Proceedings of the Nutrition Society (2014), **73**, 389–396 doi:10.1017/S0029665114000111

The Nutrition Society Irish Section Meeting was held at the Dublin Institute of Technology, Ireland on 19–21 June 2013

Conference on 'Childhood nutrition and obesity: current status and future challenges' Symposium 3: Effects of early nutrition on later health

Childhood obesity: the impact on long-term risk of metabolic and CVD is not necessarily inevitable

Sarah McMullen

Division of Nutritional Sciences, School of Biosciences, University of Nottingham, Sutton Bonington Campus, Loughborough LE12 5RD, UK

The worldwide prevalence of overweight and obesity in the adult population is estimated to be 35 %. These trends are reflected in childhood obesity prevalence, and the potential impact of early-onset obesity is of great concern. The aim of this review was to investigate the long-term implications of childhood obesity for metabolic and cardiovascular health, focusing on the independent contribution of childhood obesity to adult disease risk, as distinct from associations mediated by tracking of obesity across the lifespan. The data systematically reviewed provide little evidence to suggest that childhood overweight and obesity are independent risk factors for metabolic and cardiovascular risk during adulthood. Instead, the data demonstrate that the relationships observed are dependent on tracking of BMI between childhood and adulthood, alongside persistence of dietary patterns and physical activity. Adjustment for adult BMI uncovers unexpected negative associations between childhood BMI and adult disease, suggesting a protective effect of childhood obesity at any given level of adult BMI. Further work is required to explain these findings, both in terms of pathways and statistical artefacts. To conclude, it must be stressed that it is not suggested that childhood obesity is without negative consequence. Childhood obesity is clearly associated with a range of adverse physical and psychological outcomes. However, the data are important in supporting a positive message that the long-term consequences of childhood obesity are avoidable; and that there remains opportunity for intervention across the lifespan. This nuance in understanding long-term risk is important when considering the effectiveness of interventions at different stages of the lifespan.

Childhood: Obesity: Metabolic syndrome: Cardiovascular disease: Blood pressure

The worldwide prevalence of overweight and obesity in the adult population is currently estimated to be 35 %, rising to over 70 % in some population groups, with rates of obesity nearly doubling between 1980 and 2008[1]. This is a global phenomenon, with the prevalence of overweight and obesity in low- and middle-income countries on the rise, mirroring their transition to the obesogenic environments more commonly associated with 'Western' living. The relationship between obesity and risk of non-communicable disease in adulthood has long been established, with a wealth of evidence demonstrating the considerable impact of excess adiposity on the health and wellbeing of populations[2]. The trends in adult overweight and obesity are reflected in childhood obesity prevalence, and the potential impact of early-onset obesity is of great concern. It has been estimated that 200 million school-aged children were overweight or obese in 2010 worldwide, with a prevalence of >20 % in European states and >30 % in regions of North America[3]. In the UK, the 2007 Foresight report showed that about 8–10 % of girls and boys were obese in 2004, and this was projected to rise to an estimated 25 % by 2050[4]. The present paper considers the long-term implications of childhood obesity for metabolic and

Abbreviations: CIMT, carotid intima media thickness.

Corresponding author: S. McMullen, fax 0844 243 6001, email sarah.mcmullen@nct.org.uk

cardiovascular health, focusing on the independent contribution of childhood obesity to adult disease risk, as distinct from associations mediated by tracking of obesity and dietary-related factors across the lifespan.

Impact of childhood obesity on long-term metabolic and cardiovascular health

A large and consistent body of evidence demonstrates that overweight and obesity during childhood and adolescence have adverse consequences in terms of chronic disease risk in adulthood. This evidence has been systematically reviewed a number of times recently. In 2009, Owen *et al.*[5] reviewed the evidence of an association between BMI in childhood or early adulthood and CHD outcomes in later life, with almost all studies showing a positive association. The authors concluded that BMI from about age 7 years shows a consistently positive relation to risk of CHD in adulthood, which did not appear to be confounded by adult smoking or social class. The authors noted that the independent contribution of early obesity to CHD risk could not be established, as analyses adjusting for the effect of adult BMI were limited and inconclusive. A second systematic review[6] set out with similar objectives, but widened the inclusion criteria to include outcomes related to any adult physical morbidity or premature mortality. Again, the review demonstrated a highly consistent body of evidence that overweight and obesity in childhood and adolescence were associated with increased risk of adult morbidity and mortality, particularly related to cardiometabolic dysfunction. The largest review of this nature[7] brought together thirty-nine studies examining the association between childhood BMI and a variety of adult outcomes, including type-2 diabetes, hypertension, CHD, stroke, asthma, cancer and all-cause mortality. The review found that childhood overweight was consistently associated with increased risk of type-2 diabetes, hypertension, CHD and mortality, whereas evidence for a relationship with stroke outcomes, adult-onset asthma or cancer were mixed and inconclusive.

