Association of body mass index measured in childhood, adolescence, and young adulthood with risk of ischemic heart disease and stroke: findings from 3 historical cohort studies1–4

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ABSTRACT
Background: It is unclear whether early life body mass index (BMI; in kg/m²) is associated with adult cardiovascular disease.
Objective: The objective was to assess the association of early life BMI with the risk of ischemic heart disease (IHD) and stroke.
Design: The association between early life BMI and risk of adult mortality from IHD and stroke was assessed in 3 historical cohort studies in which height and weight had been assessed by using standard procedures. Participants were traced and linked to national mortality data. Participants in the 3 cohorts were born between 1922 and 1937, 1927 and 1956, and 1928 and 1950 and were aged 2–15, 9–18, and 16–22 y, respectively, at the time of assessment of their height and weight.
Results: Participants in all 3 cohorts had mean BMIs similar to those reported for contemporary children and young adults, but fewer of the cohort participants were overweight or obese. BMI was not associated with future risk of IHD or stroke in any cohort. The pooled (all 3 cohorts) adjusted hazard ratio per SD of early life BMI was 1.09 (95% CI: 1.01, 1.19) for IHD and 0.94 (95% CI: 0.82, 1.08) for stroke. The pooled hazard ratio of IHD when participants who were overweight or obese for their age were compared with all other participants was 1.34 (95% CI: 0.95, 1.91), and no association was found between overweight or obesity and stroke risk. The effects of BMI did not vary by cohort or by age.
Conclusion: These results do not provide strong evidence that being overweight or obese in childhood is associated with future cardiovascular disease risk.

KEY WORDS Body mass index, childhood, cardiovascular disease, life-course epidemiology

INTRODUCTION
The population prevalence of childhood obesity has increased approximately 3-fold in most industrialized countries during the past 20 y (1). It is thought that this trend will have important public health consequences. In particular, there is concern that the epidemic of childhood obesity will result in increased cardiovascular disease (CVD) risk in the future (1). However, the evidence in support of this possibility is inconclusive (2–7). Recent results from a large birth cohort of persons born in Aberdeen, Scotland, in the 1950s found that body mass index (BMI; in kg/m²) measured at a mean age of 5 y was not associated with ischemic heart disease (IHD) in adulthood (4). This result, together with results of previous studies, suggested that BMI in early childhood may not be related to future IHD risk, although greater BMI in adolescence or early adulthood may be an important risk factor for IHD (4).

In view of both the potential public health importance of an association between childhood BMI and future risk of CVD (in the context of increasing BMIs over time in childhood) and the paucity and inconclusive nature of the evidence to date, we investigated the association between early life BMI and risk of IHD and stroke in 3 study cohorts. In these cohorts, height and weight were measured between 2 and 15 y of age [the Boyd Orr cohort: participants were born between 1922 and 1937; we add longer follow-up to the results from our earlier report from this cohort (7)], between 9 and 18 y of age (the Christ’s Hospital cohort: participants were born between 1927 and 1956), and between 16 and 22 y (the Glasgow Alumni cohort: participants were born between 1928 and 1950). We included persons up to age 22 y in

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3 Supported by a United Kingdom Department of Health public health career scientist award (to DAL), a public health career scientist award funded by the Research and Development Office for Health and Personal Social Services in Northern Ireland (to PM), and a United Kingdom Medical Research Council Health of the Public Training Fellowship (to BG). The Boyd Orr cohort has received funding from the Medical Research Council, the World Cancer Research Fund, Research into Ageing, United Kingdom Survivors, the Economic and Social Research Council, the Wellcome Trust, and the British Heart Foundation. The Christ’s Hospital cohort has received funding from the University of Bristol, Cancer Research United Kingdom, and the Medical Research Council. The Glasgow Alumni Study has received funding from the Stroke Association, Chest Heart and Stroke (Scotland), United Kingdom National Health Service Research and Development CVD Programme, and the World Cancer Research Fund.
4 Reprints not available. Address correspondence to DA Lawlor, Department of Social Medicine, University of Bristol, Canynge Hall, Whiteladies Road, Bristol, BS8 2PR, United Kingdom. E-mail: d.a.lawlor@bristol.ac.uk. Received September 21, 2005. Accepted for publication January 3, 2006.
the Glasgow Alumni cohort to assess our a priori hypothesis that the association between BMI measured in later childhood or early adulthood and CVD outcomes would be stronger than that between BMI measured in childhood and CVD outcomes.

