Preventive Medicine 120 (2019) 1–7

Contents lists available at ScienceDirect

Preventive Medicine

journal homepage: www.elsevier.com/locate/ypmed

Decreases in adiposity reduce the risk of hypertension: Results from a prospective cohort of adolescents

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ARTICLE INFO

Keywords:
Adolescent
Adiposity
Blood pressure
Hypertension
Incidence

ABSTRACT

This study aimed to evaluate the effect of age-related changes in body mass index and waist circumference during adolescence on blood pressure levels and incidence of hypertension. Among the 2159 adolescents recruited at 13 years in Porto, Portugal, we evaluated those free of hypertension at baseline and followed-up at 17 years (n = 1377) - EPITeen cohort, 2003–2008. Changes in BMI percentage (BMI%) and waist circumference percentage (WC%) were evaluated continuously as the difference between 13 and 17 years, then categorized in sex-specific quartiles. Hypertension was defined as systolic and/or diastolic blood pressure ≥ 95th sex- age- and height-specific reference percentile. The association between changes in adiposity and incidence of hypertension was computed through generalized linear models with log link function and Poisson distribution [incidence rate ratios (IRR), 95% confidence intervals (95%CI)], adjusting for baseline adiposity, sex, and family history of hypertension. Overall incidence rate of hypertension was 23.8 (95%CI 19.6–28.8) per 1000 person-years. Participants presenting the highest decrease in BMI% from 13 to 17 years (1st quartile) presented lower SBP at 17y, while for those with increasing BMI% (4th quartile) SBP increased. In comparison to stable BMI% (3rd quartile), decreases in BMI% (1st quartile) were associated with 44% lower risk of hypertension at 17y (IRR = 0.56, 95%CI 0.32–0.97). Increases in BMI% (4th quartile) were associated with increased incidence, although without statistical significance (IRR = 1.11, 95%CI 0.66–1.85). Results were similar when considering changes in WC%. Decreases in BMI and WC throughout adolescence in the whole spectrum of adiposity levels presented potential benefit for blood pressure.

1. Introduction

Excess body weight is an important modifiable factor contributing to high blood pressure (Whelton et al., 2002). It has been firstly shown in adults in observational studies, but also supported by several clinical trials showing the potential of weight loss on blood pressure reduction among those with overweight and/or hypertension (Elmer et al., 2006; Siebenhofer et al., 2011; Bacon et al., 2004). In the past, primary hypertension was a rare condition in childhood, but its prevalence is increasingly higher in the young, and has been linked to the worldwide obesity epidemic (Flynn, 2013; Muntner et al., 2004).

The development and progression of cardiovascular disease is determined by long-term and cumulative exposure to different factors across the life span, including adiposity (Hardy et al., 2015), which had conducted to increasing interest on the effect of changes in adiposity at different stages of the life span - particularly at phases of intense growth. However, studies have mainly focused on adiposity changes in infancy and childhood, and less is known about the effects of adiposity changes during adolescence.

Adolescence is characterized by changes in body composition during puberty (Loomba-Albrecht and Styne, 2009), which might affect the interaction between adipocytokines, insulin and sex-steroid hormones (Siervogel et al., 2003), and consequently the long-term development of cardiometabolic diseases. Understanding how the dynamics of adiposity throughout adolescence impact on blood pressure may allow the identification of sensitive periods for intervention. Most of the previous prospective observational studies in adolescents have evaluated blood pressure in (mid-) adulthood (Juonala et al., 2011; Li et al., 2007; Siervogel et al., 2000; Sinaiko et al., 1999; Suglia et al., 2013). The consequent long follow-up periods without interim information made impossible to address the effect of short/medium-term changes, increasing the probability of exposure misclassification. The studies that

