

PEDIATRIC REVIEW

Childhood obesity and adult cardiovascular disease risk: a systematic review

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Background: Although the relationship between adult obesity and cardiovascular disease (CVD) has been shown, the relationship with childhood obesity remains unclear. Given the evidence of tracking of body mass index (BMI) from childhood to adulthood, this systematic review investigated the independent relationship between childhood BMI and adult CVD risk.

Objective: To investigate the association between childhood BMI and adult CVD risk, and whether the associations observed are independent of adult BMI.

Design: Electronic databases were searched from inception until July 2008 for studies investigating the association between childhood BMI and adult CVD risk. Two investigators independently reviewed studies for eligibility according to inclusion/exclusion criteria, extracted the data and assessed study quality using the Newcastle–Ottawa Scale.

Results: Positive associations between childhood BMI and adult blood pressure or carotid intima-media thickness were generally attenuated once adjusted for adult BMI. Associations between childhood BMI and CVD morbidity/mortality had not been adjusted and do not provide evidence of an independent relationship. Negative associations between childhood BMI and blood pressure were observed in several adjusted data sets.

Conclusions: Little evidence was found to suggest that childhood obesity is an independent risk factor for CVD risk. Instead, the data suggest that relationships observed are dependent on the tracking of BMI from childhood to adulthood. Importantly, evidence suggests that risk of raised blood pressure is highest in those who are at the lower end of the BMI scale in childhood and overweight in adulthood. The findings challenge the widely accepted view that the presence of childhood obesity is an independent risk factor for CVD and that this period should be a priority for public health intervention. Although interventions during childhood may be important in prevention of adult obesity, it is important to avoid the potential for negative consequences when the timing coincides with critical stages of neurological, behavioural and physical development.

International Journal of Obesity (2010) **34**, 18–28; doi:10.1038/ijo.2009.61; published online 12 May 2009

Keywords: childhood; blood pressure; cardiovascular disease

Background

Overweight and obesity are associated with numerous co-morbidities, such as cardiovascular disease (CVD), type 2 diabetes and certain cancers. The rising prevalence of obesity represents a global public health issue, with an estimated 30% of coronary heart disease (CHD) and ischaemic stroke and almost 60% of hypertensive disease in developed countries attributable to excess body mass index (BMI).¹ Of particular concern is the rising prevalence of obesity in children, with 32% of children and adolescents in the

United States at or above the eighty-fifth percentile of the 2000 BMI-for-age growth charts.^{2,3} Similarly in the United Kingdom, 2004 figures show the prevalence of obesity in children aged 5–17 years to be 29%.⁴ Adiposity has been shown to track from childhood into adult life, potentially augmenting the risk associated with adult obesity.^{5,6} This relationship is complex however, with the likelihood of obesity persistence related to gender, the severity of obesity and the age at which it is first present. In addition, the strength of the relationship is dependent on the obesity-defining criteria used.⁷ There is a widely held assumption that childhood obesity is a major risk factor for CVD in adulthood. However, although many studies have shown a positive relationship between childhood obesity and adult CVD risk factors,^{8,9} it remains unclear whether childhood obesity exerts an independent effect on adult cardiovascular health. Some studies suggest quite the opposite, with those

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Received 24 October 2008; revised 9 March 2009; accepted 15 March 2009; published online 12 May 2009

who were thinnest as children and overweight as adults showing the highest adult metabolic risk profile.^{7,10} Therefore, although there is much evidence to suggest that childhood obesity is a moderate risk factor for adult obesity, the independent association with adult CVD risk is less clear.

The lack of clear understanding in this area reflects a wider body of evidence relating to the complex interactions between rates of growth and adiposity at different stages of the lifecourse. Obesity and metabolic risk have been shown to be associated with maternal BMI and nutritional status during pregnancy,¹¹ low and high birth weight,¹² infant feeding practices,¹³ early postnatal growth patterns,¹⁴ rate and age of adiposity rebound¹⁵ and a variety of postnatal environmental factors. None of these factors can be treated as independent, and their segregation for investigative purposes is artificial from a life-course perspective. The interaction between growth patterns and exposures in each period may be central to the development of obesity and metabolic risk, altering the metabolic response to a subsequent obesogenic environment.¹⁶

The aim of the current review was to systematically and critically appraise the available evidence regarding the relationship between childhood obesity and adult CVD risk. The primary objective was to report on the strength of associations observed between childhood obesity and adult CVD risk. The second objective was to investigate whether the effects of childhood obesity are independent of adult BMI status.

Methods

Search strategy and selection criteria

We reviewed literature reporting results from longitudinal studies investigating the association between childhood obesity and adult CVD risk. To select articles, a computerised search of the online electronic databases PubMed (MEDLINE) and ISI Web of Science from inception up to July 2008 was performed, using the terms 'childhood', 'adult' and 'obesity'.

Eligibility of the articles was initially ascertained by screening the titles, to enable exclusion of non-relevant studies and to remove duplicates of articles identified on both databases. The abstracts and then full texts of the remaining articles were screened according to the inclusion/exclusion criteria outlined below. Additional studies were identified from the reference lists within articles meeting the selection criteria.

