Original Article

Longitudinal changes in blood pressure during weight loss and regain of weight in obese boys and girls

Jens-Christian Holm[a,b,c,d], Michael Gamborg[b], Mette Neland[e], Leigh Ward[f], Steen Gammeltoft[c], Berit L. Heitmann[b], Thorkild I.A. Sørensen[b], and Karsten K. Ibsen[d]

Objective: To investigate blood pressure (BP) in relation to changes in body mass index (BMI) in obese children during weight loss and subsequent weight regain.

Design: A longitudinal study of obese boys and girls investigated through a 12-week weight loss intervention with follow-up investigations spanning 28 months. Results shown are from baseline; day 14, 33, and 82 during weight loss; and at months 10, 16 and 28 during follow-up.

Patients: One hundred and fifteen obese children, 53 boys and 62 girls (8–15 years) with a median BMI standard deviation score (SDS) at baseline of 2.78 in boys, and 2.70 in girls. Ninety children completed the weight loss programme and 68 children entered the follow-up programme.

Methods: Height, weight, systolic blood pressure (SBP), and diastolic BP (DBP) were recorded and analysed using a general linear mixed model.

Results: Fifty-one percent of the obese children were pre or hypertensive at baseline. Both DBP and SBP declined significantly with weight loss, but a divergent response was found in the timing of the rebound in hypertension during the weight regain phase, that is DBP increased during weight regain, whereas SBP remained lower than baseline during 28 months of continuous weight regain.

Conclusion: The effect of weight reduction upon obesity-associated hypertension is noticeable and suggests the importance of an intensified childhood obesity treatment strategy in order to reduce the burden of future cardiovascular disease.

Keywords: blood pressure, BMI SDS, child, longitudinal study, obesity, weight gain, weight loss

Abbreviations: BMI SDS, body mass index standard deviation scores; BP, blood pressure; CI, confidence interval; DBP SDS, diastolic blood pressure standard deviations scores; SBP SDS, systolic blood pressure standard deviations scores

INTRODUCTION

The term obesity-hypertension acknowledges the co-pandemic of obesity and hypertension [1], in which obesity contributes to the development of hypertension in approximately 78% of men and 65% of women [2]. The Bogalusa Heart Study showed that 13% of children have increased systolic blood pressure (SBP) and that 9% have increased diastolic BP (DBP) [3], but these examinations were carried out decades ago. Thus, current childhood obesity-associated hypertension may be underestimated, since the prevalence of childhood obesity has increased significantly in recent years [4]. Recent population-based studies that have measured BP one to three times at a single visit have reported prevalence of hypertension between 4.5 and 47.6% [5,6]. Overweight and obesity in childhood is associated with increase in the incidence of cardiovascular disease (CVD) events later in adulthood [7], and obesity and its accompanying CVD complications is calculated to reduce the estimated life expectancy by 2–5 years around year 2050 in the USA, an effect comparable with the mortality from all cancers combined [8]. Such a mortality effect is predominantly attributable to hypertension and a recent large study in adults showed that especially the vascular consequences of obesity were to be held accountable for the increased morbidity and mortality seen in adults [9].

Since elevated BP is an important marker of potential later CVD, it is important to know how BP changes with concomitant changes in body mass index (BMI), and whether BP exhibits tracking over time and especially so during perturbations in weight. Tracking of BP would mean that SBP and or DBP in a group of individuals maintain a similar inter-individual rank order in the distribution in repeated measurements of BP over time. Recent, a meta-analysis of 29 independent studies on 27 820 patients showed tracking of BP from childhood into

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[a]The Children's Obesity Clinic, Department of Paediatrics, Holbæk University Hospital, Holbæk, [b]Institute of Preventive Medicine, Copenhagen University Hospital, Copenhagen, [c]Department of Clinical Biochemistry, Copenhagen University Hospital Glostrup, Glostrup, [d]Department of Paediatrics, Copenhagen University Hospital, Glostrup, [e]H.C. Andersen Children's Hospital, Odense University Hospital, Odense C, Denmark and [f]School of Chemistry and Molecular Biosciences, The University of Queensland, Brisbane, Australia

Correspondence to Jens-Christian Holm, MD, Paediatrician, Consultant, Associate Professor, PhD, Head of The Children's Obesity Clinic/The Danish Childhood Obesity Biobank, Department of Paediatrics, The University Hospital Holbæk, Smedelundsgade 60, 4300 Holbæk, Denmark. Tel: +45 59484208; fax: +45 59484209; e-mail: jhom@regionsjaelland.dk

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adolescence and recommended regular BP testing in children with normal BP measurements in order to identify hypertensive children earlier [10]. In those obese children or adolescents with hypertension, the recommendation is weight loss [11]. If tracking of BP persists irrespective of concomitant changes in weight over time, measurement of BP may be a useful tool to identify obese children of risk for future CVDs.

