06, 0.29)
TRIG ^b	0.12 (0.04, 0.21)	0.00 (−0.15, 0.15)	0.34 (0.22, 0.46)	0.12 (0.03, 0.21)
LDL	14.04 (8.26, 19.83)	−4.80 (−14.72, 5.12)	26.11 (18.67, 33.55)	1.22 (−4.73, 7.16)
HDL	−3.76 (−6.35, −1.17)	−4.53 (−8.97, −0.09)	−6.70 (−9.44, −3.96)	−2.35 (−4.54, −0.16)
Outcome 21 years	Probability of WC trajectory membership in females ^a		Probability of WC trajectory membership in males ^a	
	High, increasing	High, declining	High, increasing	High, declining
SBP	5.41 (3.62, 7.20)	0.34 (−4.00, 4.69)	9.32 (6.72, 11.92)	3.49 (0.96, 6.03)
DBP	4.90 (3.37, 6.43)	−1.29 (−4.99, 2.40)	9.60 (7.78, 11.43)	2.25 (0.46, 4.03)
HOMA-IR ^b	0.56 (0.46, 0.66)	−0.02 (−0.26, 0.21)	0.93 (0.80, 1.06)	0.26 (0.14, 0.39)
TRIG ^b	0.14 (0.06, 0.23)	−0.00 (−0.22, 0.21)	0.37 (0.27, 0.47)	0.10 (−0.00, 0.19)
LDL	12.31 (6.55, 18.07)	−4.37 (−18.20, 9.45)	22.50 (15.87, 29.12)	1.15 (−5.37, 7.67)
HDL	−5.56 (−8.12, −2.99)	−3.49 (−9.64, 2.67)	−5.67 (−8.11, −3.23)	−1.82 (−4.22, 0.58)

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; HDL, high-density lipoprotein cholesterol; HOMA-IR, homeostatic model assessment; LDL, low-density lipoprotein cholesterol; SBP, systolic blood pressure; TRIG, triglycerides; WC, waist circumference. ^aTrajectory 'normal' is the reference group. ^bResults are presented for the log-transformed variable.

increasing' trajectory (more frequently females) had a high BMI/WC in adolescence and gained BMI/WC more rapidly, thereafter, presenting the highest prevalence of obesity and the worst profile of CV risk factors at 21 years of age, particularly in males. A small group (more frequently males) had a high BMI/WC in early adolescence but it declined from adolescence-to-early adulthood. Among 'high, declining' group, in females the CV risk factors at 21 years did not differ from normal group, whereas for males, although worse than those in the normal group, CV risk factors were more favorable than those in the 'high, increasing'. In addition to the identification of trajectories, we also found that adiposity changes from 13 to 21 years were associated with unfavorable values of the CV risk factors evaluated, and excessive increases between 17 and 21 years of age (moving up in relative position for BMI in the population) were particularly influential. These results were similar using either BMI or WC.

Strengths and limitations

Major strengths of this study include the use of both BMI and WC and applying innovative modeling techniques for the identification of trajectories, allowing the study of the effect of cumulative exposure to adiposity on CV risk factors, and not only the effect of the adiposity in a specific age. In addition, in a period under characterized—transition from adolescence-to-adulthood, our study adds information on the specific effect of adiposity changes at different ages. We used repeated measurements of adiposity objectively measured under standardized procedures, as well as repeated measurements of many confounders, from a population-based cohort, enabling the generalizability of the results.

Nonetheless, potential limitations of the study exist. Losses to follow-up and item non-response led to missing data. We conducted analyses using multiple imputation for BMI, WC and covariates including the main predictors of missing data, which would have reduced selection bias. However, our final models

Table 3. Adjusted regression coefficients (mean change) for cardiovascular risk factors at 21 years of age per standard deviation increase in BMI and in WC at different ages (13, 17 and 21 years) in the EPITeen cohort, Porto, Portugal—missing covariates imputed ($m=30$ imputations)