It is important to note that all three systematic reviews commented on the unknown independent contribution of childhood obesity[5–7], as distinct from the contribution mediated by tracking of BMI from childhood into adult life. Of the studies reported, only a few had adjusted for adult BMI and, where adjustments had been made, the results were found to be inconclusive. Discussion and commentary in this area often stray towards asserting that childhood obesity is an independent risk factor for adult disease, giving the impression of a permanency of effect and weighting the argument for prioritising childhood for weight management interventions. This may at first seem like a subtlety in the reporting of the data, but is in fact very important when considering identification of at-risk groups and the relative impact of the timing of interventions on their long-term effectiveness. The present review will first consider potential mediators of the relationship between childhood obesity and adult disease risk, focusing on the tracking of BMI and related behavioural factors across the lifespan, before reviewing the evidence of an independent association between childhood BMI and adult disease risk.

Tracking of BMI from childhood to adulthood

The associations observed between childhood obesity and adult disease risk are likely to be partially mediated by tracking of BMI from childhood to adulthood, with the increased likelihood that overweight or obese children become overweight or obese adults explaining their increased risk of disease. The extent to which this explains the associations is an important question in terms of the relative contribution of exposures at different stages of the lifespan to risk of disease in adulthood. In 2008, Singh *et al.*[8] published a systematic review of data relating to the persistence of childhood overweight and obesity. Studies were selected if they had a prospective or retrospective longitudinal design, and had taken at least one anthropometric measurement of BMI, skin fold or waist circumference during youth (age ≤18 years) and during adulthood (age ≥19 years). Such data had been collected as part of eighteen different studies and the data published in twenty-five articles. From these, Singh *et al.* extracted estimates of the risk or proportions of overweight youth who went on to become overweight adults and compared these with non-overweight youth. As expected, all studies showed an increased risk for overweight or obese youth to become overweight adults. However, there was considerable variability in the estimated risks, reflecting homogeneity between studies in terms of the anthropometric methods used, the interval between childhood and adulthood measurements, and the criteria used to classify BMI. Based on the high-quality studies, the risk of overweight or obese children or adolescents becoming overweight or obese adults was at least twice as high as their normal-weight counterparts, with the highest relative risk reported being 22·3. The persistence of overweight was generally higher with increasing BMI (i.e. the risk of adult overweight was greater for obese compared with overweight children) and with increasing age (i.e. the risk of adult overweight was greater for overweight and obese adolescents compared with children). The percentage of overweight adolescents becoming overweight adults varied between 22 and 58 %. Overall, the percentage of obese adolescents becoming overweight/obese adults varied between 24 and 90 %. The authors termed the persistence of overweight into adulthood as 'moderate', but also noted that the majority of overweight adults were not overweight during childhood.

It is an inevitable limitation of using longitudinal life-course data that the populations generally are not contemporary. The persistence of overweight in current generations, which have a greater prevalence of obesity[1] and a more obesogenic environment[9], may therefore be greater than that reported to date. However, at present, these data must be relied on to give us the best current estimate of BMI tracking. The moderate level of tracking

of BMI from childhood to adulthood[8] may be explained by a combination of genetic and environmental factors[10–13], and is likely to partially mediate the increased risk of adult disease in those who were overweight in childhood. The genetic influences on adiposity and tracking of BMI across the lifespan are beyond the scope of this review, but have been reviewed elsewhere[13]. The tracking of two key modifiable behaviours related to adiposity will be reviewed briefly, before considering the independent effects of childhood obesity on adult disease risk.