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https://doi.org/10.1016/j.ypmed.2018.12.017
Received 19 June 2018; Received in revised form 14 November 2018; Accepted 24 December 2018
Available online 27 December 2018

specifically investigated the short and medium-term effect of adiposity/anthropometrics changes evaluated changes as continuous variables, but focused only on increases in adiposity (Maximova et al., 2010; Lawlor et al., 2010; Tybor et al., 2011; Horta et al., 2003). No previous study have evaluated the effect of changes in adiposity/anthropometrics measured as a continuous quantity, separately for those presenting an increase or a decrease in adiposity. Two studies have also addressed the effect of changes in body mass index category on adolescent blood pressure (Lawlor et al., 2010; Parker et al., 2016). This approach also addresses decreases in BMI - for example, changing from overweight or obese status to normal category, however, it only quantifies the effect of changing a category, which is dependent on the magnitude of the change and on the initial position of the subject in relation to the cut-off used. Additionally, inconsistent results regarding potential sex-differences in the association between changes in adiposity indicators and blood pressure in adolescence have been reported (Maximova et al., 2010; Lawlor et al., 2010; Tybor et al., 2011; Parker et al., 2016).

Therefore, we studied the effect on blood pressure levels and incidence of hypertension of age-related changes in indicators of total and central adiposity during adolescence, addressing both decreases and increases in adiposity using continuous variables, and changes in adiposity category.

2. Methods

Eligible participants were adolescents from the Epidemiological Health Investigation of Teenagers in Porto (EPITeen) cohort. As previously reported (Ramos and Barros, 2007), in 2003/2004 a cohort of adolescents born in 1990 and enrolled at public and private schools in Porto, Portugal, was assembled. All the 27 public and 19 from the 24 private schools in Porto accepted to participate, and 2159 (77.5%) of the 2786 eligible participants accepted to participate. In the second evaluation in 2007/2008, 1716 participants were re-evaluated and mean duration of follow-up was 38.4 months (standard deviation = 5.3). Participants were on average 13.7 (0.34) and 16.8 years (0.48), at the first and second waves, respectively.

The Ethics Committee of Hospital S. João approved this project and appropriate standard procedures were developed to guarantee data confidentiality and protection. Parents and adolescents received written and oral information explaining the purpose and design of the study and written informed consent was obtained from both.

For this analysis, participants with hypertension ($n = 251$) or missing values on blood pressure ($n = 137$) at baseline were excluded, and therefore eligible participants were the 1771 at risk of developing hypertension. We excluded those with missing data on blood pressure at 17 years ($n = 32$), weight, height or waist circumference at 13 or 17 years ($n = 17$), and additionally 345 were lost to follow-up. Therefore, analysis included 1377 participants.

Among the eligible participants, baseline characteristics of the participants included and those excluded from this study were similar with regard to sex, BMI categories, median waist circumference, and mean systolic and diastolic blood pressure at 13 years of age. A higher proportion of participants included in the study had highly educated parents (Supplementary Table S1).

2.1. Data collection

Both evaluations followed the same procedures. Standardised self-administered questionnaires were used and a physical examination was performed at school by a trained team of health professionals.

2.2. Adiposity measures

Weight and height of the participants were obtained in light indoor clothes and no shoes. Weight was measured in kilograms to the nearest tenth, using a bioelectrical impedance scale and height was measured in centimetres to the nearest tenth, using a portable stadiometer. Waist circumference (WC) 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 WC were used as indicators of total and central adiposity, respectively, and changes in adiposity indicators were examined using two approaches. Firstly, changes were measured based on the continuous variables of adiposity at each age. BMI percentage (BMI%) was calculated at 13 and at 17 years as the percentage difference from the reference median BMI (Kuczmarski et al., 2002), applying the formula BMI% = 100 $\log_e$ (BMI/median BMI reference for age and sex) (Cole, 2000). Similarly, waist circumference percentage (WC%) was calculated applying the same formula and using as reference the median waist circumference from the percentiles for European-American children and adolescents (Fernandez et al., 2004). Changes in BMI% and WC% were computed as the difference in the adiposity measure between 13 and 17 years of age (for example, BMI% 17y minus BMI% 13y). This continuous variable was then categorized in sex-specific quartiles, for each adiposity measure. For example, a decrease in BMI% means that the adolescent moved closer to the median BMI from the reference population and can be interpreted as a decrease in BMI, according to what was expected for their age and sex.