SUBJECTS AND METHODS

Boyd Orr cohort

The Boyd Orr cohort is a historical cohort study based on the long-term follow-up of 4999 children who were surveyed in the Carnegie Trust’s study of family diet and health in pre-World War II (ie, 1937–1939) Great Britain (8). Cohort members were born between 1922 and 1937. In 1988, the original paper records from this survey were obtained, and the data were entered into an electronic database. Participants were linked to (ie, flagged with) the National Health Service Central Register (NHSCR) to obtain mortality data, and 4397 (88%) were successfully traced and flagged. Full details of the original survey and of the tracing and flagging of the participants are described elsewhere (9). Briefly, 1343 families (with 4999 children aged 0–19 y) living in 16 areas of England and Scotland were surveyed during a 2-y period between 1937 and 1939. Approval for the revitalization of the Boyd Orr study was provided by United Bristol’s Hospital Trust Local Research Ethics Committee.

The occupation of the head of the household recorded at the time of the survey was used to classify social class. In all but 2 of the survey areas, the children underwent a detailed physical examination, which included measurements of height and weight by using standard research protocols (8). Weight and height were measured only on this occasion. For the current analysis, we have included participants who were aged 2–15 y when examined, because few of the participants were >15 y at the time of examination, and BMI in children <2 y old is difficult to interpret. A total of 2586 participants were successfully traced and had anthropometric measurements between the ages of 2 and 15 y.

Christ’s Hospital cohort

The Christ’s Hospital cohort is a historical cohort study based on the long-term follow-up of 3175 children who attended the single-sex (male) Christ’s Hospital school (a private boarding school, which also enrolled a small number of orphaned boys) between 1936 and 1969. While the children attended Christ’s Hospital school, their height and weight were measured regularly with the use of protocols originally developed by the school’s medical officer, Gerald Edward Friend, MD, an influential figure in the field of schoolchildren’s nutrition (10, 11). Participants were flagged with the NHSCR to obtain mortality data, and 2593 (81%) were successfully traced and flagged. The South West Multi-Centre Research Ethics Committee approved the tracing of this cohort.

In the current study, we used the measurements, taken at school entry and exit examinations, from the growth record cards. At school entry, the age range of participants was 9–18 y, but 99% were aged 9–12 y, and only those participants are included in the analyses of school entry BMI. Similarly, at school exit, the full age range was 9–18 y, but only the 96% who were aged 15–18 y are included in the analyses of school exit BMIs. The father’s occupation when the participant was in school has been used to classify social class. The final analysis included 1420 participants, who were traced and had entry or exit school anthropometric measurements in the above-mentioned age ranges and for whom there was socioeconomic data.

Glasgow Alumni cohort

The Glasgow Alumni study is a historical cohort study based on the long-term follow-up of 15 322 students who attended Glasgow University between 1948 and 1968 and for whom detailed student health data were collected by using protocols devised by Parnell (12) and used by Parnell and his colleagues for their Nuffield Foundation–sponsored research of student health. Of these 15 322 students, 12 755 (83%) were successfully traced and flagged with the NHSCR. Full details of the methods were previously described (13). The father’s occupation, recorded at the time of each student’s examination, was used to classify social class. Students were asked whether they smoked and the amount that they smoked and were classified as never or current smokers. Students’ heights and weights were measured, on the occasion of entry to university, by a physician with ≥3 y clinical experience (13). The age range of all students who attended Glasgow University during the period of the student assessments was 16–69 y. Because we are interested in the association of BMI in early life with future risk of CVD, we excluded participants who were aged ≥23 y at the time of their student physical examination. In total, 10 555 participants who were traced and had BMI measured when they were aged <23 y are included in this analysis.