Outcome 21 years	Exposure (years)	Females		Males	
		BMI z-score	WC z-score	BMI z-score	WC z-score
SBP	13	1.45 (0.78, 2.12)	1.25 (0.56, 1.94)	2.11 (1.31, 2.90)	1.99 (1.21, 2.78)
	17	1.78 (1.14, 2.41)	1.40 (0.76, 2.03)	2.31 (1.57, 3.05)	2.30 (1.57, 3.03)
	21	2.08 (1.49, 2.67)	1.82 (1.22, 2.40)	3.27 (2.59, 3.96)	3.19 (2.50, 3.87)
DBP	13	1.06 (0.50, 1.61)	0.88 (0.30, 1.46)	1.68 (1.13, 2.24)	1.58 (1.03, 2.13)
	17	1.42 (0.88, 1.96)	1.30 (0.76, 1.84)	1.88 (1.35, 2.41)	1.76 (1.24, 2.29)
	21	1.65 (1.14, 2.15)	1.43 (0.93, 1.93)	2.45 (1.95, 2.94)	2.50 (2.01, 3.00)
HOMA-IR ^a	13	0.09 (0.05, 0.13)	0.09 (0.05, 0.13)	0.17 (0.12, 0.21)	0.16 (0.12, 0.21)
	17	0.11 (0.07, 0.14)	0.10 (0.06, 0.14)	0.18 (0.14, 0.22)	0.19 (0.15, 0.23)
	21	0.18 (0.15, 0.22)	0.19 (0.15, 0.22)	0.25 (0.21, 0.28)	0.26 (0.22, 0.29)
TRIG ^a	13	0.02 (−0.01, 0.05)	0.04 (0.00, 0.07)	0.08 (0.05, 0.11)	0.08 (0.05, 0.11)
	17	0.01 (−0.02, 0.04)	0.03 (0.00, 0.06)	0.08 (0.05, 0.11)	0.09 (0.06, 0.12)
	21	0.05 (0.02, 0.08)	0.06 (0.03, 0.09)	0.10 (0.07, 0.13)	0.11 (0.08, 0.14)
LDL	13	1.40 (−0.72, 3.53)	0.34 (−1.83, 2.52)	4.06 (2.06, 6.05)	2.79 (0.78, 4.80)
	17	2.50 (0.47, 4.53)	1.97 (−0.05, 3.99)	4.26 (2.34, 6.17)	3.04 (1.15, 4.93)
	21	4.19 (2.29, 6.08)	3.25 (1.36, 5.14)	6.76 (4.54, 8.12)	5.67 (3.89, 7.45)
HDL	13	−1.22 (−2.16, −0.28)	−1.49 (−2.44, −0.53)	−1.38 (−2.11, −0.64)	−1.23 (−1.99, −0.47)
	17	−1.49 (−2.39, −0.59)	−1.68 (−2.58, −0.79)	−1.73 (−2.44, −1.03)	−1.50 (−2.19, −0.81)
	21	−1.16 (−2.01, −0.31)	−1.58 (−2.42, −0.74)	−2.02 (−2.68, −1.36)	−1.78 (−2.44, −1.12)

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; HDL, high-density lipoprotein cholesterol; HOMA-IR, homeostatic model assessment; LDL, low-density lipoprotein cholesterol; SBP, systolic blood pressure; TRIG: triglycerides; WC: waist circumference. ^aResults are presented for the log-transformed variable. N ranges between 864 and 903 for females, and 806 and 853 for males, depending on the outcome. Estimates were adjusted for birth weight; mother's smoking during pregnancy; parental education; household occupational position; family history of hypertension, diabetes or dyslipidaemia (according to the outcome); parental BMI z-score; and participant's practice of sports.