Secondly, we also examined changes in the categories of BMI and WC defined according to standard references. At each age, adolescents were classified according to the age- and sex-specific BMI reference percentiles developed by the U.S. Centers for Disease Control and Prevention (Kuczmarski et al., 2002) in three categories: thin/normal (BMI < 85th percentile), overweight (BMI ≥85th & < 95th percentile) and obese (BMI ≥95th percentile). For WC, the 75th percentile for European-American adolescents from the age- sex- and ethnicity-specific WC references (Fernandez et al., 2004) derived from the Third National Health and Nutrition Examination Survey (NHANES III) was used to classify adolescents in two categories: normal WC (< 75th percentile) and high WC (≥75th percentile). For changes in BMI category between the two ages, adolescents were classified in four groups according to their classification at 13 and at 17 years, respectively: normal/normal; overweight-obese/normal; normal/overweight-obese; and overweight-obese/overweight-obese. For changes in WC category, defined according to the 75th percentile, the four groups were: normal/normal; high/normal; normal/high; high/high.

2.3. Blood pressure

In both study waves, blood pressure was measured with a mercury sphygmomanometer by auscultation, following the recommendations of the American Academy of Pediatrics (Anon, 2004). After at least 10 min of rest, two blood pressure readings were taken separately by at least 5 min. A third measure was taken when the difference between the first two readings was higher than 5 mmHg. Hypertension was defined according to the quantitative criteria of the American Academy of Pediatrics (Anon, 2004) as systolic (SBP) and/or diastolic blood pressure (DBP) above the 95th percentile for sex, age and height; prehypertension as SBP and/or DBP above the 90th percentile, but both below the 95th percentile; and normal blood pressure defined as both SBP and DBP below the 90th percentile. In our analyses, the outcome considered was hypertension at 17 years, versus normal and prehypertension categories combined.

2.4. Covariates

Family history of a medical diagnosis of hypertension was asked separately to the mother and the father, and then combined as: positive, when at least one of the adolescent's parents had the diagnosis; negative, when both parents reported no diagnosis; or non-classifiable, when the available information showed no diagnosis for one of the parents, but missing regarding the other.

2.5. Statistical analysis

A linear regression model was fitted to estimate the association between adiposity changes and continuous systolic blood pressure at 17 years. Estimates were adjusted for height at 17 years, adiposity measure at 13 years, sex and family history of hypertension.

Incidence rate ratios (IRR) and respective 95% confidence intervals (95% CI) were computed through generalized linear models with log link function and Poisson distribution. The total person-time at risk was calculated, and the log of person-months was included as the offset variable. Firstly, for each adiposity measure (BMI% and WC%), we computed the association between changes in adiposity, measured based on continuous changes, and incidence of hypertension. Model 1 was adjusted for adiposity measure at 13 years, and model 2 was further adjusted for sex and family history of hypertension. Secondly, we also measured the association of changes in BMI and WC category between 13 and 17 years with incidence of hypertension. Estimates were adjusted for sex and family history of hypertension (model 3).

Statistical analysis was conducted using SPSS (IBM Corp. Released 2014. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.), and the significance level was set at 0.05 for two-sided tests.

3. Results

Regarding changes in adiposity indicators between 13 and 17 years, participants classified in the first quartile of changes in BMI% presented a decrease in BMI% with a mean of −13.3%; in the second quartile a decrease in adiposity was also registered but of lower magnitude (mean of −4.9%); the third quartile represents those with stable adiposity (mean of −0.2%, varying between −2.9% and 2.6%); and the fourth quartile represents those with an increase in adiposity (mean of 6.7%). For quartiles of changes in WC%, the mean values of WC% change in each quartile were − 13.4%, −5.3%, −0.9% and 6.1%, respectively from the first to the fourth quartile.