Tracking of obesity-related behaviours from childhood to adulthood

Dietary intake and physical activity are two key modifiable behaviours related to risk of obesity. It is important to consider how these factors track between childhood and adulthood, and therefore contribute to the persistence of overweight and obesity. A recent systematic review[14] identified thirty-eight longitudinal studies, which assessed at least one measure of diet, physical activity or inactivity at baseline (aged <18 years) and at follow-up (at least 5 years after baseline and aged >18 years). The majority of studies investigated tracking of physical activity (twenty-seven papers describing sixteen cohorts) rather than dietary intake (eleven papers describing five cohorts), and these outcomes were generally reported separately. Despite the considerable challenges associated with measuring complex behaviours over time, the review demonstrated clear evidence of tracking of both physical activity and diet between childhood and adulthood, with the strength of tracking of a similar order for both behaviours. The emphasis of the studies included was primarily on cardiovascular risk, with dietary assessment focusing on dietary patterns or specific nutrients rather than the total energy intake *per se*. However, the dietary pattern is predictive of obesity risk, with energy dense, high-fat, low-fibre patterns prospectively associated with excess adiposity during childhood and adolescence[15]. In addition, the dietary pattern data are useful for identifying at-risk groups or overall dietary behaviours to target with intervention[16,17].

Craigie *et al.*[14] identified a clear need for further investigation of tracking of diet and physical activity within the context of obesity risk. Limitations surrounding population dietary assessment and long-term follow-up mean that the evidence base is relatively weak, with several studies having a short follow-up period and inconclusive results. Data from the Young Finns Study enabled the assessment of dietary patterns over a longer-term period of 21 years[18]. The study identified two substantially different dietary patterns, termed 'traditional' and 'health conscious', which were clearly identifiable across the three study points. Food choices expressed as dietary pattern scores showed tracking across the 21-year period (1980–2001), with Spearman's correlation coefficients of about 0·35, reasonable considering the time interval, transition from childhood to adulthood and the short term measurement of food consumption used. Approximately 30–40 % of subjects originally belonging to the extreme quintiles of the energy-adjusted pattern scores persisted in the same quintile 6 and 21 years later. Within this same study population, significant tracking of physical activity and inactivity were also observed from adolescence to young adulthood[19]. Similarly to the tracking of BMI, the strength of tracking of both diet and physical activity was generally greater with increasing age at baseline, suggesting greater stability of obesity-related behaviours from late adolescence *v.* earlier childhood and with shorter interval between baseline and follow-up[14]. Similar findings were observed when investigating the tracking of blood pressure, a key cardiovascular risk factor associated with obesity[20].

Independent effects of childhood obesity on adult disease risk

The data reviewed demonstrate tracking of overweight and obesity, as well as two primary modifiable behaviours related to risk of obesity, from childhood to adulthood[8,14,19], providing a pathway by which the risk of adult disease could originate from childhood. However, it is important to consider whether a component of the association between childhood obesity and adult disease risk could be independent of adult BMI. For example, if overweight or obese children shift to a healthy weight during the late adolescence or the early adulthood period, does their risk reduce to that of healthy-weight adults who have no history of childhood obesity? Similarly, are obese adults who have been obese since childhood at greater risk than those who were a healthy weight during childhood? While not a primary focus of the research reviewed so far, this subtlety in the data is an important point when considering the permanency of effects of childhood dietary behaviours and the relative impact of interventions at different stages of the life-course.

The general concept that the nutritional status during the developmental period can have permanent lifelong consequences is well supported. There is a wealth of information from human epidemiology and animal modelling studies to demonstrate that nutrition during early life can impact on developmental processes in a way that permanently affects the organ structure, physiological function and gene regulation, thereby affecting the risk of developing a range of disease risk factors and outcomes in adult life[21]. However, it remains unclear whether childhood overweight could have similar remodelling effects such that, even if a cohort of overweight children achieved a healthy BMI in adulthood, the increased risk associated with their childhood obesity remained. Previous systematic reviews have clearly demonstrated an association between childhood BMI and adult disease risk, but have also highlighted a gap in the evidence base surrounding the unknown independent contribution of childhood BMI[5–7]. We therefore systematically reviewed the literature with the specific objective of assessing whether the association between childhood BMI and adult disease risk were fully dependent on adult BMI[22,23].