The inclusion criteria were:

- (1) Childhood measures of BMI at one or more ages of childhood (0–12 years) or adolescence (13–18 years). All measurements were taken by health professionals or trained investigators.
- (2) Childhood BMI status calculated using US Center for Disease Control (CDC) percentile charts³ or International Obesity Task Force charts (IOTF),¹⁷ and childhood

overweight and obese defined as within those criterion (CDC: >eighty-fifth centile = at risk of overweight, >ninety-fifth centile = overweight; IOTF percentiles track back from World Health Organisation Adult Guidelines¹⁸ of $\geq 25 \text{ kg/m}^2$ overweight and ≥ 30 obese).

OR

Childhood BMI status treated as a continuous variable and association with adult outcome assessed by regression or correlation.

- (3) Adult overweight and obese defined according to World Health Organisation Guidelines¹⁸ as overweight when $\text{BMI} \geq 25 \text{ kg/m}^2$ and obese when $\text{BMI} \geq 30 \text{ kg/m}^2$.
 - (4) One or more biomarkers of CVD risk measured at one or more ages in adulthood (defined as >18 years), for example, blood pressure, carotid intima-media thickness (CIMT). All measurements were taken by health professionals or trained investigators.
- OR
- CVD outcomes/cause of death extracted from secure registers.
- (5) Studies carried out in westernised, developed countries.
 - (6) Articles in English language.

The exclusion criteria were:

- (1) Studies where participants were part of an obesity intervention/health promotion programme.
- (2) Studies where the individuals involved were all part of a selected group, for example, childhood cancer survivors, preterm babies, diabetics and so on.
- (3) Studies in which exposure or outcome had been self reported.
- (4) Childhood or adult overweight/obese defined using arbitrary cut-off points.
- (5) Reviews, rather than original data.

Two investigators (LJL and SM) independently reviewed studies for eligibility according to the criteria above. Agreement was good ($\kappa = 99\%$) and any differences were agreed by consensus. The selection process and number of articles excluded at each stage of this process are shown in Figure 1.

Data extraction

Where childhood BMI had been treated as a continuous variable, regression or correlation coefficients were extracted together with the statistical significance of the associations (where provided). Where childhood BMI had been categorised according to criteria for overweight and obesity, hazard ratios or relative risks and confidence intervals (CIs) were extracted together with statistical significance of the effect (where provided). These data are summarised in Table 1.

Quality assessment

The key aspects of study quality specific to this systematic review were assessed during initial paper screening and selection.

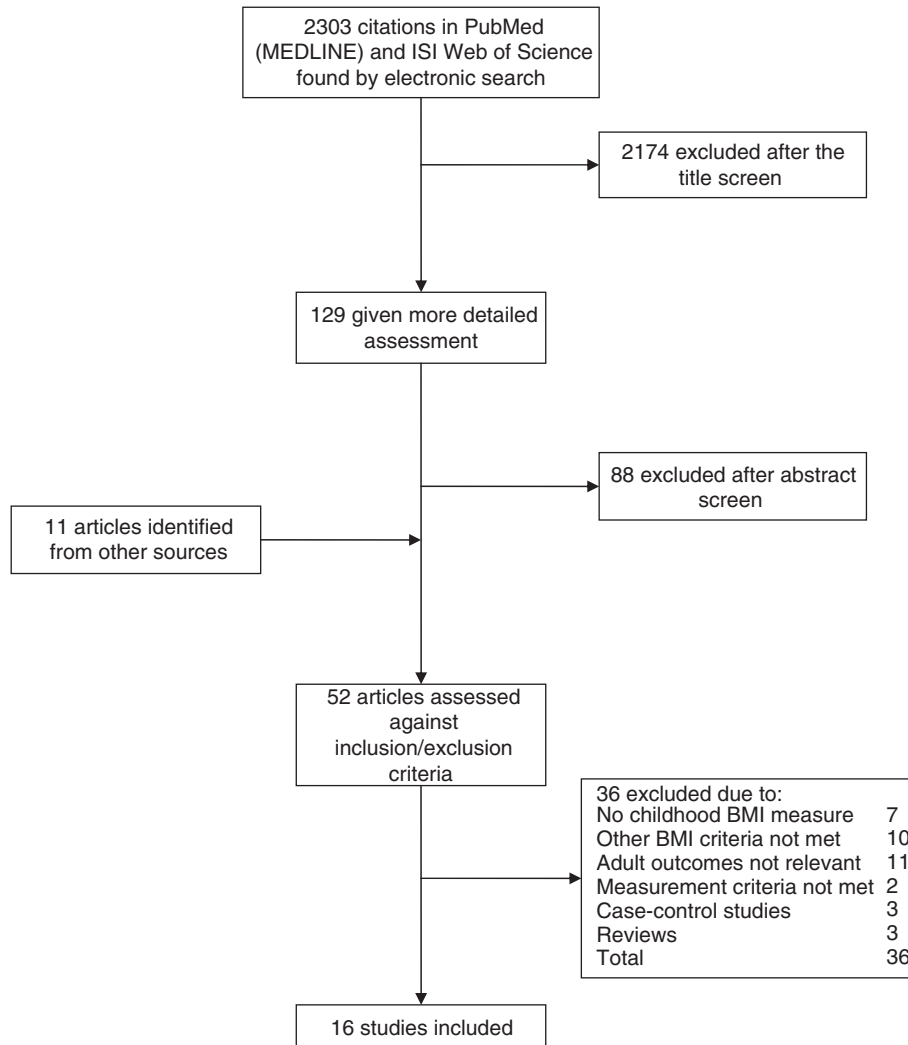


Figure 1 Flowchart of the search and selection process.