In the present longitudinal study, concomitant changes of BP and weight were measured in obese children in order to evaluate the degree of elevated BP associated with baseline obesity and the relationship between BP and obesity during weight loss and regain of weight. Further, it is investigated whether SBP and DBP exhibit tracking despite perturbations in weight.

METHODS

Design

Groups of obese children were examined on day 1 (baseline), 14, 33, and 82 during the weight loss programme, and at month 10, 16, and 28 during follow-up. The weight loss programme has been described in detail elsewhere [12,13]. Briefly, the institution 'Julemærkehjemmet', Skælskør, Denmark offers a 3-month precisely planned and evaluated weight-reduction regimen consisting of a restricted low-fat diet with a fixed level of energy intake at 6500–7000 kJ per day combined with an obligatory physical activity programme. Follow-up examinations were carried out at the Paediatric Department at the University Hospital in Glostrup. During follow-up no planned interventions were performed.

Examinations included interviews and measurement of weight, height, and BP. During the study, 232 children were identified as eligible to participate with 115 agreeing to do so. Ninety children completed the weight loss programme, 68 engaged in follow-up, and 44 children completed all examinations in the follow-up programme. Data regarding baseline characteristics and development of BMI standard deviation scores (SDS) during weight loss and regain have previously been published [12,13].

The Scientific Ethical Committee of Copenhagen approved the study, and written informed consent was obtained from all participants, as well as from their parents according to the Helsinki Declaration.

Procedures

Height was measured by stadiometer to the nearest 5 mm. Weight was measured to the nearest 0.1 kg on a SECA Delta Scale, model 707, S&W.

Body mass index was calculated as weight divided by height squared. BMI SDS was calculated by the LMS method where the optimal power to obtain normality is calculated for each of a series of age groups and the trend summarized by a smooth (L) curve. Trends in the mean (M) and coefficient of variation (S) are similarly smoothed. The resulting L, M and S curves contain the information to draw any centile curve comparing the calculated BMI with the distribution of BMI in a representative Danish population of the same age and sex [14] in order to evaluate the degree of overweight and obesity irrespective of sex and age during growth and development.

Blood pressure was measured manually on the right arm by a mercury sphygmomanometer. Three measurements were recorded in the supine position after a 5-min rest. The average of three recordings was used for analysis. SBP was read at the first Korotkoff sound and DBP at the disappearance of the pulse sound (phase V). On the basis of sex, height and height-specific BP percentiles [5], the measured SBP and DBP were compared with the distribution of BP in an American reference population with the same sex and height from where BP SDS were calculated in correspondence with the guideline of the European Society of Hypertension [11].

Statistical methods

The longitudinal development of BP during weight loss and weight regain and the association between BMI SDS and BP SDS was modelled using a generalized linear mixed model [15]. The mean value of BP SDS is modelled as a function of time, both unadjusted and adjusted for BMI SDS.

In order to minimize bias originating from the missing observations during the longitudinal analysis, we chose an unstructured model for the covariance [16].

Children were assessed as having elevated BP by the proportion of children who exceeded the age, sex, and height-specific 90th, 95th, and 99th percentiles in the BP charts, respectively [5].

Tracking was investigated using partial correlation coefficients between the first measures of SBP and DBP and later measures of BP in the same child adjusted for BMI SDS at both measurements.

RESULTS

One hundred and fifteen children (62 girls) with a median age of 12.1 years (range 8–15 years) and a median weight of 63.2 kg in boys and 67.8 kg in girls were enrolled in a weight loss programme; 90 children completed the programme, as 25 children were excluded, primarily due to refusal of intravenous sampling. Of the 68 children included in the follow-up programme, 44 children completed follow-up examinations, yielding retention rates of 78% during weight loss and 65% during follow-up. Children dropping out were not different with respect to baseline age, but those dropping out (BMI SDS of 2.91 ± 0.60) were a little heavier than those that remained (BMI SDS of 2.62 ± 0.57) in the study ($P = 0.023$) [12].