Studies were selected for inclusion in the systematic reviews if they had a measure of BMI in childhood (aged ≤18 years, either classified according to the center for disease control (CDC)[24] or international obesity taskforce cutoffs (IOTF) guidelines[25] or analysed as a continuous variable) and a marker of metabolic or CVD risk or outcome in adult life (age >18 years). Regression coefficients or estimates of relative risk were extracted from each study, and the reviews extended those previously published by explicitly searching for analyses which had adjusted for adult BMI. Reasonable quality was established through the inclusion and exclusion criteria; for example, studies were excluded if they used arbitrary BMI thresholds for overweight and obesity, or if the data were self-reported. However, the quality assessment using the Newcastle–Ottawa Scale[26] identified some reasonably consistent weaknesses. The majority of studies failed to demonstrate that the outcome was not already present during childhood and assessed disease risk markers in the cohort at an adult age which was considered too young for outcomes to be shown adequately. In contrast, those studies which assessed risk markers at an older age or focused on actual disease outcomes or mortality inevitably used populations which were less contemporary. Regression coefficients or estimates of the relative risk could be extracted from all studies, but there was considerable heterogeneity in the data presented. Most notably, 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.

Despite methodological heterogeneity, the findings were relatively consistent. Similarly to other systematic reviews[5–7], the studies consistently showed positive associations between childhood BMI and adult disease risk, across a range of metabolic and cardiovascular measures. However, there was very limited and weak evidence that childhood obesity is an independent risk factor for adult disease. The majority of analyses that adjusted for adult BMI showed attenuation of the associations between childhood BMI and adult disease risk, indicating that the associations were mediated by tracking of BMI from childhood to adulthood.

Peripheral blood pressure was one of the most common risk factors assessed as an outcome in the studies selected. Of the eight studies considering the relationship between childhood BMI and adult blood pressure[27–34], six showed positive associations[27–29,32–34]. However, when adjusted for adult BMI, only two associations remained positive[32,33] and four studies demonstrated significant negative associations (i.e. lower BMI in childhood was associated with greater adult blood pressure)[29,30,32,34]. These included the two studies with the oldest adult cohorts[30,34], which scored well in terms of quality of assessment and would be expected to give a better representation of lifetime risk of developing hypertension. Of the two studies that showed a positive association in the adjusted data set, one had the fewest number of participants and the adult age was young[33]. There were therefore very few hypertensive cases to consider (16/130 men). Six studies considered the association between childhood BMI and carotid intima media thickness (CIMT)[30,35–39], with five of these studies showing a positive association[35–39]. However, after adjusting for adult BMI only one positive association remained, and this was for the cumulative change in BMI from childhood to adulthood[39]. It must be noted that these studies assessed CIMT at a relatively young age in adulthood, so may be limited in their ability to determine the long-term risk associated with childhood obesity. The one exception was the study by Wright *et al.*[30] which measured CIMT at age 50 years and showed no association with childhood BMI. Using data from the Bogalusa Heart Study, Freedman *et al.*[37] showed no relationship between childhood BMI status and adult CIMT among adults who were of normal BMI. Interestingly, those in the 90th centile for CIMT actually had lower BMI up to age 7 years.

Analyses of the association between childhood BMI and circulating biomarkers of metabolic function showed a similar pattern. The relationship with total cholesterol was variable between studies[28–30,40], but both of the analyses which adjusted for adult BMI showed a negative association between the total cholesterol and childhood BMI[29,30]. A positive association between plasma LDL cholesterol and BMI[29], and negative associations between HDL cholesterol and BMI[28,29] were observed, but these were attenuated or reversed in the adjusted data sets. Similarly the data were mixed for TAG in the unadjusted data sets[28–30,41], but only negative associations were reported for data sets adjusted for BMI[29,30]. Three out of six[28–30,42–44] studies looking at insulin concentrations or resistance showed a positive association with childhood BMI[28,29,42], but these were again attenuated or reversed with adjustment for BMI. Similarly to the cardiovascular outcomes, the two studies using older adult cohorts showed negative relationships with childhood BMI[30,43].

The studies which assessed metabolic and CVD outcomes rather than risk factors were of better quality in terms of length of follow-up[45–47]. However, the nature of these studies meant that no adjustments for adult BMI were made. Only one paper used type-2 diabetes mortality as an outcome measure and found no association with childhood BMI status[48]. Mixed results were found for the risk of metabolic syndrome, with the only study to adjust for adult BMI showing a negative association[41].