For inclusion in the review, studies had to fulfil the following qualitative criteria relating to study design and methodology:

- (1) Childhood exposure and adult outcomes measured in the same individuals, that is, prospective or historical follow-up and case-control designs,
- (2) Exposures and outcomes measured by trained investigators or health professionals or extracted from secure records,
- (3) Where childhood BMI was categorised into weight categories, CDC³ and IOTF¹⁷ thresholds for overweight and obesity were used.

The Newcastle–Ottawa Scale (Table 2) was then used to assess the quality of studies, which passed the defined criteria for inclusion, based on recommendations by the Cochrane Non-Randomised Studies Methods Working Group and two reviews

on the subject of epidemiological quality assessment.^{19,20} Details of the scales can be found at http://www.ohri.ca/programs/clinical_epidemiology/oxford.htm. This scale is designed to assess cohort or case-control studies on the basis of: (1) Selection of cohort or cases/controls; (2) Comparability of cohorts or cases/controls; (3) Assessment of exposure and outcome. High quality characteristics within each of these items were awarded a star, up to a maximum of four stars for selection, two stars for comparability and three stars for assessment. This assessment tool avoids the reporting of summary scores, which have been shown to be unreliable and difficult to interpret,²⁰ and is designed specifically for non-randomised studies. Two investigators (LJL and SM) independently assessed study quality according to the criteria in Table 2. Agreement was good ($\kappa = 93 \cdot 8\%$) and differences were agreed by consensus. Results from the quality assessment are summarised in Table 3.

Table 1 Characteristics of the selected studies grouped by outcome measurement

Reference	Childhood age	Adult age	Population	n	Tracking of BMI	Effect Size	Effect of adjusting for adult BMI
<i>Blood pressure</i>							
Burke et al. ²²	9, 12, 15, 18	25	Males and females in Australia born 1976	600	r = 0.575–0.824***	Duration of overweight/obese was not a predictor of systolic or diastolic blood pressure	N/A
Field et al. ²¹	8–15	18–26	Males and females in Boston, USA born 1963–1970	286	Observed but data not shown	Males (n = 130) SBP r = +0.5 mm Hg per BMI unit. Females SBP–NS DBP–NS both males and females Change in BMI–NS (data not shown) OR for hypertension as young adult compared with <seventy-fifth centile: >eighty-fifth percentile–OR = 5.1 (95% CI 1.4–18.1) SBP r = +0.08***, and DBP r = +0.09***	Not adjusted Not adjusted Not adjusted OR = 5.1 but authors state 'CIs slightly wider' –data not shown SBP r = –0.07***, and DBP r = –0.05
Freedman et al. ³²	5–17	18–37	Males and females in Louisiana, USA born 1959–1968; BHS	2617	r = 0.58	Men–NS Women: SBP r = –1.29* mm Hg per BMI unit at age 2, and r = +1.45* mm Hg per s.d. change in body size from age 7 to 15. All other ages NS.	Authors state 'Smaller effects, but still significant' (Data not shown).
Hardy et al. ²³	2, 4, 7, 15	43	Men and women in GB, born 1946	3157	Not calculated	SBP r = +0.14 to 0.38* for childhood BMI SBP r = +0.16 to 0.44* for change in BMI DBP r = +0.10 to 0.34* for childhood BMI for some ages, but not all DBP r from +0.12 to 0.27* for change in BMI	Not adjusted Not adjusted
Lauer and Clarke ¹⁰	7–18	20–30	Males and females, Iowa, USA, born 1950–1960s; MS	2445	r = 0.45 – 0.74*	SBP r = +1.1 mm Hg per 1 s.d. increase in BMI (age 7), +2.1 (age 11) and +3.1 (age 16) DBP r = +0.9 mm Hg per 1 s.d. increase in BMI (age 7), +1.6 (age 11) and +2.1 (age 16)	Not adjusted
Li et al. ³³	7, 11, 16	45	Males and females in GB, born 1958	9297	Observed but data not shown	SBP r = +0.16*** (BMI at age 7–12) and SBP r = +0.18*** (BMI at age 13–18) DBP–data not reported	Not adjusted
Sinaiko et al. ⁹	7–18	23	Males and females in Minneapolis, USA born 1970–1971 MCCBPS	679	r = 0.612***	Men–NS Women–NS	Men–NS Women–NS at age 13 r = –0.15 and –0.16 for SBP and DBP at age 9
Wright et al. ⁷	9, 13	50	Males and females in Newcastle, UK born 1947 NTFS	412	r = 0.24–0.39		
<i>Carotid intima-media thickness</i>							
Freedman et al. ⁸	4–18	33 ± 3	Males and females in Louisiana, USA born 1959–1968; BHS	513	(r = 0.58 observed in 2001 BHS study)	Age 11–14 r = +0.15**, 15–18 r = +0.22*** <11 was NS But no significant differences in mean CIMT in adults who were non-obese, regardless of their childhood BMI.	+ve association, but magnitude reduced (data not shown)
Freedman et al. ³¹	2–14	23–42	Males and females in Louisiana, USA born 1959–1968; BHS	1142	(r = 0.58 observed in 2001 BHS study)	Initial BMI r = +0.13*** Cumulative BMI r = +0.15***	Not adjusted r = +0.08**
Juonala et al. ²⁵	3, 6, 9, 12, 15, 18	24–39	Males and females in Finland, born 1962–1977 YFS	2260	r = 0.30–0.65***	NS at ages 3, 6, 9 or 15 Age 12, r = +0.18***, Age 18, r = +0.12*	NS
Oren et al. ³⁰	12–16	27–30	Males and females in the Netherlands, born 1963–1968	750	r = 0.62 (M) r = 0.65 (F)	r = +3.1 μm (95% CI 2.1–4.0) per 1 s.d. BMI	NS
Raitakari et al. ²⁸	3, 6, 9, 12, 15, 18	24–39	Males and females in Finland, born 1962–1977 YFS	2229	Not reported	r = +0.009 mm** per 1 s.d. BMI and 1 unit change in age	NS