Table 1 presents mean SBP and DBP values and the incidence rate of hypertension at 17 years according to baseline characteristics and changes in adiposity between 13 and 17 years. The overall incidence rate of hypertension was 23.8 (95% CI 19.6–28.8) per 1000 person-

Table 1
Systolic and diastolic blood pressure at 17 years and incidence rate of hypertension, according to baseline characteristics and changes in adiposity between 13 and 17 years (n = 1377) – EPITeen cohort, Portugal, 2003–2008.

		SBP (mmHg)	DBP (mmHg)	Hypertension
	n (%)	Mean (SD)		IR (95% CI) Per 1000 person-years
Overall	1377	114.1 (11.2)	67.2 (8.6)	23.8 (19.6–28.8)
Sex				
Females	716 (52.0)	110.5 (10.0)	65.8 (8.1)	22.9 (17.5–30.0)
Males	661 (48.0)	118.0 (11.2)	68.7 (8.8)	24.7 (18.8–32.4)
Family history hypertension				
Negative	498 (36.2)	113.2 (11.0)	66.5 (8.3)	22.8 (16.4–31.6)
Positive	466 (33.8)	115.3 (11.8)	68.0 (8.8)	26.3 (19.2–36.0)
Non-classifiable	413 (30.0)	113.8 (10.7)	67.2 (8.6)	22.2 (15.5–31.7)
BMI at 13 years[a]				
Normal/thinness	1089 (79.1)	113.3 (10.8)	66.8 (8.6)	19.2 (15.1–24.4)
Overweight	195 (14.2)	115.8 (12.3)	67.9 (8.4)	30.4 (19.4–47.6)
Obesity	93 (6.8)	119.7 (12.2)	70.3 (8.5)	64.0 (40.8–100.4)
WC at 13 years[b]				
Normal	1077 (78.2)	113.4 (11.0)	66.9 (8.6)	19.1 (15.0–24.3)
High	300 (21.8)	116.5 (11.9)	68.4 (8.5)	40.5 (29.6–55.4)
Changes BMI%				
1st Q ('highest decrease')	344 (25.0)	113.3 (12.0)	66.2 (7.8)	23.2 (15.8–34.0)
2nd Q ('decrease')	344 (25.0)	113.4 (10.7)	66.6 (8.5)	18.2 (11.7–28.2)
3rd Q ('stable')	345 (25.1)	113.9 (11.4)	67.5 (8.9)	26.2 (18.2–37.7)
4th Q ('increase')	344 (25.0)	115.7 (10.7)	68.5 (8.9)	27.6 (19.3–39.5)
Changes WC%				
1st Q ('highest decrease')	344 (25.0)	112.7 (11.3)	66.5 (7.9)	18.3 (11.9–28.1)
2nd Q ('decrease')	345 (25.1)	112.1 (10.6)	65.6 (8.0)	13.2 (8.0–22.0)
3rd Q ('stable')	344 (25.0)	115.5 (11.8)	67.7 (8.7)	34.0 (24.6–46.9)
4th Q ('increase')	344 (25.0)	116.1 (10.6)	69.0 (9.3)	30.6 (21.6–43.2)
Changes in BMI category[a]				
Normal/normal	1049 (76.2)	113.0 (10.6)	66.6 (8.4)	16.9 (13.0–21.9)
Overw.-obese/normal	115 (8.4)	113.7 (12.4)	66.6 (8.1)	18.8 (8.9–39.4)
Normal/Overw.-obese	40 (2.9)	121.6 (13.2)	72.4 (10.5)	80.3 (43.2–14.9)
Overw.-obese/Overw.-obese	173 (12.6)	119.3 (11.9)	70.1 (8.6)	56.5 (39.7–80.3)
Changes in WC category[b]				
Normal/normal	1041 (75.6)	113.2 (10.8)	66.7 (8.4)	18.2 (14.2–23.4)
High/normal	174 (12.6)	113.6 (11.2)	66.5 (8.0)	22.7 (13.2–39.2)
Normal/high	36 (2.6)	119.8 (13.0)	72.1 (11.8)	45.7 (19.0–109.9)
High/high	126 (9.2)	120.6 (11.6)	71.2 (8.4)	66.3 (45.1–97.4)

BMI%: body mass index percentage; DBP: diastolic blood pressure; IR: incidence rate; SBP: systolic blood pressure; WC%: waist circumference percentage.