To summarise, there was very limited and weak evidence that childhood obesity is an independent risk factor for adult disease. Instead, the associations appeared dependent on tracking of BMI from childhood to adulthood, with the majority of studies which adjusted for adult BMI showing attenuation or reversal of the associations observed. This conclusion has been supported by a more recent review[7], which set out with similar objectives and included a wider spectrum of adult disease (e.g. asthma and cancers). Interestingly, the analyses adjusted for adult BMI were more suggestive of an inverse association between childhood BMI and adult disease risk factors[22,23]. Children at the lower end of the BMI range appeared most susceptible to the metabolic risks associated with adult obesity, including

dyslipidaemia, elevated blood pressure (and, less convincingly, insulin resistance). Additionally obese adults appeared more likely to exhibit healthier metabolic profiles if they were also obese in childhood, with childhood obesity conferring a protective effect if BMI was reduced in adulthood.

While these patterns in the data became clear after systematically extracting unadjusted and adjusted data sets for the purpose of review, there is very little comment on the attenuated or negative associations in the individual papers or narrative reviews on the subject. Interpretation or reporting bias seems implicit in driving the focus on the more intuitive positive associations between childhood obesity and adult disease risk in the unadjusted data sets.

Statistical considerations: the reversal paradox

In highlighting the predominance of negative associations in the adjusted data sets, it must be noted that there are potential analytical issues associated with the use of statistical adjustment for an exposure measure in this way. Anthropometric measures are often considered to be confounders for health-related outcomes, with regression analyses adjusted accordingly. However, in many instances, body weight or BMI are not true confounders but part of the causal pathway between exposure and outcome[49]. In the data sets being discussed in this review, adjusted and unadjusted effect estimates are being compared which distinguish the indirect effect of childhood BMI (i.e. acting through adult BMI as the specified intermediate) from its direct effects (i.e. acting via pathways independent of adult BMI). Using this method of decomposition of effects[50], if adjustment for the proposed intermediate exposure greatly attenuates the association between exposure and outcome, it is inferred that the exposure's effect is mediated predominantly through a pathway involving that intermediate. If minimal attenuation is observed, it is assumed that the exposure is acting through pathways which are independent of the proposed intermediate, in this case adult BMI. However, there are potential issues with the use of statistical adjustment in this way, as demonstrated in a noteworthy statistical simulation experiment conducted by Tu *et al.*[51]. Computer simulations of three hypothetical relations between birth-weight and adult blood pressure were used to investigate the effect of statistically adjusting for adult weight, as a potential mediator of the relationship. An association between birth weight and blood pressure could be induced, exaggerated or reversed by adjustment for adult body weight, depending on the simulated direction of the unadjusted association and the strength of the correlations between adult body weight and exposure or outcome. Of particular relevance to the data sets systematically reviewed by ourselves, the simulated modest positive relationship between birthweight and blood pressure (Scenario 3) could be reversed by strengthening the correlations between these variables and the proposed intermediate adult weight. Given the strength of association between adult BMI and CVD risk factors, it is plausible that the associations between childhood BMI and CVD risk factors could be at risk of the same reversal paradox when adjustments for adult BMI are made. Therefore, while the data are clear in terms of demonstrating an attenuation of the association between childhood BMI and adult CVD risk when adjusting for adult BMI, the reverse associations observed must be interpreted with caution.

Could childhood obesity be protective at a given level of adult BMI?

Although the inverse associations between childhood BMI and adult disease risk that are observed after adjustment for adult BMI are somewhat counterintuitive, it is important not to perpetuate any interpretation bias by only attempting to explain them as a possible statistical artefact. It is known that there are considerable variations between individuals in the level of adiposity at which insulin resistance is exhibited; some relatively lean individuals are insulin resistant, whereas some very obese individuals are not[52]. Obese individuals who present as 'metabolically normal' are of considerable interest, with 16·6 % of obese adults categorised as metabolically healthy using relatively stringent criteria[53]. Uncertainty surrounds the important question of what determines the point at which an otherwise 'healthy' storage tissue begins to promote the development of components of the metabolic syndrome. Importantly for the research questions being examined in this review, metabolically normal obesity has been associated with an earlier onset of obesity[54] and insulin resistance has been found to be progressively lower with longer duration of obesity[55]. These studies were based on small samples of the population, but the data are consistent with the hypothesis that childhood obesity may offer protection against the metabolic effects of obesity in adulthood. Adipocyte size is inversely related to insulin sensitivity[56] and risk of type II diabetes[57]. Obese individuals with relatively few large adipocytes exhibit lower insulin sensitivity than those with the same degree of obesity but many small fat cells[56,57]. Of particular relevance to this project is the evidence that obesity with relatively small adipocytes has been associated with onset during childhood[58]. Adipocyte number, size and relative distribution between different adipose tissue depots are all therefore implicated in determining the metabolic consequences of a positive energy imbalance. The mechanisms responsible for the development of different patterns of adipose morphology are unknown. It is of particular interest that these are related to early life factors, but further research is required to understand the influence of excess adiposity during childhood on adipocyte number, size and relative distribution between depots.