At baseline, the median BMI SDS was 2.79 in boys and 2.70 in girls. The median BMI SDS was reduced by 20% in boys, and by 19% in girls [12]. Nearly all children were unable to sustain their lower body weight or BMI during the 28 months of follow-up. Overall, during weight regain BMI SDS increased relative to end weight loss weight by 31% in boys and by 32% in girls, respectively [13].

At the time of enrolment the mean (±SD) SBP and DBP in boys were SBP 122.9 ± 12.4 and DBP 79.9 ± 9.9, respectively, and in girls, SBP 120.6 ± 13.8 and DBP 80.8 ± 11.2, respectively.

Table 1 shows BP defined as percentage of children with BP within the BP percentiles 90–95, 95–99, and above the

TABLE 1. The degree of hypertension in obese children as illustrated with relative proportions of children with BP SDS within the 90–95 percentiles (prehypertension), within the 95–99 percentiles (stage 1 hypertension) and with BP SDS above the 99th BP percentile (stage 2 hypertension) during weight loss and subsequent weight regain in boys and girls

	Days				Months		
	1	14	33	82	10	16	28
Boys							
N	56	46	44	42	29	26	24
DBP							
% in 90–95	10.7	13.0	4.6	2.4	10.3	11.5	16.7
% in 95–99	25.0	8.7	11.4	9.5	6.9	11.5	4.2
% >99	17.9	2.2	0	0	0	7.7	12.5
SBP							
% in 90–95	12.5	10.9	11.4	14.6	3.5	7.7	4.2
% in 95–99	16.1	10.9	4.5	4.8	6.9	0	12.5
% >99	19.6	4.4	0	0	0	0	8.3
Girls							
N	61	52	49	47	33	33	22
DBP							
% in 90–95	19.7	13.5	10.2	8.5	15.2	15.2	31.8
% in 95–99	24.6	11.6	12.2	19.2	12.1	6.1	18.2
% >99	13.1	5.8	4.1	2.1	3.0	6.1	0
SBP							
% in 90–95	13.1	9.6	10.2	2.1	9.1	3.0	18.2
% in 95–99	19.7	11.5	8.2	8.5	3.0	3.0	9.1
% >99	16.4	13.5	6.1	0	3.0	0	4.6

BMI SDS, body mass index standard deviation scores; DBP SDS, diastolic blood pressure standard deviations scores; prehypertension (% in 90–95), percentage of children within the BP percentiles 90–95; SBP SDS, systolic blood pressure standard deviations scores, stage 1 hypertension (% in 95–99); percentage of children within the BP percentiles 95–99, stage 2 hypertension (% >99); percentage of children with a BP above the 99th BP percentile.

99th percentile of the American reference population values. Approximately, 50% of all obese children had a median BP above the 90th percentile (BP SDS above 1.28) in both sexes at baseline suggesting prehypertension or grade 1 or 2 hypertension (Table 1).

Both systolic and diastolic pressures decreased continuously during weight loss in boys and girls and were almost normalized during intervention. During weight regain, a divergent development of the SBP and DBP was observed. During the first 16 months of weight regain, BMI SDS increased 0.50 in both boys and girls, but the SBP remained low in both sexes. The lowest SBP was recorded at 16 months when the mean BP SDS was 0.0 and 0.1 in boys and girls, respectively. In fact, it was not until the last visit at 28 months, that the SBP increased again at a time when the children had regained weight continuously in more than 2 years to a level exceeding baseline weight. However, at this stage SBP had still not reached the degree of hypertension seen at baseline. The DBP, on the contrary, started to rise along with increases in the degree of obesity as soon as the children were discharged from the weight loss programme.

Figure 1 shows the development of BMI SDS, DBP and SBP SDS during weight loss and weight regain in boys and girls, both with and without adjustment of BP with BMI. However, multivariate regression analysis of changes in SBP and DBP with concomitant changes in BMI SDS showed a positive association with BMI SDS, that is a 1 SD increase in BMI SDS was associated with a 0.41 SD higher SBP SDS [confidence interval (CI) 0.19–0.62, $P = 0.0004$] in boys and a 0.42 SD higher SBP SDS (CI 0.21–0.64, $P = 0.0003$) in girls. The relationship between DBP and BMI SDS was weak, a 1 SD increase in BMI SDS being associated with a 0.18 SD higher SBP SDS (CI 0.02–0.34, $P = 0.03$) in boys and a 0.14 SD higher SBP SDS (CI −0.04 to 0.32, $P = 0.14$) in girls.