Statistical analyses

For all 3 cohorts, the International Classification of Disease (ICD) codes used to define IHD were 410–414, 429.2 (ICD-9), and I20–25, I51.6 (ICD-10), and those used to define stroke were I60–I69, G45 (ICD-10). Internally standardized age and sex z scores for BMI were generated for participants in each cohort so that comparisons could be made across cohorts, despite the fact that BMI was measured at different ages and in males and females. In addition, overweight and obesity were categorized by using the age- and sex-specific thresholds for children that correspond to a BMI ≥25 (for overweight) and ≥30 (for obesity) in adulthood by means of models of growth trajectories from population samples (14). The childhood equivalents of these adult thresholds were derived by Cole et al (14) from models of growth trajectories with age, which were based on samples from several different countries. These childhood equivalents cover the age range 2–18 y, whereas, for participants ≥18 y old, we used the standard adult cutoffs of BMI ≥25 for overweight and BMI ≥30 for obesity.

Data were analyzed by using Cox proportional hazards regression models, with participants’ age as the time axis. Contributions to risk were censored at the earliest of 1) emigration date; 2) death from a cause other than the outcome of interest; and 3) the last date of mortality tracing for each cohort: 28 February 2003 for the Boyd Orr cohort and 30 November 2004 for the Christ’s Hospital and Glasgow Alumni cohorts. Proportionality assumptions were assessed by inspection of cumulative hazard function plots (Nelson-Aalen) on a logged axis. No evidence was observed for any violation of the proportionality assumptions. In the Boyd Orr cohort, robust SEs, taking account of nonindependence between siblings within the sample, were used to estimate all SEs and P values. The other 2 cohorts did not include siblings. Adjustment was made for family social class in all 3 cohorts.
Information on participant smoking at the time of BMI assessment was available only in the Glasgow Alumni cohort. In adulthood, smoking can have an important masking effect on the association between BMI and future CVD, because long-term smokers often have lower BMIs but are at greater risk because of their smoking. Therefore, in the Glasgow Alumni cohort only, we performed stratified analyses (in smokers and never smokers) and examined whether statistical evidence showed an interaction between smoking and BMI for CVD outcomes and whether smoking confounded any association. To examine whether the effect of early life BMI and mortality from either IHD or stroke varied by age in early life, we performed stratified analyses (in smokers and never smokers) with the overweight participants. For the Christ’s Hospital (persons who attended a private male boarding school) and the Glasgow Alumni (persons who attended university in the 1950s and 1960s) cohorts, few participants came from lower socioeconomic groups; this is to be expected, given the source of these cohorts. In contrast, ≥50% of the participants of the Boyd Orr cohort came from lower socioeconomic groups, which reflects the selection of deprived families for this study.

No strong statistical evidence was observed that the effect of BMI on the risk of either IHD or stroke varied between males and females in the Boyd Orr cohort or the Glasgow Alumni cohort (P for interaction ≥ 0.16), and so all results are presented for both sexes combined. The unadjusted and adjusted associations of BMI and being overweight or obese with risk of IHD and stroke for each of the 3 cohorts are shown in Table 1. No strong statistical evidence was observed of a linear association between BMI and being overweight or obese with risk of IHD and stroke in any of the individual cohorts. However, estimates were imprecise, and, in the Boyd Orr cohort, they were of borderline statistical significance at the conventional 5% level. No strong statistical evidence was observed in any of the cohorts that being overweight or obese at age 18-22 y was associated with future mortality from CVD.