Methodological considerations: sampling and assessment

Given the long-term nature of the associations being examined in this literature, it is inevitable that the childhood assessments were made in cohorts studied before

the current obesity epidemic. It has been shown that the persistence of overweight between childhood and adulthood is generally higher with increasing childhood BMI[8]. Widespread and extreme obesity are more common now[1], combined with an obesogenic environment[9]; so current estimates may underestimate the strength of tracking of obesity between childhood and adulthood in contemporary populations. Additionally, research has demonstrated that many obese children already manifest some metabolic complications, including impaired glucose tolerance, dyslipidaemia, hypertension, fatty liver disease and systemic low-grade inflammation[59–61]. Cross-sectional analysis of obese children showed that the prevalence of metabolic syndrome increased directly with the degree of obesity[60], with levels of insulin resistance exacerbated by increased deposition of lipid in the visceral and intramyocellular compartments at any given BMI[62]. While the reviewed data sets only provide weak evidence that an association between childhood and adult disease risk exists independently of adult BMI, it remains a possibility that the levels of childhood obesity in contemporary society may have a greater permanency of effect. Increased understanding of the particular phenotypic characteristics, which are associated with the presence of obesity-related cardiometabolic dysfunction during childhood and adolescence itself remains an important area of research.

Another limitation of the majority of longitudinal cohort studies published to date is that they rely on BMI data as a measure of adiposity, when it is known to reflect both fat and fat-free mass. This is a particularly important point when considering the association between BMI and metabolic disease, given the opposing influences which abdominal adipose tissue and skeletal muscle have on insulin sensitivity and glucose disposal[63]. BMI is also highly age-dependent in children, with a progressive increase in lean (as well as fat) mass throughout childhood and adolescence[64]. Interestingly, Wright *et al.*[30] showed a relatively weak correlation between childhood and adulthood BMI, likely to reflect the increasing contribution of other factors to adult body composition as the follow-up period lengthens. This study also found that percentage body fat during adulthood was not associated with childhood BMI, despite childhood and adult BMI being correlated. Overrepresentation of children with a lower lean body mass at the lower end of the BMI scale may complicate interpretation of the associations observed, given the known tracking of build[64] and involvement of lean mass in glucose metabolism[63].

Conclusion

The data reviewed provide little evidence to suggest that childhood overweight and obesity is an independent risk factor for metabolic and cardiovascular risk during adulthood, and that which does exist should be considered weak. Instead, the data demonstrate that the relationships observed are dependent on tracking of BMI between childhood and adulthood, alongside persistence of dietary and physical activity behaviours. Adjustment for adult BMI uncovers unexpected negative associations between childhood BMI and adult risk factors, suggesting a protective effect of childhood obesity at any given level of adult BMI. Further investigation is required to explain these findings, both in terms of potential biological pathways and statistical artefacts. It is important to stress at this point that it is not being suggested that childhood obesity is without negative consequence. Childhood obesity is clearly associated with a range of adverse physical, psychological and social outcomes[7,59–61,65]. In addition, the tracking of adiposity and related behaviours from childhood to adulthood increases the risk of morbidity and mortality related to chronic disease in adulthood. However, the data are important in supporting the positive message that the long-term consequences of childhood obesity are avoidable; and that there remains opportunity for intervention across the lifespan. This is in contrast to the notion that childhood obesity has permanent irreversible effects on cardiovascular health, and supports the well-established evidence that weight loss in adulthood can lead to important positive health outcomes. This nuance in understanding long-term risk is particularly important when considering the effectiveness of interventions at different stages of the lifespan. Using an established risk factor focused modelling tool Dynamic Modelling for Health Impact Assessment, it has been demonstrated that reducing obesity prevalence in adulthood has much greater outcomes in terms of chronic disease and life expectancy than the same reduction in obesity prevalence during childhood[66]. In addition, the health gains associated with a large reduction in childhood obesity were offset by a relatively small increase in risk of becoming overweight or obese in adulthood. It is important to target interventions to the stages of the life-course at which they are most likely to be effective and which offer the best long-term benefits. This has to be balanced against the potential for negative consequences if the timing of intervention coincides with critical stages of neurological, behavioural and physical developments. Understanding the pathways by which childhood obesity influences long-term disease risk will help inform the design and focus the targets of health promotion programmes during these sensitive stages.