Table 2 shows correlation coefficients between BMI SDS and SBP SDS and between BMI SDS and DBP SDS during weight loss and regain in boys and girls. Significant correlations were seen at baseline and at the measurement at 14 days in girls.

Table 3 shows partial correlation coefficients of repeated measures of SBP and DBP in boys and girls, in which the baseline measurement is compared with later measurements adjusted for BMI. These analyses did not reveal tracking of SBP and DBP in boys and girls during weight loss and regain.

DISCUSSION

The present longitudinal study shows that obesity-related hypertension is treatable by weight reduction and that there exists a discrepancy between the development of the SBP and DBP during weight regain in children. Whereas the mean DBP rose, as soon as the children were discharged from the weight loss programme, the mean SBP continued to remain low during follow-up despite the children regaining weight during this entire period. That SBP remained low beyond the weight regain phase was a surprising finding, which may suggest that it is not the increased body weight *per se* that determines the SBP in children during weight regain. The finding of a divergent SBP and DBP development during weight regain in children indicates a more complicated effect of weight changes with a prolonged beneficial effect of weight loss on SBP, despite ongoing weight regain. Therefore, other factors like conduit and

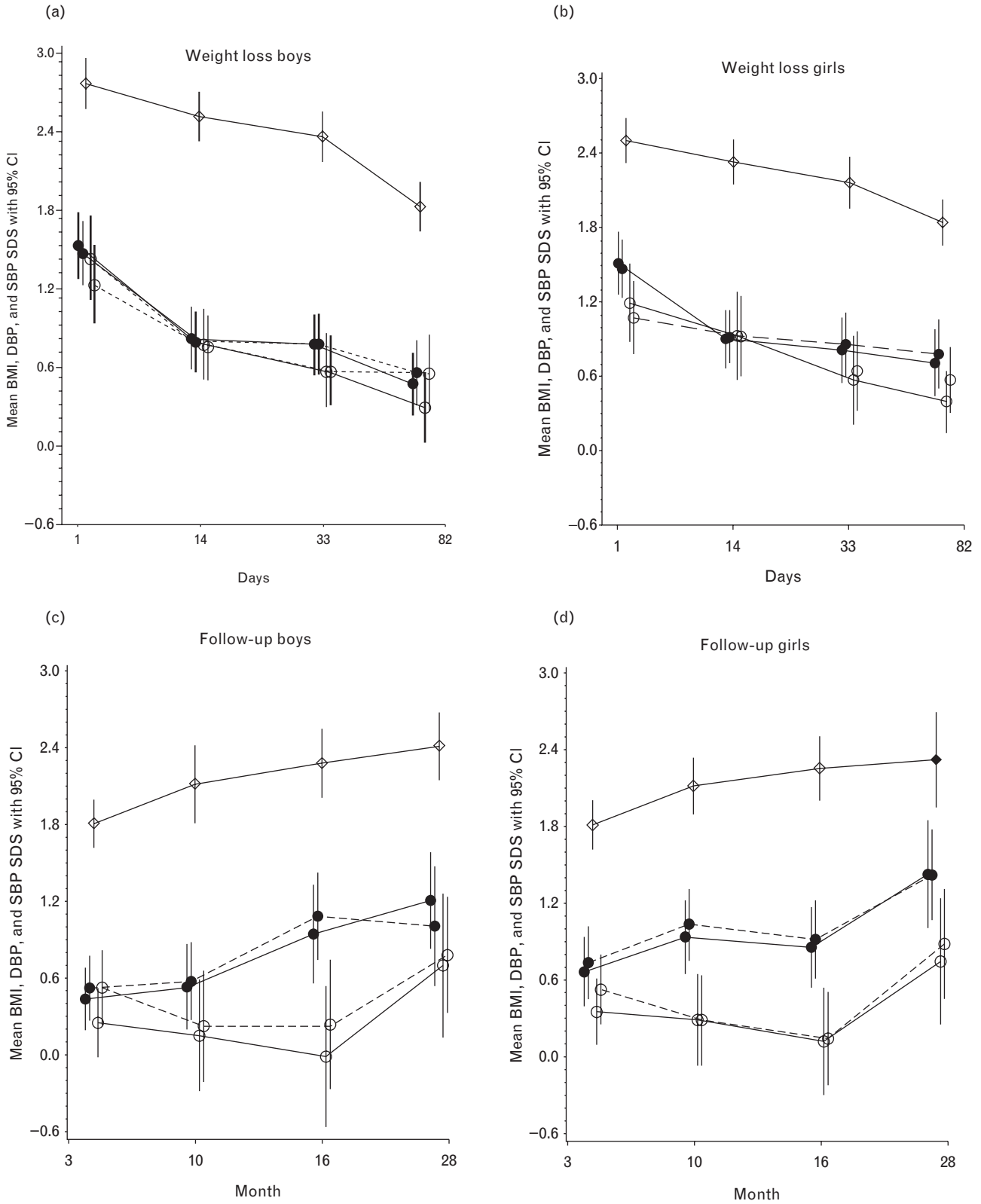

FIGURE 1 Changes in BMI SDS, SBP and DBP SDS during weight loss in boys (a) and girls (b) and during weight regain in boys (c) and girls (d). SBP and DBP SDS are also shown after multiple regression analysis showing only subtle changes in both systolic and diastolic BP after adjustment for concomitant changes of BMI SDS. Adjusted BP estimates were corrected for concurrent BMI SDS by a generalized linear mixed regression model. Bars indicate standard deviations. BMI SDS, body mass index standard deviation scores; DBP SDS, diastolic blood pressure standard deviations scores; SBP SDS, systolic blood pressure standard deviations scores. ◇, BMI; ●, DBP; ○, SBP; ——, crude; - - -, BMI adjusted.

TABLE 2. Correlation coefficients between BMI SDS and SBP SDS and between BMI SDS and DBP SDS with associated *P* values

	Days				Months		
	1	14	33	82	10	16	28
Boys							
N	52	45	34	42	25	23	19
BMI SDS and SBP SDS	*0.54*	*0.31*	0.12	0.16	−0.01	0.26	0.29
P	*	*0.04*	0.50	0.30	0.96	0.22	0.22
BMI SDS and DBP SDS	*0.46*	0.06	−0.03	0.19	−0.23	0.06	−0.09