[a] BMI classified according to the CDC growth charts (Kuczmarski et al., 2002).

[b] Waist circumference classified according to percentiles for European-American children and adolescents (Fernandez et al., 2004); high WC corresponds to values ≥75th percentile.

Table 2
Association between changes in adiposity from 13 to 17 years, measured based on the continuous change in adiposity, and systolic blood pressure at 17 years (n = 1293) – EPITeen cohort, Portugal, 2003–2008.

	Adjusted β (95% CI)[a]	Adjusted β (95% CI)[b]
Changes BMI%		
1st Q ('highest decrease')	−0.768 (−2.365; 0.829)	−2.864 (−4.478; −1.250)
2nd Q ('decrease')	−0.454 (−2.051; 1.142)	−0.961 (−2.496; 0.574)
3rd Q ('stable')	1	1
4th Q ('increase')	2.141 (0.544; 3.739)	2.337 (0.806; 3.868)
Changes WC%		
1st Q ('highest decrease')	−2.863 (−4.448; −1.278)	−5.212 (−6.831; −3.594)
2nd Q ('decrease')	−3.473 (−5.057; −1.890)	−4.065 (−5.594; −2.536)
3rd Q ('stable')	1	1
4th Q ('increase')	0.576 (−1.009; 2.161)	1.037 (−0.480; 2.554)

BMI%: body mass index percentage; WC%: waist circumference percentage.
[a] Adjusted for height at 17 years.
[b] Adjusted for height at 17 years, adiposity levels at 13 years, sex and family history of hypertension.

years. The mean blood pressure levels and the incidence rate of hypertension were higher among males, adolescents with family history of disease, in those with higher levels of BMI and WC at baseline, and in adolescents in the category of increases in BMI and WC (4th quartile). Regarding changes in standard categories of adiposity, changes to a lower category of adiposity (from the overweight-obese to normal BMI category, and from high to normal WC) were more frequent than changes to a higher category. The lowest incidence rate of hypertension was found among adolescents maintaining the normal adiposity category, while the highest incidence rate among those maintaining or changing to a higher category of adiposity.

Results using continuous SBP as outcome (Table 2) showed that participants presenting the highest decrease in BMI% from 13 to 17 years (1st quartile) presented lower SBP at 17 years (β = −2.864 mmHg, 95% CI -4.478; −1.250), while for those with increasing BMI% (4th quartile) SBP increased on average by 2.337 (95% CI 0.806; 3.868). Similar results were found for changes in WC%. Regarding the association with hypertension, after adjustment for baseline adiposity, sex, and family history of hypertension, changes in BMI% and in WC% were significantly associated with incidence of hypertension at 17 years (Table 3). In comparison to stable BMI% (3rd quartile), decreases in BMI% from 13 to 17 years were associated with lower incidence hypertension at 17 years: IRR = 0.56, 95% CI: 0.32–0.97 for those in the first quartile (presenting the highest decrease), and IRR = 0.63, 95% CI: 0.36–1.12 for the second quartile. Increases in BMI% (4th quartile) were associated with higher incidence of hypertension, although statistical significance was not attained (IRR = 1.11, 95% CI: 0.66–1.85). Similar results were found for changes in WC%: the decrease was associated with about 65% lower incidence of hypertension for both the first and second quartiles.

When the associations were computed for changes in standard categories of BMI (Table 4), and in comparison to adolescents in the category thin/normal at both ages, those who shifted to the overweight-obese category presented the highest risk of incident hypertension (IRR = 4.74, 95% CI: 2.41–9.31). The risk of those maintaining in the overweight-obese category was 3.34 (2.14–5.18). For changes in WC category, in comparison to those with normal WC at both ages, the highest risk of incident hypertension was found in the adolescents with high WC (≥75th percentile) at both ages (IRR: 3.62, 95% CI: 2.28–5.76), and shifting to the high WC category also increased the risk of hypertension (IRR: 2.47, 95% CI: 0.799–6.16). Adolescents changing from higher to lower BMI and WC categories presented risk of hypertension comparable to those maintaining in the normal category.