### RESULTS

Participant characteristics for each cohort are shown in Table 1. For all 3 cohorts, <0.5% of the participants were obese, and, in all remaining analyses, the obese participants are combined with the overweight participants. For the Christ’s Hospital (persons who attended a private male boarding school) and the Glasgow Alumni (persons who attended university in the 1950s and 1960s) cohorts, few participants came from lower socioeconomic groups; this is to be expected, given the source of these cohorts. In contrast, ≥50% of the participants of the Boyd Orr cohort came from lower socioeconomic groups, which reflects the selection of deprived families for this study.
In Table 2, the effects on IHD and stroke of BMI that was based on height and weight assessments at the school exit examination (at age 15-18 y) in the Christ’s Hospital study are presented. The effects based on height and weight examinations at the school entry examination (at age 9-12 y) did not differ substantively from those at the exit examination, as shown in Figure 1 and Figure 2.

Of the Glasgow Alumni participants, 34% were smokers. Smoking at this early age (16–22 y) was associated with increased risk of CVD [hazard ratio (HR) comparing smokers to never smokers: 1.48 (95% CI: 1.16, 1.89)], and this association was not altered by adjustment for family social class. Smoking was not related to BMI or being overweight or obese; 34% of participants who were normal-weight were smokers, whereas 35% of participants who were overweight or obese were smokers ($P = 0.5$). The effect of BMI assessed either as a continuous $z$ score or as a dichotomy comparing overweight or obese with normal-weight on IHD or stroke did not differ significantly between smokers and nonsmokers ($P$ for interaction $> 0.5$). When we adjusted for the effect of smoking in any of the associations assessed within the Glasgow Alumni cohort, no effect was observed on the HRs.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Boyd Orr cohort $^2$</th>
<th>Christ’s Hospital cohort $^2$</th>
<th>Glasgow Alumni cohort $^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>IHD death</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Per BMI $z$ score</td>
<td>1.13 (0.99, 1.28)$^6$</td>
<td>1.14 (1.00, 1.30)</td>
<td>1.09 (0.97, 1.23)</td>
</tr>
<tr>
<td>$P$ linear trend</td>
<td>0.07</td>
<td>0.05</td>
<td>0.1</td>
</tr>
<tr>
<td>Normal BMI (kg/m$^2$)</td>
<td>0.6</td>
<td>0.5</td>
<td>0.9</td>
</tr>
<tr>
<td>Overweight or obesity</td>
<td>1.33 (0.65, 2.70)</td>
<td>1.34 (0.66, 2.72)</td>
<td>1.39 (0.87, 2.21)</td>
</tr>
<tr>
<td>$P$</td>
<td>0.4</td>
<td>0.4</td>
<td>0.2</td>
</tr>
</tbody>
</table>

| Stroke death | | | |
| Per BMI $z$ score | 0.96 (0.76, 1.22) | 0.97 (0.77, 1.23) | 0.95 (0.80, 1.13) |
| $P$ linear trend | 0.8 | 0.8 | 0.5 |
| Normal BMI (kg/m$^2$) | 0.8 | 0.8 | 0.9 |
| Overweight or obesity | 0.49 (0.07, 3.56) | 0.51 (0.07, 3.71) | 1.41 (0.74, 2.69) |
| $P$ | 0.5 | 0.5 | 0.3 |

$^1$ HR, hazard ratio. All $P$ values were computed from likelihood ratio tests.

$^2$ Included both males and females; birth years of participants were 1922–1937; age at assessment of height and weight was 2–15 y; the total number of participants was 2586, of whom 230 died of IHD and 72 died of a stroke during the follow-up period.

$^3$ Included males only; birth years of participants were 1927–1956; age at assessment of height and weight was 15–18 y (exit examination); the total number of participants was 1420, of whom 73 died of IHD and 21 died of a stroke during the follow-up period.