P	*0.0005*	0.7	0.86	0.23	0.27	0.78	0.72
Girls							
N	58	52	44	46	30	30	20
BMI SDS and SBP SDS	*0.31*	*0.35*	*0.41*	0.20	0.05	*0.43*	−0.14
P	*0.02*	*0.01*	*0.006*	0.18	0.77	*0.02*	0.56
BMI SDS and DBP SDS	*0.39*	*0.32*	0.04	−0.03	−0.22	0.32	−0.31
P	*0.002*	*0.02*	0.78	0.86	0.25	0.09	0.18

BMI SDS, body mass index standard deviation scores; DBP SDS, diastolic blood pressure standard deviations scores; SBP SDS, systolic blood pressure standard deviations scores.
*Implies a *P* value below 0.0001, other significant *P* values are in italics.

resistance artery endothelial function might be of importance [17] in the central arterial stiffening that determines SBP together with cardiac output. In the paediatric group, precise and reliable noninvasive tests for atherosclerosis in youth are not yet fully established, but have the potential to improve our ability to estimate future risk for heart attack and stroke [18].

In the present study, weight loss was an effective treatment for obesity-associated hypertension in children, since BP almost normalized during weight loss. This is in line with previous findings in children and adults in whom weight loss was associated with a decreased prevalence of hypertension [19]. Similarly, BP increased during weight regain in the present study, but did, however, not reach the degree of hypertension seen at baseline even after 28 months of continuous weight regain. These results stress that weight reduction has a beneficial effect upon hypertension not only during weight loss but also into the phase of weight regain. In line with the development of hypertension during weight regain, it has been shown in children that a higher BMI during development is associated with a higher BP [20] and in adults that a 5% weight gain increased the risk of hypertension by 30% in a 4-year period [21].

Hypertension was primarily seen at baseline, although 25% of the children were pre or hypertensive at 2 weeks into the weight loss programme. The degree of hypertension seen at baseline might be due to a white-coat effect. Nevertheless, the rapid weight loss seen after baseline may have reduced hypertension effectively as well as also seen in previous studies [22]. An alternative explanation may be that leptin in the same children has been found to decline rapidly in the first 12 days of weight loss [12], which may result in a decreased stimulation of the sympathetic nervous system and/or decreased renal sodium re-absorption and ameliorated pressure natriuresis, which again may have reduced BP [23].