Table 1 (continued)

Reference	Childhood age	Adult age	Population	n	Tracking of BMI	Effect Size	Effect of adjusting for adult BMI
Wright <i>et al.</i> ⁷	9, 13	50	Males and females in Newcastle, UK born 1947 NTFS	412	$r = 0.24-0.39$	Men-NS Women-NS	Men-NS Women-NS
<i>Disease outcomes</i>							
Eriksson <i>et al.</i> ²⁷	6-16	Up to 71	Males in Helsinki, Finland, born 1924-1933	3641	NA	HR associated with 1 s.d. increase in BMI was 1.15 (95% CI 1.03-1.29) at age 7, to 1.18 (1.07-1.31) at age 15.	Not adjusted
Lawlor <i>et al.</i> ²⁴	5	55	Males and females in Aberdeen, UK, born 1950s	11 106	NA	NS	Not adjusted
Lawlor <i>et al.</i> ²⁶	2-15 (BO) 15-18 (CH) 16-18 (GA)	Min 50	Males and females in England/Scotland (BO), males at CH school; males and females at Glasgow University (GA), born 1922-1956	14 831	NA	NS for studies individually When studies were pooled NS for stroke mortality, and for IHD HR of 1.09 (95% CI 1.01-1.19) per BMI z-score. But comparing overweight/obese to normal weight the HRs were NS.	Not adjusted

Abbreviations: BHS, Bogalusa Heart Study; BO, Boyd Orr Cohort; CH, Christ's Hospital school; CI, confidence intervals; DBP, diastolic blood pressure; GA, Glasgow Alumni. CHD, coronary heart disease; HR, hazard ratios; IHD, ischaemic heart disease; MCBPS, Minneapolis Children's Blood Pressure Study; MS, Muscatine study; NA, not applicable; NS, not significant; NTFS, Newcastle Thousand Families Cohort; OR, odds ratios; s.d., standard deviation; SBP, systolic blood pressure; YFS, Young Finns Study. * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$.

Results

Sixteen articles fulfilled the selection criteria and a summary of the main characteristics and results are shown in Table 1. All studies, apart from one, were published in the last 10 years.

Quality assessment

The quality scores assessed according to the Newcastle-Ottawa Scale varied between studies (Table 3), even though a reasonable level of quality had been established through the inclusion/exclusion criteria. On the basis of sample selection, the studies scored highly with either three or four stars out of four. Only one study²¹ scored four stars, and all the other studies that scored three failed on not showing that the outcome of interest was absent in childhood. For comparability there was more variation, with five studies scoring no stars, nine scoring one star and only two studies^{22,23} scoring two. This variation was because of differences in accounting for confounding factors (Table 2). Although age and gender were generally accounted for, socioeconomic status was not in most studies. Some studies adjusted for current BMI, but not necessarily in all the analyses, and a star was only awarded where it was taken into account consistently whenever relevant. For assessment, all studies scored either two or three stars. Of those that only scored two, most were not awarded the third because the adult cohort was considered too young for the outcome to be shown adequately.

Most studies did not adopt cut-off points to define childhood overweight and obese, but treated childhood BMI as a continuous variable for the purposes of statistical analysis. This variable was most commonly presented as childhood BMI or BMI z-scores, but also as the change in BMI or BMI z-scores between age categories. Studies that did employ cut-off points used a variety of definitions of overweight and obesity. We specified that they should be those recommended by either the US CDC³ or IOTF,¹⁷ to ensure appropriate classification of children as overweight or obese and to enable comparison between studies. Studies using arbitrary cut-off points were therefore excluded. The variety of statistical approaches used made it difficult to directly compare results across the selected studies. However, regression coefficients or estimates of relative risk could be extracted from all studies.

