

## PEDIATRIC EDITORIAL

# Placing the cardiovascular risk of childhood obesity in perspective

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The study by Lloyd *et al.*<sup>1</sup> is a timely review of the evidence for an association between childhood body mass index (BMI) and adult blood pressure, carotid intima media thickness (IMT) and cardiovascular morbidity or mortality. Cardiovascular risk is often cited as a major reason to actively treat established overweight and obesity in childhood, and to prevent the appearance of overweight. There are of course numerous reasons to treat childhood overweight and obesity, including current medical morbidity, rather than just a future risk of disease. That there are no defined levels of risk for any of the classic cardiovascular risk factors in children also makes interpretation of future risk reduction difficult. The systematic review by Lloyd *et al.*<sup>1</sup> suggests that the evidence that childhood overweight and obesity are independent risk factors for adult cardiovascular disease is limited and highlights a number of the methodological issues in the studies that have examined this association to date.

First, the included studies were not examinations of contemporary cohorts and, in some cases, the childhood period dated back more than 50 years. The prevalence of childhood overweight and obesity in these historical cohorts is lower than those in contemporary cohorts, with the significant rise in childhood overweight and obesity occurring over the past two decades. The rise in prevalence rates of more extreme levels of obesity may also be a more powerful driver for the association with future cardiovascular disease risk. Thus, it is conceivable that current studies incorporating young adults or current era children would result in quite different findings.

Second, all the included studies have used BMI as the measure of both childhood and adult adiposity. As identified by the authors, BMI does not directly measure fat mass and, although clinically useful, it is relatively insensitive in discriminating between lean body mass and fat mass.<sup>2</sup> This may potentially result in misclassification of a subject's true degree of adiposity. Moreover, a number of the studies have assessed children of a wide age range at a single time point using BMI rather than BMI z-score as a measure of childhood adiposity. The BMI z-score is an essential adjustment made for both age and gender in order to allow valid comparison between individual time points or between studies. In

addition, a statistical adjustment for adult BMI was carried out in only some of the studies.

Waist circumference measures as an indicator of central or visceral obesity, which seems to convey the highest risk from cardiovascular disease, are generally not available in the cohorts. It has been observed that waist circumference z-scores are increasing at a more rapid rate than BMI z-scores in contemporary child cohorts,<sup>3</sup> and may better reflect the risks of childhood obesity for adult cardiovascular outcomes.<sup>4</sup>

Third, there is variability between studies on whether biochemical markers were reported. The majority of studies have reported blood pressure and carotid IMT outcomes in young as opposed to older adults. As the authors of this systematic review point out, a longer time frame may be necessary in order to observe an effect of childhood obesity on such measures.

Finally, information about puberty is generally missing from cohorts. Puberty spans a relatively short time period of 2–5 years and may be only recorded retrospectively and relatively inaccurately. This is unfortunate as puberty is a significant confounder when considering cardiovascular risk profiles. The physical and physiological effects of puberty are multiple, with gender dimorphism. There is a dramatic change in height and weight. Gender differences in fat mass are apparent before puberty, but puberty produces further changes in fat deposition that are testosterone and estradiol dependent. Subcutaneous fat is reduced in males and visceral adipose stores increase. In females, subcutaneous fat increases in a gynoid distribution and there is some increase in visceral fat. However, 20% of females who gain weight in puberty have male patterning or android obesity, often associated with polycystic ovaries, which carry an increased risk of cardiovascular risk in adulthood. Thus, puberty is one of the risk time points for the development of obesity in childhood.<sup>5</sup> Estradiol increases HDL-cholesterol, whereas progesterone and androgens have a deleterious effect on cholesterol profile. Puberty is also associated with a physiological insulin resistance, secondary to increased growth hormone secretion, which may be exacerbated by overweight and which is more marked in females.<sup>6</sup> Overweight and obesity in females are associated with early menarche, which in turn leads to higher adult BMI, greater and more persistent insulin resistance and a more adverse cardiovascular risk profile.<sup>7</sup>

For all these reasons it is difficult to conclude, from the evidence currently available, what influence, if any,

childhood overweight and obesity have on cardiovascular risk, independent of adult obesity. The call by the authors of this systematic review for further large population-based prospective studies that incorporate a contemporary era of children is thus timely. Such studies may help to determine whether there are critical windows during childhood in which increased body fatness might be more influential, such as puberty, and also whether changes from low to high body fatness are important. However, the length of study time required does not sit easily with research funding timetables and the increasing pharmaceutical interventions for cardiovascular risk factors may preclude the definitive study ever being accomplished.

In the interim, there is much evidence to indicate that obesity in childhood exerts an adverse influence on vascular structure and function in childhood itself. Arterial endothelial and smooth muscle dysfunction, both key steps in the development of atherosclerosis, have been observed in obese children<sup>8–11</sup> Obese children show increased arterial stiffness,<sup>8,11</sup> which in adult populations has been shown to be associated with adverse cardiovascular outcomes.<sup>12,13</sup> A number of studies have reported higher IMT in obese compared with lean children and a reduction in IMT occurring with diet, physical activity and/or weight loss.<sup>14–16</sup> These factors, combined with the well-described tracking of obesity into adulthood, the greater clustering of cardiovascular risk factors with increasing levels of childhood obesity, including the presence of proinflammatory factors,<sup>17–19</sup> the presence of significant obesity-related morbidity in childhood, including fatty liver and psychosocial distress<sup>20</sup> and the important independent risk of adult obesity for cardiovascular disease, strongly argue for public health lifestyle interventions to target childhood overweight and obesity decades before the appearance of symptomatic cardiovascular disease.

## Conflict of interest

The authors declare no conflict of interest.

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