Acknowledgements

The two systematic reviews conducted by the author were in collaboration with Dr Louise Lloyd and Professor Simon Langley-Evans at the University of Nottingham. The author would also like to thank the other colleagues in the School of Biosciences at the University of Nottingham for their discussion around the theories in this review paper, in particular Professor Michael Lomax, Dr John Brameld and Professor Andrew Salter.

Financial Support

The two systematic reviews discussed in this review were originally funded by the Rank Prize Funds.

Conflicts of Interest

None.

Authorship

The author was solely responsible for all aspects of preparation of this paper.

References

1. World Health Organisation. World Health Statistics 2013. http://www.who.int/gho/publications/world_health_statistics/2013/en/index.html (accessed 14 November 2013).
2. Visscher TLS & Seidell JC (2001) The public health impact of obesity. *Annu. Rev Public Health* **22**, 355–375.
3. International Association for the Study of Obesity (2012) http://www.iaso.org/iotf/obesity/obesitytheglobalepidemic/ (accessed 14 November 2013).
4. Foresight (2008) *Tackling Obesities: Future Choices – Project Report*, 2nd ed. London: The Stationery Office, UK.
5. Owen CG, Whincup PH, Orfei L *et al.* (2009) Is body mass index before middle age related to coronary heart disease risk in later life? Evidence from observational studies. *Int J Obes* **33**, 866–877.
6. Reilly JJ & Kelly J (2011) Long-term impact of overweight and obesity in childhood and adolescence on morbidity and premature mortality in adulthood: systematic review. *Int J Obes* **35**, 891–898.
7. Park MH, Falconer C, Viner RM *et al.* (2012) The impact of childhood obesity on morbidity and mortality in adulthood: a systematic review. *Obes Rev* **13**, 985–1000.
8. Singh AS, Mulder C, Twisk JWR *et al.* (2008) Tracking of childhood overweight into adulthood: a systematic review of the literature. *Obes Rev* **9**, 474–488.
9. Lobstein T (2008) Child obesity: what can be done and who will do it? *Proc Nutr Soc* **67**, 301–306.
10. Silventoinen K, Bartels M, Posthuma D *et al.* (2007) Genetic regulation of growth in height and weight from 3 to 12 years of age: a longitudinal study of Dutch twin children. *Twin Res Hum Genet* **10**, 354–363.
11. Haworth CMA, Carnell S, Meaburn EL *et al.* (2008) Increasing heritability of BMI and stronger associations with the FTO gene over childhood. *Obesity* **16**, 2663–2668.
12. Wardle J, Carnell S, Haworth CMA *et al.* (2008) Evidence for a strong genetic influence on childhood adiposity despite the force of the obesogenic environment. *Am J Clin Nutr* **87**, 398–404.
13. Silventoinen K & Kaprio J (2009) Genetics of tracking of body mass index from birth to late middle age: evidence from Twin and Family Studies. *Obes Facts* **2**, 196–202.
14. Craigie AM, Lake AA, Kelly SA *et al.* (2011) Tracking of obesity-related behaviours from childhood to adulthood: a systematic review. *Maturitas* **70**, 266–284.
15. Ambrosini GL, Emmett PM, Northstone K *et al.* (2012) Identification of a dietary pattern prospectively associated with increased adiposity during childhood and adolescence. *Int J Obes* **36**, 1299–1305.
16. van Dam RM (2005) New approaches to the study of dietary patterns. *Br J Nutr* **93**, 573–574.
17. Slattery ML (2008) Defining dietary consumption: is the sum greater than its parts? *Am J Clin Nutr* **88**, 14–15.
18. Mikkila V, Rasanen L, Raitakari OT *et al.* (2005) Consistent dietary patterns identified from childhood to adulthood: the cardiovascular risk in young Finns study. *Br J Nutr* **93**, 923–931.