$^4$ Included males and females; birth years of participants were 1928–1950; age at assessment of height and weight was 16–22 y; the total number of participants was 10 555, of whom 280 died of IHD and 144 died of a stroke during the follow-up period.

$^5$ Adjusted for age, sex (Boyd Orr and Glasgow Alumni), social class, and smoking (Glasgow Alumni only).

$^6$ $z$; 95% CI in parentheses (all such values).

$^7$ Too few cases.

FIGURE 1. Association of early life body mass index (BMI) with ischemic heart disease (IHD) mortality in 3 historical cohorts stratified by age at assessment of height and weight. The horizontal line represents the null value of 1.0.

FIGURE 2. Association of early life body mass index (BMI) with stroke mortality in 3 historical cohorts stratified by age at assessment of height and weight. The horizontal line represents the null value of 1.0.
TABLE 3
Pooled (from 3 historical cohorts) adjusted hazard ratios of the associations of BMI with mortality from ischemic heart disease (IHD) and stroke

<table>
<thead>
<tr>
<th></th>
<th>Random effects model</th>
<th>Fixed effects model</th>
</tr>
</thead>
<tbody>
<tr>
<td>IHD death</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Per BMI z score</td>
<td>1.09 (0.99, 1.19)</td>
<td>1.09 (1.01, 1.19)</td>
</tr>
<tr>
<td>$P$ for linear trend</td>
<td>0.06</td>
<td>0.04</td>
</tr>
<tr>
<td>Normal BMI (kg/m²)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Overweight or obesity</td>
<td>1.34 (0.93, 1.95)</td>
<td>1.34 (0.95, 1.91)</td>
</tr>
<tr>
<td>$P$</td>
<td>0.12</td>
<td>0.10</td>
</tr>
<tr>
<td>Stroke death</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Per BMI z score</td>
<td>0.94 (0.81, 1.11)</td>
<td>0.94 (0.82, 1.08)</td>
</tr>
<tr>
<td>$P$ for linear trend</td>
<td>0.4</td>
<td>0.4</td>
</tr>
<tr>
<td>Normal BMI (kg/m²)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Overweight or obesity</td>
<td>1.30 (0.70, 2.42)</td>
<td>1.30 (0.72, 2.37)</td>
</tr>
<tr>
<td>$P$</td>
<td>0.4</td>
<td>0.4</td>
</tr>
</tbody>
</table>

n = 14,561 participants included in these analyses; 583 deaths were due to IHD and 237 deaths were due to stroke. All $P$ values computed from $z$ scores.

The HRs for the effect of BMI on IHD for each study stratified by age at which height and weight were measured are shown in Figure 1. Similar effects with stroke as the outcome are shown in Figure 2. Within each study, no evidence was found that the effect of BMI on the risk of either IHD or stroke differed by the age at which height and weight were assessed (age group $\times$ BMI interaction, $P > 0.2$). Similarly, the effect of overweight or obesity did not differ by age within the cohorts (age group $\times$ overweight $\times$ obesity interaction, $P > 0.6$).

The pooled (across all 3 cohorts) adjusted HRs for IHD and stroke are shown in Table 3. We had decided a priori to pool the effects by using a random effects model. However, because no evidence of heterogeneity was observed between the studies, we present here results from both the random and fixed effects models. Evidence of a linear association was observed between early life BMI and IHD mortality. No strong statistical evidence was observed of a linear association between early life BMI and stroke mortality from stroke or between overweight or obesity in early life and either IHD or stroke. No strong statistical evidence of heterogeneity was observed between the 3 studies (all $P$ values $> 0.4$). In Table 3, the results from the exit examination were used for the Christ’s Hospital cohort, but use of the entry examination results instead did not result in estimates that were substantively different from those presented.