The ages at which exposures and outcomes were measured differed substantially between studies, ranging from 2 to 18 years for childhood BMI and 18-71 for adult outcome. Some studies²⁴ used one childhood age as their exposure, whereas others²⁵ used several cohorts of children at different ages. Most studies, however, used longitudinal data from the same individuals, so had several BMI readings in childhood for each individual. Historical cohort studies generally included adult outcomes at older ages, and there-

Table 2 Assessment of quality for a cohort study: adapted from Newcastle–Ottawa Scale. Stars were awarded if the criteria shown in italics were met

Selection

1. Representativeness of the intervention cohort
 - (a) *truly representative of children in the contemporary western world*
 - (b) *somewhat representative of children in the contemporary western world*
 - (c) selected group of patients, for example, only certain socioeconomic groups/areas
 - (d) no description of the derivation of the cohort
2. Selection of the non-intervention cohort (in this case ‘normal weight’ during childhood)
 - (a) *drawn from the same community as the intervention cohort* (in this case ‘at risk of overweight’ or ‘overweight/obese’ during childhood)
 - (b) drawn from a different source
 - (c) no description of the derivation of the non-intervention cohort
3. Ascertainment of exposure
 - (a) *measurement by trained health professional*
 - (b) *secure record*
 - (c) written self report
 - (d) other/no description
4. Demonstration that outcome of interest was not present at start of study
 - (a) *yes*
 - (b) no

Comparability

1. Comparability of cohorts on the basis of the design or analysis
 - (a) *study states that age, sex and adult BMI are controlled for in statistical analysis*
 - (b) *study states that socio-economic status is controlled for in statistical analysis*

Assessment

1. Assessment of outcome
 - (a) *independent assessment by trained health care professional*
 - (b) *record linkage*
 - (c) self report
 - (d) other/no description
2. Was follow-up long enough for outcomes to occur
 - (a) *yes, if mean adult age > 35*
 - (b) no, if mean adult age \leq 35
3. Adequacy of follow-up of cohorts
 - (a) *complete follow-up: all subjects accounted for*
 - (b) *subjects lost to follow-up unlikely to introduce bias: number lost \leq 20%, or description of those lost suggesting no different from those followed*
 - (c) follow-up rate < 80% and no description of those lost
 - (d) no statement

fore scored higher within the assessment criteria (Table 2), whereas the prospective studies mainly considered young to middle-aged adults. Year of birth also varied from the 1920s^{26,27} up to the 1970s.^{9,25,28}

Adult outcomes were more homogenous, with blood pressure measured as both systolic and diastolic, and hypertension defined as per the World Health Organisation Guidelines²⁹ in all studies. Three studies measured CIMT in the common carotid far wall,^{25,28,30} whereas two studies^{8,31} averaged measurements from the far walls of the common carotid, carotid bifurcation and internal carotid. The sixth study⁷ did not provide details. Mortality and morbidity outcomes were all identified from the UK National Health Service Central Register, the Scottish Morbidity Register or the Finland National Mortality Register.

Main results

Blood pressure

Eight studies considered the impact of childhood BMI on adult blood pressure (Table 3). Three studies showed positive correlations between childhood BMI and systolic blood pressure (SBP) and diastolic blood pressure (DBP),^{10,32,33} and a further three studies showed a positive association with SBP only.^{9,21,23} All but two of these studies^{23,28} observed significant tracking of childhood BMI into adulthood, yet two studies did not adjust for adult BMI^{9,10} meaning that the independent effects of childhood BMI were not tested. These studies scored poorly in quality assessment of the comparability criteria (Table 2).

Of the studies that did adjust for adult BMI, two showed that the positive associations remained.^{21,23} Field *et al.*²¹

Table 3 Summary of the associations between childhood BMI and CVD risk reported in the selected studies and the study scores (*) for three quality criteria

Reference	Association with childhood BMI ^a	Association adjusted for adult BMI ^a	Newcastle–Ottawa Scale		
			Selection (maximum 4*)	Comparability (maximum 2*)	Assessment (maximum 3*)
<i>Blood pressure</i>					
Burke <i>et al.</i> ²²	↔	Not applicable	***	**	**
Field <i>et al.</i> ²¹	+ ↔	+	****	*	**
Freedman <i>et al.</i> ³²	+	–	***	*	**
Hardy <i>et al.</i> ²³	+ ↔ –	+	***	**	**
Lauer and Clarke, ¹⁰	+	Not adjusted	***		**
Li <i>et al.</i> ³³	+	–	***	*	***
Sinaiko <i>et al.</i> ⁹	+	Not adjusted	***		**
Wright <i>et al.</i> ⁷	↔	↔ –	***	*	***
<i>Carotid intima-media thickness</i>					
Freedman <i>et al.</i> ⁸	+ ↔	+ ↔	***	*	**
Freedman <i>et al.</i> ³¹	+	Not all adjusted	***		***
Juonala <i>et al.</i> ²⁵	+ ↔	↔	***	*	**
Oren <i>et al.</i> ³⁰	+	↔	***	*	**
Raitakari <i>et al.</i> ²⁸	+	↔	***	*	**
Wright <i>et al.</i> ⁷	↔	↔	***	*	***
<i>Disease outcomes</i>					
Eriksson <i>et al.</i> ²⁷	+	Not adjusted	***		***
Lawlor <i>et al.</i> ²⁴	↔	Not adjusted	***	*	***
Lawlor <i>et al.</i> ²⁶	↔	Not adjusted	***	*	***