During the phase of weight regain, the increase in DBP was expected; however, the degree of the diastolic hypertension at baseline was unexpected, since DBP is less pronounced in children [24]. In adults, diastolic hypertension correlates well with the degree of target end-organ damage [25]. In childhood, hypertension is often associated with an increased left-ventricular mass [6] and an increased carotid intima–media thickness [26]. The degree of diastolic hypertension in the present study may indicate the seriousness of obesity-mediated hypertension in these children.

TABLE 3. Partial correlation coefficients between baseline systolic and diastolic BP compared to later measurements of systolic and diastolic BP in the same individual, respectively, during weight loss and follow-up adjusted for BMI SDS and pubertal development

	Days				Months		
Day 1 vs.	1	14	33	81	10	16	28
Boys							
N	52	42	31	39	30	21	17
DBP SDS	1.0	0.28	0.12	−0.09	−0.05	0.37	0.20
P		–	–	–	–	–	–
SBP SDS	1.0	0.14	0.05	0.33	0.19	0.04	0.61
P		–	–	0.04	–	–	0.02
Girls							
N	58	48	42	44	30	30	20
DBP SDS	1.0	0.44	0.22	0.23	0.10	0.16	0.12
P		0.002	–	–	–	–	–
SBP SDS	1.0	0.30	0.26	0.23	−0.08	−0.16	0.61
P		0.04	–	–	–	–	0.007

SBP SDS, systolic blood pressure standard deviations scores; DBP SDS, diastolic blood pressure standard deviations scores; – implies a *P* value above 0.05.
Numbers of children were lower, since the tracking analyses required that the same individuals had two consecutive measures of the same biomarker in each interval.

A high prevalence of hypertension among obese Danish children in the present study was observed. At baseline, approximately half of the children had a SBP and DBP that was greater than the 90th BP percentile given age, height, and sex. Changes in SBP and DBP during weight loss and regain were not altered significantly after adjustment of concomitant changes in BMI SDS over time during weight loss and regain. Further, SBP and DBP exhibited positive correlations with BMI SDS, but only at baseline in boys and in the first two measurements in girls. However, in the multivariate models, SBP exhibited significant associations with BMI SDS over time, whereas the associations between DBP and BMI SDS over time were weak. Altogether, these findings suggest that BP is significantly associated with BMI SDS at baseline, but relatively independent of concomitant changes in BMI SDS during changes in weight. In line with this finding, a study in adults showed that changes in body weight have a great influence on arterial hypertension though independent of the effect of the attained weight [27]. Further, Sjöström *et al.* showed a decline in BP as expected by weight loss following bariatric surgery, but whereas weight reduction had a dramatic effect on the 8-year incidence of diabetes [odds ratio (OR) 0.16, 95% CI 0.07–0.36], it had no effect on the 8-year incidence of hypertension, which again shows a tendency for detachment of BP from concurrent body weight [28]. These findings need replication in prospective childhood obesity-hypertension studies in order to ascertain the beneficial effect of weight loss upon childhood-induced hypertension in later adolescence and adulthood irrespective of BMI over time.

Interestingly, neither SBP nor DBP exhibited tracking during changes in weight in the obese boys and girls in the present study, despite BP having been found to track from childhood to adulthood in a meta-analysis [10]. A lower statistical power due to decreasing number of participants over time in the present study may have resulted in a type 2 error even though the weight loss and regain *per se* may have biased tracking over time as well, since the partial correlation coefficient tracking estimates were adjusted for concomitant changes in BMI SDS.

The present study had some limitations. Despite significant findings, drop-out and resulting attrition of numbers of children participating may have weakened the established relationships and associations between changes in BMI SDS and BP in the present study. Although much effort had been expended to increase retention, those dropping out did not differ in baseline characteristics from those completing the study except that they were a slightly heavier.

Last, the present study did not include detailed individual reports of dietary fat, energy intake, and physical activity, but it would be of interest in future studies to investigate to what extent the relationship between body weight changes and changes in BP is induced by the concomitant changes in these behavioural features and whether they may modify the effect of body weight changes on BP.

In conclusion, weight reduction is effective in reducing the obesity-mediated BP burden. Despite continuous weight regain, SBP remained low during continuous weight regain in obese children, whereas DBP relapsed in alignment with increases in obesity. If a diminished degree of hypertension is maintained over time a decreased cardiovascular risk profile may be attained in these young people, but maintenance of a lowered weight is of primary significance.

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Conflicts of interest

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All authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research project.

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