3.1. Sensitivity analyses

Further adjustment for sociodemographic and behavioural factors (parental education, dietary intake, physical activity, smoking and alcohol consumption) was tested, but as results remained unchanged, those data are presented only as supplementary material (Supplementary Table S2). The interaction between baseline adiposity and changes in adiposity was not statistically significant and analysis only in normal weight adolescents at baseline showed similar associations (Supplementary Table S3).

Table 3
Association between changes in adiposity from 13 to 17 years, measured based on the continuous change in adiposity, and incidence of hypertension (n = 1377) – EPITeen cohort, Portugal, 2003–2008.

	Crude IRR (95% CI)	Model 1 IRR (95% CI)	Model 2 IRR (95% CI)
Changes BMI%			
1st Q ('highest decrease')	0.88 (0.52–1.50)	0.56 (0.32–0.97)	0.56 (0.32–0.97)
2nd Q ('decrease')	0.69 (0.39–1.22)	0.63 (0.36–1.12)	0.63 (0.36–1.12)
3rd Q ('stable')	1	1	1
4th Q ('increase')	1.05 (0.63–1.76)	1.11 (0.66–1.84)	1.11 (0.66–1.85)
	p-trend = 0.306	p-trend = 0.005	p-trend = 0.005
Changes WC%			
1st Q ('highest decrease')	0.54 (0.32–0.92)	0.34 (0.19–0.59)	0.33 (0.19–0.58)
2nd Q ('decrease')	0.39 (0.21–0.71)	0.34 (0.19–0.63)	0.34 (0.19–0.63)
3rd Q ('stable')	1	1	1
4th Q ('increase')	0.90 (0.56–1.44)	0.98 (0.61–1.58)	0.98 (0.61–1.58)
	p-trend = 0.006	p-trend < 0.001	p-trend < 0.001

Model 1: adjusted for adiposity levels at 13 years; Model 2: model 1 + sex and family history of hypertension.
BMI%: body mass index percentage; IRR: incidence rate ratio; WC%: waist circumference percentage.

Table 4
Association of changes in BMI category and in WC category between 13 and 17 years with incidence of hypertension (n = 1377) – EPITeen cohort, Portugal, 2003–2008.

	Crude IRR (95% CI)	Model 3 IRR (95% CI)
Changes in BMI category[a]		
13 y/17 y		
Normal/normal	1	1
Overweight-obese/normal	1.11 (0.51–2.43)	1.10 (0.50–2.42)
Normal/overweight-obese	4.75 (2.42–9.30)	4.74 (2.41–9.31)
Overweight-obese/overweight-obese	3.34 (2.16–5.17)	3.34 (2.14–5.18)
	p-trend < 0.001	p-trend < 0.001
Changes in WC category[b]		
13 y/17 y		
Normal/normal	1	1
High/normal	1.25 (0.68–2.27)	1.24 (0.68–2.26)
Normal/high	2.51 (1.01–6.24)	2.47 (0.99–6.16)
High/high	3.63 (2.30–5.75)	3.62 (2.28–5.76)
	p-trend < 0.001	p-trend < 0.001

Model 3: adjusted for sex and family history of hypertension.
BMI: body mass index; WC: waist circumference.
[a] BMI classified according to the CDC Growth Charts (Kuczmarski et al., 2002).
[b] Waist circumference classified according to percentiles for European-American children and adolescents (Fernandez et al., 2004); high WC corresponds to values ≥75th percentile.

Sex-interaction terms were not statistically significant in the models evaluating the association between changes in adiposity and incidence of hypertension.