DISCUSSION

We found no strong statistical evidence for a linear association between BMI and future risk of IHD and stroke within each individual cohort study examined here. However, results for each individual cohort study were imprecise, and, when data from the 3 cohorts were pooled, evidence was observed of a linear association between early life BMI and IHD mortality. No strong statistical evidence was observed that overweight or obesity was associated with increased IHD in these cohorts, either individually or when they were pooled together, and no strong evidence that early life BMI or overweight or obesity was associated with greater mortality from stroke in adulthood. We could find no strong evidence to support our hypothesis that the effect of early life BMI on later CVD would be greater when the age at which height and weight were measured was greater (ie, from early childhood through adolescence to early adulthood).

Our mean values for BMI for each cohort are surprisingly similar to mean values for children of similar ages in contemporary Britain (16). For example, mean BMI values in boys and girls aged 2–9 y in the Health Survey for England (16) measured between 1995 and 2002 were all between 16 and 17, which do not differ significantly from the values of 16.0 and 16.1 for participants in the Boyd Orr cohort (Table 1). Similarly, mean BMI values for 15-y-old boys and girls in the Health Survey for England (16) measured between 1995 and 2002 were all between 20 and 21, which do not differ significantly from the values of $\approx 21.6$ and 21.5 for the BMI exit measurements in the Christ’s Hospital and Glasgow Alumni cohorts, respectively. However, almost none of the participants in any of our 3 cohorts fell into the obese category, and only 4–6% in each cohort were categorized as overweight. These values compare with a finding of obesity in 0.9% of boys and 1.2% of girls aged 9.6% of boys and 11.7% of girls in British growth surveys conducted between 1978 and 1993 by using thresholds identical to those used here (14). Thus, the relatively low levels of overweight or obesity in our cohorts may explain the lack of strong statistical evidence for associations between early life overweight or obesity and CVD outcomes. This possibility holds true, particularly, if any association is largely driven by an effect of extreme obesity in early life, rather than being continuous across the BMI distribution. Bearing in mind the greater prevalence of obesity in contemporary populations of children than in those populations examined here, the modest effect on IHD in our cohorts may translate into greater risks of future IHD in obese children in contemporary populations.

The possibility that our findings may not be generalizable to contemporary populations of children, among whom the prevalence of obesity is greater than that among the studied populations, is a limitation of our study, but it highlights one of the important difficulties of examining the associations of early life factors with future disease outcomes. Historical cohorts may not be representative of contemporary children and young adults in terms of exposure distribution (in this case, BMI), but studies of contemporary children have the limitation of not having disease outcomes. One approach, therefore, is to consider results from historical cohorts with disease outcomes, as we have done here, together with results of associations with risk factors in contemporary children.

Of studies assessing the relation of BMI with CVD risk factors in contemporary children, many (17–21) but not all (2) studies found that contemporary overweight and obese children and adolescents have more adverse lipid and insulin concentrations and blood pressure measurements than do nonoverweight (normal-weight) children. In one cross-sectional study, severely obese ($\geq$95th percentile) children had greater arterial stiffness than did normal-weight children, but no difference in carotid intima-media thickness was observed between the 2 groups (22). In a second, similar study, both arterial stiffness and carotid intima-media thickness were greater in severely obese 6–14-y-olds than in the other children, and this effect attenuated toward the null after adjustment for insulin resistance (23). Although one explanation for our null findings of the effect of overweight or obesity is that there were too few obese children in these historical cohorts (as compared with contemporary children) to find an association, an alternative explanation is that...
overweight or obesity per se is not an adverse CVD risk factor if other risk factors predisposing to a vascular event are well controlled. In particular, childhood obesity may not result in a greater CVD risk if other risk factors remain well controlled in the intervening years. One limitation of the current analysis is the lack of data on biological and lifestyle risk factors across the life course, which could be used to assess this issue further. In addition, we do not have information on adult BMI.