Abbreviation: BMI, body mass index. ^a+, Positive correlation; ↔, no significant correlation; –, negative correlation; multiple annotations reflect differing associations found within paper, e.g., in different age groups.

showed an odds ratio for hypertension in adulthood of 5.1 (95% CI: 1.4, 18.1) in those with childhood BMI over eighty-fifth centile relative to those under the seventy-fifth centile. Once adjusted for adult BMI, it was reported that the odds ratio for hypertension remained at 5.1 but that the confidence intervals became wider, but this data was not shown. Hardy *et al.*²³ reported a positive correlation between SBP and standard deviation change in BMI from age 7 to 15, when adjusted for adult BMI. However, the strength and significance of this correlation was not shown and no significant positive correlations were observed for other age groups, either for change in BMI or initial BMI.

In contrast, four studies showed a negative correlation between childhood BMI and adult blood pressure in their adjusted data sets^{7,23,32,33} (that is, lower BMI in childhood was associated with greater adult blood pressure). Freedman *et al.*³² reported a weak positive correlation between childhood BMI and adult SBP or diastolic blood pressure, but this became negative once adjusted for adult BMI (that is, an increase in childhood BMI was associated with a decrease in adult blood pressure). A change from a positive to negative correlation when adjusted for adult BMI was also observed by Li *et al.*³³ Wright *et al.*⁷ reported a negative correlation between female BMI at age 9 and adult SBP or diastolic blood pressure when adjusted for adult BMI. However, this was not the case at age 13, or in males at either time-point. Hardy *et al.*²³ showed no significant association between childhood BMI and adult blood pressure in males, but a negative correlation in females aged 2. This finding was

reported to persist after adjusting for adult BMI, but the relevant data was not included in the article. The studies by Li *et al.*³³ and Hardy *et al.*²³ scored higher within the assessment criteria (Table 2) as outcome measurements were made at an age when they were more likely to have occurred (45 and 50 year old, respectively). In contrast, the other studies assessed outcomes at an average of 18–27 years of age.

Carotid intima-media thickness

Six studies considered the impact of childhood BMI on CIMT and five of these studies showed a positive association between the two variables.^{8,25,28,30,31} However, after adjusting for adult BMI only the cumulative change in BMI from one study³¹ remained significant. An additional two studies showed positive associations with some age groups but not others.^{8,25} Freedman *et al.*⁸ found no significant correlations between adult CIMT and BMI under the age of 11, but positive correlations at ages 11–18. However, the magnitude of these associations was reduced once adjusted for adult BMI (data not shown in original article). The findings of this study also indicated that among adults who were of normal BMI, there was no relationship between childhood BMI status and adult CIMT. Juonala *et al.*²⁵ reported no significant associations between BMI at ages 3, 6, 9 or 15 and CIMT 21 years later, but positive correlations with BMI at ages 12 and 18. However, these differences became non-significant once adjusted for adult BMI. The final study⁷ showed no significant correlations, either before or after

adjusting for adult BMI. The quality of the studies within this CIMT grouping was relatively consistent, but a general weakness of all studies was the young age at which outcome measurements had been made. The exception to this was the study by Wright *et al.*,⁷ which measured CIMT at 50 years of age and showed no association with childhood BMI.

Disease outcomes

Three studies looked at the impact of childhood BMI on coronary or ischaemic heart disease and stroke incidence. These studies scored relatively highly on assessment criteria (Table 2), having measured disease outcomes at an age when they would be likely to have occurred. One study²⁴ found no significantly increased risk of CHD and stroke incidence in adults who were classified as overweight or obese as children. A second study by the same authors²⁶ pooled data from three historical cohorts and found no increased risk of stroke, but a small increased risk of ischaemic heart disease mortality. The final study²⁷ reported that childhood BMI was positively associated with CHD mortality. None of these studies made adjustment for adult BMI and were, therefore, considered of poor quality in terms of comparability.

Discussion

Cardiovascular disease represents a global public health issue and accounts for nearly half of all deaths in Europe.⁴ The adult risk factors for CVD have been well characterised, and it is estimated that around a third of CHD and ischaemic stroke is attributable to excess adiposity.¹ Although the relationship between adult obesity and CVD risk has been shown, the relationship with childhood obesity remains less clear. Given the evidence of tracking of BMI from childhood to adulthood,^{5,6} this review aimed to investigate the independence of relationships between childhood BMI and adult CVD risk. This is of considerable importance for the design of appropriate and targeted public health interventions. Our findings, to some extent, challenge the widely accepted view that the presence of childhood obesity is an independent factor for CVD and that this period should be a priority for public health intervention. The studies selected according to stringent criteria focused on the relationship of childhood BMI with blood pressure and CIMT as risk factors for CVD, as well as CVD disease endpoints.