4. Discussion

Results from our prospective observational study showed that changes in indicators of total and central adiposity during adolescence had a strong effect on blood pressure. Decreases in adiposity were associated with lower systolic blood pressure at 17 years of age and lower risk of hypertension, and this risk reduction was present in both sexes, and even in normal weight adolescents. Additionally, the analysis of changes in adiposity category showed that adolescents changing from higher to lower BMI and WC categories presented risk of hypertension comparable to those maintaining in the normal category.

4.1. Methodological considerations

While changes in BMI in adulthood can be measured as the difference in the BMI raw values between two ages, the use of BMI in adolescence raises methodological problems due to increases in height in this stage of life. In our study, we calculated BMI percentage which is the percentage difference from median BMI from the reference population (Kuczmarski et al., 2002). Sex- and age-specific BMI z-scores according to a reference population are often used to evaluate changes in adiposity, however, studies have shown that BMI percentage is a better alternative to measure changes in adiposity in children (Cole et al., 2005; Kakinami et al., 2014).

Hypertension was defined according to the mean values of two readings of blood pressure obtained on a single occasion, and not on at least 3 separate occasions as recommended in clinical practice (Anon, 2004), which may have resulted in the overestimation of hypertension incidence. Nevertheless, overestimation due to white-coat effect was minimized in our study by the assessment of blood pressure at school, in adolescents' usual environment, and adolescents were already familiar with the study and its procedures, since they were participating for the second time in the project. Nevertheless, if prevalence/incidence of hypertension is overestimated, the association between changes in adiposity and risk of hypertension is likely to be underestimated, assuming that misclassification of hypertension is non-differential according to the exposure.

The main strengths of our study are the population-based nature and the prospective design, with the assessment of different confounder variables. Participants from our cohort are representative of 13-year-old adolescents from Porto, since they were recruited at schools within ages of compulsory education, and a high participation was registered (77.5%). Although we excluded some participants due to losses to follow-up or missing information, exclusions were non-differential for the main variables under study among the eligible participants, supporting the external validity of our findings. The population-based nature of our study allowed to estimate the effect of decreases in adiposity not related to specific interventions in high-risk groups, but rather decreases observed in a population-based sample (Rose, 1985), and therefore contributes for the quantification of the potential gains of interventions at the population level.

4.2. Interpretation of findings

We found a high incidence of hypertension between 13 and 17 years of age in our sample, higher than those reported in studies evaluating incidence of hypertension at similar ages in other countries (Parker et al., 2016; Obarzanek et al., 2010). However, it is consistent with previous studies showing high incidence and higher mean levels of blood pressure in the Portuguese population in comparison with other European countries (Pereira et al., 2012; Macedo et al., 2005; Danaei et al., 2011).

Our results suggest that for a given BMI at early adolescence, subsequent decreases in BMI, even in a short period of time, were associated with lower SBP at 17 years, and lower risk of hypertension. To our knowledge there are no studies on blood pressure using a directly comparable methodology in terms of changes in BMI percentage. While we measured continuous changes in adiposity and then separately addressed the effect of increasing or decreasing adiposity, other observational studies evaluated changes in adiposity as a continuous variable focusing only on the effect of increases in adiposity (Maximova et al., 2010; Lawlor et al., 2010). These studies have shown that increases in adiposity during adolescence were associated with an increase in SBP (Maximova et al., 2010), or with increased risk of high SBP (Lawlor et al., 2010), but the effect of decreases in adiposity were not quantified. Therefore, our approach extends the previous evidence showing that there is potential benefit of decreases in adiposity for hypertension prevention, even in normal weight individuals. This is in

accordance to previous studies showing that, even within normal ranges, adiposity is positively associated with risk of health outcomes, such as cardiovascular and all-cause mortality (Twig et al., 2016).

On the other hand, in our study the increase in BMI/WC in this period was associated with increased incidence of hypertension, although statistical significance was not reached. The lack of significance may be explained by the fact that most participants in the category of increases in adiposity were normal weight or thin at 13 years, and were still in the same category at 17 years. Results using continuous SBP as outcome showed that the increase in adiposity was significantly associated with higher SBP at 17 years.