Table 4. Adjusted regression coefficients for cardiovascular risk factors at 21 years of age per standard deviation increase in BMI and in WC during different periods (13–17 years; 17–21 years) in the EPITeen cohort, Porto, Portugal—missing covariates imputed ($m=30$ imputations)

Outcome 21 years	Exposure (years)	Females		Males	
		BMI z-score	WC z-score	BMI z-score	WC z-score
SBP	13–17	1.79 (0.48, 3.10)	1.05 (0.10, 1.99)	2.03 (0.47, 3.59)	1.97 (0.70, 3.23)
	17–21	1.99 (1.01, 2.97)	1.67 (0.85, 2.48)	3.83 (2.67, 4.98)	3.01 (1.99, 4.03)
DBP	13–17	1.72 (0.63, 2.80)	1.36 (0.57, 2.14)	1.58 (0.50, 2.66)	1.41 (0.53, 2.29)
	17–21	1.56 (0.72, 2.40)	1.07 (0.37, 1.76)	2.80 (1.97, 3.64)	2.70 (1.97, 3.44)
HOMA-IR ^a	13–17	0.10 (0.03, 0.18)	0.08 (0.02, 0.13)	0.15 (0.07, 0.23)	0.16 (0.09, 0.22)
	17–21	0.27 (0.21, 0.32)	0.22 (0.18, 0.27)	0.30 (0.24, 0.36)	0.27 (0.22, 0.33)
TRIG ^a	13–17	−0.01 (−0.07, 0.05)	0.01 (−0.03, 0.06)	0.04 (−0.02, 0.10)	0.07 (0.02, 0.12)
	17–21	0.12 (0.07, 0.16)	0.07 (0.03, 0.11)	0.10 (0.05, 0.15)	0.11 (0.07, 0.15)
LDL	13–17	4.29 (0.25, 8.33)	3.39 (0.39, 6.39)	2.81 (−1.06, 6.68)	2.34 (−0.87, 5.54)
	17–21	6.16 (2.99, 9.34)	3.72 (1.11, 6.33)	8.62 (5.63, 11.62)	7.98 (5.33, 10.64)
HDL	13–17	−1.54 (−3.33, 0.26)	−1.36 (−2.67, −0.04)	−1.92 (−3.34, −0.50)	−1.44 (−2.66, −0.23)
	17–21	−0.10 (−1.50, 1.30)	−0.94 (−2.10, 0.21)	−1.92 (−3.04, −0.80)	−1.68 (−3.33, −0.69)

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; HDL, high-density lipoprotein cholesterol; HOMA-IR, homeostatic model assessment; LDL, low-density lipoprotein cholesterol; SBP, systolic blood pressure; TRIG, triglycerides; WC, waist circumference. ^aResults are presented for the log-transformed variable. N ranges between 864 and 903 for females, and 806 and 853 for males, depending on the outcome. Estimates were adjusted for birth weight; mother's smoking during pregnancy; parental education; household occupational position; family history of hypertension, diabetes or dyslipidaemia (according to the outcome); parental BMI z-score; and participant's practice of sports.

were fitted only to participants with measured outcomes in the third study wave. Attrition in the third wave was higher among participants with lower parental education, and among those obese at the recruitment age. The underrepresentation of obese participants may have led to an underestimation of the associations reported in our study.

Interpretation of findings

Information on growth trajectories in the period from adolescence-to-adulthood is limited. To our knowledge, five

studies have identified BMI trajectories in this age period using similar methodology^{11,30–33} and found three to four distinct trajectories, with some groups being similar to the trajectories 'normal' and 'high, increasing' identified in our study. A declining trajectory was only identified in two of these studies.^{11,32} Ziyab *et al.*¹¹ using data from infancy to 18 years, identified an 'early transient overweight' trajectory. However, this trajectory was characterized by a decline in BMI z-score from 1 to 10 years of age, and a stabilization from 10 to 18 years, whereas the declining trajectory in our study presented declining values of BMI more

pronounced from 17 to 21 years of age, than from 13 to 17 years. In Canada's National Longitudinal Survey of Children and Youth³² a decreasing trajectory was also identified from age 1 to 20 years and the decrease in BMI values was more evident in females, as we also found in our study, although it occurred at earlier ages in their study—from early to mid-adolescence. The small sample size of the group 'high, declining' identified in our sample, particularly in females, limited our ability to explore in depth the characteristics of this group.