The current study and previous studies that examined the association of childhood or early life adiposity with future CVD risk have used BMI as an indicator of adiposity (2–7). Although BMI is widely used in clinical practice and research, it is easy to measure, and is more reproducible than is skinfold-thickness or waist circumference measurement (3), it may not be the best indicator of adiposity in childhood (24). In the Boyd Orr cohort, BMI in childhood was correlated with lean mass index (r = 0.18) but not fat mass index, percentage body fat, or waist circumference measured 65 y later (r = 0.04, −0.06, and 0.04, respectively) in a small subgroup (n = 799) of the original cohort. In small studies of obese children and adolescents, evidence exists that central or intraabdominal adiposity, assessed by magnetic resonance imaging or waist circumference, is a stronger predictor of insulin resistance, glucose intolerance, and dyslipidemia than is BMI (25–27). Although historical cohort studies in which participants have disease outcomes are unlikely to have more direct measurements of childhood adiposity, it will be valuable in the future to see whether differences are observed between the predictive ability of childhood BMI and the direct measurement of the percentages of lean and fat mass with respect to CVD risk in modern birth cohort studies, such as the Avon Longitudinal Study of Parents and Children (28), that include both indirect anthropometric assessment of adiposity and dual-energy X-ray absorptiometry assessment of fat and lean mass.

In some adult studies, null associations between BMI and CVD risk may be the result of reverse causality or of masking by smoking (29). In the current study, in which BMI is measured early in life, reverse causality is an unlikely explanation for the weak associations found. Smoking can mask the effect of BMI because long-term smokers tend to have low BMI but are at increased risk of CVD. In the Glasgow Alumni cohort, despite the fact that 35% of subjects were smokers at the time that their BMI was assessed and despite a strong association between smoking at this young age and future risk of IHD and stroke, no effect modification or confounding was observed on the associations of BMI with IHD or stroke by smoking. This is most likely a result of the fact that, because of the subjects’ age, the duration of smoking would have been short, and smoking would be unlikely to have had a marked effect on their BMI. Smoking in adulthood could not confound the association between childhood BMI and future CVD risk, because smoking in adulthood could not directly influence childhood BMI. To mediate any effect, one would have to suggest that childhood BMI had a direct effect on whether these study participants went on to be smokers in adulthood, which seems unlikely.

In conclusion, we found no strong statistical evidence in 3 historical cohort studies for an association between early life overweight or obesity and future mortality from IHD or stroke. We postulate 3 possible reasons for these findings. First, if increased risk is associated only with extreme childhood obesity, then the low levels of obesity in these historical cohorts may mean that no association should be anticipated. If this is the case with childhood BMI distributions in contemporary populations that are right-skewed (meaning that a greater proportion are obese and that the mean BMI is higher in this group), then, in contemporary children, overweight or obesity could have a marked influence on future CVD risk and population trends. A second explanation is that overweight or obesity in childhood may not be associated with future risk if other risk factors across the life course are absent or well controlled. Studies with repeated measurements of a range of CVD risk factors from across the life course are required to examine this possibility. Finally, BMI, which combines fat and lean mass, is a poor indicator of adiposity and distribution of adiposity in childhood. In the future, results from studies of contemporary children that have direct assessments of lean and fat mass will be able to provide a more definitive assessment of the effect of early life adiposity and its distribution on future CVD risk.

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DAL devised the study design, undertook the analyses, wrote the first draft of the manuscript, and coordinated the final version. RMM and DG are principal investigators for the Boyd Orr cohort and contributed to developing the study design. BG and PM are principal investigators for the Glasgow Alumni cohort. SE is one of the principal investigators for the Boyd Orr cohort. JS and YB-S are principal investigators for the Christ’s Hospital cohort. GDS is one of the principal investigators for the Glasgow Alumni, Christ’s Hospital, and Boyd Orr cohorts and contributed to developing the study design. RMM, DG, BG, PM, SE, JS, YB-S, and GDS contributed to writing the manuscript. None of the authors had a personal or financial conflict of interest.

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