The analysis of changes in adiposity indicators based on continuous quantity adds information in relation to changes in categories of adiposity, since it evaluates the effect of any change in adiposity, while changes in BMI category are dependent on the initial position of the subject's BMI in relation to the cut-off. However, as the two approaches may be complementary, we also analysed the effect of changes in adiposity categories on blood pressure and our results are in accordance to those from two other studies in adolescents (Lawlor et al., 2010; Parker et al., 2016). Data from a retrospective cohort of subjects from three health systems in the U.S. showed that adolescents (12–17 years) who shifted to or maintained the obesity category had three times increased risk of incident hypertension over a median of 3.1 years of follow-up, in comparison to those maintaining a normal weight (Parker et al., 2016). These results are of similar magnitude of those found in our study, although we have evaluated changes from normal BMI to overweight and obesity combined. Lawlor et al. (2010) evaluated changes in BMI category from 9–12 to 15–16 years in the ALSPAC cohort and showed that in comparison to adolescents who were normal weight at both ages, those increasing to or maintaining in overweight/obesity category presented the highest odds of high systolic blood pressure at 15–16 years. The magnitude of the association was lower, in comparison to our results, but while we evaluated incident hypertension, in that study the outcome was defined as high SBP ($\geq$130 mmHg) (Lawlor et al., 2010). In our study, we also found that adolescents decreasing from overweight/obese category to normal BMI presented risk of hypertension comparable to adolescents maintaining in the normal category, which is in accordance to the findings in the U.S. adolescents (Parker et al., 2016) and to those found in the ALSPAC cohort for girls (Lawlor et al., 2010). Data from the ALSPAC cohort showed that boys in that category, although decreasing BMI, presented higher risk of high SBP, in comparison to those maintaining in the normal category, but lower than the risk of participants that were overweight/obese at both ages. These sex-differences were not found in our study, and are also not supported by other studies, using either the continuous approach or changes in categories (Maximova et al., 2010; Tybor et al., 2011; Parker et al., 2016).

To the best of our knowledge no other studies have addressed changes in WC category, but two studies addressing the effect of increases in continuous WC and in BMI reported results similar for both measures (Maximova et al., 2010; Lawlor et al., 2010), while another study found that WC had additional potential for the prediction of changes in blood pressure during adolescence, in comparison to BMI (Tybor et al., 2011). Therefore, evidence is still inconsistent regarding the superiority of WC over BMI for the prediction of health risks, as described also in adults (Bosy-Westphal et al., 2006; Carmienke et al., 2013; Janssen et al., 2004), and further studies are warranted to clarify if the effect of central adiposity on cardiometabolic factors is similar to total adiposity.

Our study suggests that adolescence, specifically the period between 13 and 17 years, may be a sensitive period for changes in adiposity with relevant impact on blood pressure. Although adiposity at early adolescence is particularly relevant for future blood pressure, decreases in BMI and WC throughout adolescence, even in normal weight individuals, are likely to reduce the risk of hypertension, and therefore the future risk of cardiovascular disease. In addition to strategies for childhood obesity prevention, interventions on adolescent adiposity should take advantage of changes in adiposity occurring at this stage of life.

Conflict of interest

The authors declare no conflict of interest.

Funding

This study was funded by FEDER through the Operational Programme Competitiveness and Internationalization and national funding from the Foundation for Science and Technology – FCT (Portuguese Ministry of Science, Technology and Higher Education) (POCI-01- 0145-FEDER- 016829), under the project “A longitudinal approach to metabolically healthy obesity: from inflammation to cardiovascular risk profile“(Ref. FCT PTDC/DTP-EPI/6506/2014) and the Unidade de Investigação em Epidemiologia - Instituto de Saúde Pública da Universidade do Porto (EPIUnit) (POCI-01- 0145-FEDER-006862; Ref. UID/DTP/04750/2013). Individual grants to JA (SFRH/BD/78153/2011) and to HB (SFRH/BSAB/113778/2015) by the Portuguese Foundation for Science and Technology – FCT are gratefully acknowledged.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ypmed.2018.12.017.

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