'High, increasing' trajectory presented the worst levels of CV risk factors at 21 years of age, whereas the levels in the 'high, declining' trajectory were closer to those in the 'normal' group. This finding is also in accordance to other study that found higher systolic and diastolic blood pressure at 18 years in the delayed overweight trajectory in comparison to the 'normal' trajectory, but still smaller than the values found for the early persistent obesity trajectory.¹¹ Regarding studies in other age ranges, in the Raine Study,⁷ those in increasing trajectories from birth to 14 years presented the highest insulin resistance levels at 14 years, whereas the outcome in those from declining trajectories was similar to those in the reference trajectory ('Optimal growth'). Girls in the 'upward percentile crossing' trajectory from 5 to 15 years had highest metabolic risk factors at 15 years, whereas the 'delayed downward percentile crossing' presented similar levels in comparison to the '50th percentile tracking'.⁹ These results and those from our study suggest that excessive gains in adiposity during the pediatric ages are associated with adverse CV risk factors, partly because it is likely to result in high current BMI. This is supported by the sex-differences in the association between 'high, declining' trajectory and the CV risk factors in our study. In females there was a marked decrease in BMI between 13 and 21 years in this trajectory, but the final BMI mean value was closer to the mean BMI value in the 'normal' trajectory and this resulted in no statistically significant differences in the outcomes between these two trajectories. In males, there was a small decline in BMI mean values, but the difference in BMI values at 21 years in comparison to the 'normal' trajectory was higher than in females, resulting in increased values of CV risk factors at 21 years, although of lower magnitude in comparison to the 'high, increasing' group.

To our knowledge, this is the first study addressing waist circumference trajectories in the period from adolescence-to-adulthood. Trajectories of WC were similar to the BMI trajectories, and associations of WC trajectories with CV risk factors at 21 years were of the same magnitude to those found for BMI trajectories. Although WC is described as a measure of central or abdominal adiposity, it is highly correlated to BMI (correlations around 0.8 in females and 0.9 in males at each age, in our study). Other studies have found that BMI and WC perform similarly in the association with CV risk factors.^{34–36}

We found that changes in adiposity, both from 13 to 17 years and from 17 to 21 years, were associated to unfavorable CV risk parameters at 21 years, but the magnitude was stronger for the later period. These results suggest that changes in adiposity in these specific ages (17 to 21 years) are more relevant for CV risk factors. During early and mid-adolescence the effect of adiposity changes in CV risk factors may be of lower magnitude, as other factors such as hormonal changes related to puberty may also influence lipid and insulin levels.^{37,38} The comparison of changes in the specific periods evaluated here with other studies is difficult due to the differences in the periods evaluated, but two studies using data from the 1958 British birth cohort, and evaluating similar periods (11–16 years and 16–23 years) also found stronger associations for the changes in BMI from 16 to 23 years with adult glycosylated hemoglobin²⁴ and blood pressure at 45 years.³⁹ However, this could be because the period is closer in time to the outcome, rather than an effect of this specific period (17–21 years) under study, as described in other studies.^{22–24,39}

In conclusion, our study identified three distinct trajectories of BMI and WC from adolescence-to-adulthood, and showed a benefit on the cardiovascular risk profile for those in the declining adiposity trajectory. The similar results for the two adiposity measures support that both BMI and WC are surrogates of global adiposity. In addition, increases in BMI and WC, particularly recent changes from late adolescence-to-young adulthood, had a strong positive association with traditional cardiovascular risk factors. Our results highlight the importance of promote a healthy BMI at all ages to prevent unfavorable cardiovascular risk factors and future disease.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ACKNOWLEDGEMENTS

This study was supported by national funding from the Portuguese Foundation for Science and Technology—FCT (Portuguese Ministry of Education and Science) within the Epidemiology Research Unit—Institute of Public Health, University of Porto (UID/DTP/047507/2013). The Population, Policy and Practice Programme was formed in 2014, incorporating the activities of the Centre for Paediatric Epidemiology and Biostatistics, which was supported in part by the Medical Research Council in its capacity as the MRC Centre of Epidemiology for Child Health (award G0400546). Research at the GOSH/UCL Institute of Child Health is supported in part by the Department of Health's NIHR Biomedical Research Centres. An individual grant to JA (SFRH/BD/78153/2011) by the Portuguese Foundation for Science and Technology—FCT is gratefully acknowledged.

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