Hypertension

Hypertension is a well-characterised risk factor for CVD,¹ with ~50% of CHD and 75% of stroke in developed countries attributable to raised blood pressure.⁴ Recent literature has suggested that high childhood BMI is associated with increased risk of raised blood pressure in later life. However, this systematic review suggests that the relationships observed between childhood BMI and adult

blood pressure cannot be considered independent of adult BMI. Evidence of an independent positive relationship between childhood BMI and adult blood pressure was reported in just two studies,^{21,23} neither of which included the relevant adjusted data in the paper (confidence intervals²¹ or correlation statistics²³). The study by Field *et al.*²¹ had the fewest participants and the adult age was young (18–26 years old). As a consequence there were very few hypertensive cases to consider (16 hypertensive men/130) and the results need to be viewed with caution. Evidence of a positive independent association between childhood BMI and adult blood pressure is therefore considered weak.

In contrast, the remaining three studies which adjusted for adult BMI provided evidence of a negative relationship between childhood BMI and adult blood pressure.^{7,32,33} The Wright *et al.*⁷ and Li *et al.*³³ studies had the oldest adult cohorts (age 45 and 50, respectively) and therefore scored well in terms of assessment criteria (Table 2). These studies would be expected to give a better representation of lifetime risk of developing hypertension, and both showed negative associations between childhood BMI and adult blood pressure. These findings suggest that it is those who were of lower BMI as children and overweight as adults who are at greatest risk of high blood pressure.

The balance of the data therefore seem to suggest that avoiding overweight during childhood fails to provide any protection against the effects of obesity in adulthood and may even increase risk in individuals that go on to be obese. In addition, those who are obese in childhood and go on to be normal weight as adults do not seem to be at any increased risk of raised blood pressure. Again, this suggests that childhood obesity is not an independent risk factor for adult hypertension. Instead, it may be the increase in relative adiposity between childhood and adulthood, which has particularly detrimental effects. Indeed, Lauer *et al.*¹⁰ observed that the strongest predictor of high adult blood pressure was a change from being at the lower end of the BMI scale in childhood to the higher end in adulthood. Li *et al.*³³ reported that the effect of adult BMI on blood pressure and risk of hypertension was strongest for those who had been in the lowest BMI decile as children. Alternatively, early life programming of metabolic function according to childhood body composition could alter the metabolic response to adiposity in later life.³⁴ These complex interactions are worthy of further study, including the potential mechanisms underlying them.

Carotid-intima thickness

Thickening of the carotid intima-media is considered to be a marker of atherosclerosis and has been associated with increased incidence of CHD and stroke.^{35,36} CIMT is correlated with adult BMI^{37,38} and recent studies have suggested that it is also associated with childhood BMI. However, this systematic review only found two studies, which show a positive independent association between childhood BMI

and adult CIMT. These studies focused on two different samples from the Bogalusa Heart Cohort^{8,31} and quality assessment highlighted weaknesses in their design and interpretation. Freedman *et al.*⁸ failed to include the key data in the paper (significance of correlation) and did not therefore provide empirical evidence of an independent association. The second study by Freedman *et al.*³¹ showed increased adult CIMT in those with a cumulative increase in BMI between childhood and adulthood, but not necessarily an independent effect of childhood BMI. The latter could have been addressed by adjusting the association between childhood BMI and CIMT, but this data was not included. In the same studies, mean CIMT in non-obese adults did not differ between those who had been obese as children and those who had not,⁸ suggesting that childhood obesity did not exert an independent effect. When comparing women in the tenth and ninetieth centiles for adult CIMT, those in the ninetieth centile actually had lower BMI up to the age of 7 years.³¹ These findings were not given any weighting in the authors' interpretation of the data in contrast to the weak correlation data, indicating a certain degree of interpretation bias. An important limitation highlighted by Freedman *et al.* is that replicate CIMT measurements were only moderately correlated in their studies ($r = 0.68^8$ and 0.85^{31}), suggesting poor reproducibility of the technique. Issues in the measurement of the technique have been reviewed earlier.³⁹

The remaining studies showed no association between childhood BMI and adult CIMT once adjusted for adult BMI. In support of this, Juonala *et al.*²⁵ also observed that individuals who were overweight as a child but normal weight as adults did not have significantly different mean adult CIMT to those who were normal weight throughout childhood and adulthood. With the exception of the Wright study,⁷ these longitudinal studies considered young adults rather than those in middle or old age. It is possible that the follow-up period was not long enough to observe effects on CIMT. The increase in CIMT associated with atherosclerosis generally has a very slow progression.³⁹ A CIMT of over 900 μm is considered to be the level at which CIMT is associated with atherosclerosis.⁴⁰ The mean CIMT in these studies ranged from ~ 500 to 800 μm , which was therefore not high enough to be regarded as clinically significant. The exception to this was the mean adult CIMT in males in the second Freedman study,³¹ which was $870 \pm 100 \mu\text{m}$. However, after controlling for adult BMI, adult CIMT increased by 16 μm per 1-unit change in childhood BMI z-score, which is only 1.84% of the mean for males. This difference is very small and unlikely to have any clinically relevant impact. This cohort contained a higher proportion of black men (26%) than other studies, and this sub-group was shown to have higher mean CIMT than white men. Despite a longer follow-up period to age 50 in the Wright study⁷, CIMT remained below that estimated to be associated with atherosclerosis and showed no association with childhood BMI. There is therefore little evidence of an independent relationship between childhood BMI and CIMT, and that which does exist should be considered weak.

Cardiovascular disease outcomes

Studies investigating the relationship between childhood BMI and CVD risk factors in early adult life provide a useful indication of the impact of childhood BMI on long-term cardiovascular health. However, relationships observed at this level cannot be assumed to reflect a relationship with risk of morbidity or mortality from CVD in later life. Long-term follow-up of cohort studies to assess disease endpoints is required to fully test these hypotheses. Only three such studies met the inclusion criteria for this review, and all were of a historical nature. Although two of these studies provided evidence of a relationship between childhood BMI and CHD²⁷ or ischaemic heart disease²⁶ mortality, neither adjusted for adult BMI and cannot therefore provide evidence of an independent effect of childhood BMI. These studies therefore scored poorly for comparability, somewhat outweighing the advantages gained by them measuring outcome in the cohort at an older age. The third study showed that men who died from CHD had a higher childhood BMI than those who did not.²⁴ However, their BMI was on the sixtieth centile for the population as a whole and therefore still well within the normal weight range for the population. Although historical cohort studies provide a unique opportunity to assess long-term effects of early life factors, it should be remembered that the populations studied cannot be considered contemporary and do not therefore reflect current lifestyles and dietary behaviours. Funding support for long-term follow-up of current prospective cohort studies, which focus on contemporary populations and allow for stronger control over confounding, will enable better understanding of the impact of early life factors on long-term CVD risk.

Final conclusions

In summary, this review has found little evidence to suggest that childhood overweight and obesity is an independent risk factor for increased blood pressure, CIMT or CVD morbidity or mortality. That which does exist should be considered weak, according to our quality assessment. A possible explanation for the absence of an association could be the higher relative contribution that lean body mass and bony frame make to BMI in children.^{7,41} Although most of the studies in this review showed moderate tracking of BMI from childhood to adulthood, this is not necessarily true of the whole field⁴² and may be partly explained by tracking of build. Interestingly, Wright *et al.*⁷ showed a weaker correlation between childhood and adult BMI. This may reflect differing contributors to and incidence of childhood obesity in this less contemporary 1940's cohort, or simply the increasing contribution of other factors to adult obesity risk as the follow-up period lengthens. This study also considered percentage body fat as an adult and found it was not associated with childhood BMI despite childhood and adult BMI being moderately correlated. Over-representation of children with a lower lean body mass

in groups at the lower end of the BMI scale may explain the negative associations observed. More detailed analysis of body composition in future prospective cohort studies should improve understanding of this relationship. Continued follow-up of current prospective cohorts will also provide a better representation of the contribution of childhood obesity to lifetime risk. At present, however, the data suggest that any relationship observed is dependent on the tracking of BMI from childhood to adulthood. Importantly, the evidence suggests that the risk of raised blood pressure is highest in those who were of lower BMI in childhood and overweight in adulthood. This is contrary to original hypotheses and requires further investigation.

In contrast to the findings of this review, bias in the reporting and review of studies in this area suggests stronger evidence that a positive relationship exists between childhood BMI and adult CVD risk. Indeed, during this systematic review it became apparent that data relating to positive relationships were highlighted and discussed much more readily than data showing an insignificant or negative relationship, often with little consideration for the adjustment for adult BMI. Examples of this include two of the selected publications from the Bogalusa Heart Study, in which overall conclusions emphasised weak correlation data. In contrast, little emphasis was given to data in the same papers showing no difference in adult CIMT risk between non-obese and obese children⁸ and that those in the ninetieth centile for adult CIMT actually had lower BMI up to the age of 7 years.³¹

Although there is currently no compelling evidence to support independent effects of childhood obesity on CVD risk, it is important not to underestimate the potential problems caused by childhood obesity because of the potential for tracking into adulthood,⁶ where obesity is firmly established as a risk for co-morbidities. However, this review also highlights potential long-term risks of being underweight during childhood. Public Health initiatives must therefore continue to promote healthy lifestyles in children, whilst stressing the importance of maintaining weight within the normal range. Careful consideration is required as to the approach and targeting of obesity interventions. Although interventions must target the stages of the life-course which offer the best long-term benefits, it is important to avoid the potential for negative consequences when the timing coincides with critical stages of neurological, behavioural and physical development.⁴³ It is hoped that this review can contribute to discussion in this area.

Acknowledgements

LJ Lloyd was supported by a graduate studentship from the Organix Foundation.

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