19. Raitakari OT, Porkka KVK, Taimela S *et al.* (1994) Effects of persistent physical activity and inactivity on coronary risk-factors in children and young adults – the cardiovascular risk in young Finns study. *Am J Epidemiol* **140**, 195–205.
20. Chen X & Wang Y (2008) Tracking of blood pressure from childhood to adulthood – a systematic review and meta-regression analysis. *Circulation* **117**, 3171–3180.
21. Langley-Evans SC & McMullen S (2010) Developmental origins of adult disease. *Med Princ Pract* **19**, 87–98.
22. Lloyd LJ, Langley-Evans SC & McMullen S (2010) Childhood obesity and adult cardiovascular disease risk: a systematic review. *Int J Obes* **34**, 18–28.
23. Lloyd LJ, Langley-Evans SC & McMullen S (2012) Childhood obesity and risk of the adult metabolic syndrome: a systematic review. *Int J Obes* **36**, 1–11.
24. Kuczmarski RJ, Ogden CL, Grummer-Strawn LM *et al.* (2000) CDC growth charts: United States. *Adv Data* **314**, 1–27.
25. Cole TJ, Bellizzi MC, Flegal KM *et al.* (2000) Establishing a standard definition for child overweight and obesity worldwide: international survey. *BMJ* **320**, 1240–1243.
26. Wells GASB, O'Connell D, Peterson J *et al.* (2013) The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp (accessed 14 November 2013).
27. Lauer RM & Clarke WR (1989) Childhood risk-factors for high adult blood pressure – the Muscatine Study. *Pediatr* **84**, 633–641.
28. Sinaiko AR, Donahue RP, Jacobs DR *et al.* (1999) Relation of weight and rate of increase in weight during childhood and adolescence to body size, blood pressure, fasting insulin, and lipids in young adults – the Minneapolis Children's Blood Pressure Study. *Circulation* **99**, 1471–1476.
29. Freedman DS, Khan LK, Dietz WH *et al.* (2001) Relationship of childhood obesity to coronary heart disease risk factors in adulthood: the Bogalusa Heart Study. *Pediatrics* **108**, 712–718.
30. Wright CM, Parker L, Lamont D *et al.* (2001) Implications of childhood obesity for adult health: findings from thousand families cohort study. *BMJ* **323**, 1280–1284.
31. Burke V, Beilin LJ, Dunbar D *et al.* (2004) Associations between blood pressure and overweight defined by new standards for body mass index in childhood. *Prev Med* **38**, 558–564.
32. Hardy R, Wadsworth ME, Langenberg C *et al.* (2004) Birthweight, childhood growth, and blood pressure at 43 years in a British birth cohort. *Int J Epidemiol* **33**, 121–129.
33. Field AE, Cook NR & Gillman MW (2005) Weight status in childhood as a predictor of becoming overweight or hypertensive in early adulthood. *Obes Res* **13**, 163–169.
34. Li L, Law C & Power C (2007) Body mass index throughout the life-course and blood pressure in mid-adult life: a birth cohort study. *J Hypertens* **25**, 1215–1223.
35. Oren A, Vos LE, Uiterwaal CS *et al.* (2003) Change in body mass index from adolescence to young adulthood and increased carotid intima-media thickness at 28 years of age: the Atherosclerosis Risk in Young Adults study. *Int J Obes Relat Metab Disord* **27**, 1383–1390.
36. Raitakari OT, Juonalta M, Viikari JS *et al.* (2003) Cardiovascular risk factors in childhood as predictors of

carotid artery intima-media thickness in adulthood. *Circulation* **108**, 719–720.
37. Freedman DS, Dietz WH, Tang R *et al.* (2004) The relation of obesity throughout life to carotid intima-media thickness in adulthood: the Bogalusa Heart Study. *Int J Obes Relat Metab Disord* **28**, 159–166.
38. Juonala M, Raitakari M, SAV J *et al.* (2006) Obesity in youth is not an independent predictor of carotid IMT in adulthood. The Cardiovascular Risk in Young Finns Study. *Atherosclerosis* **185**, 388–393.
39. Freedman DS, Patel DA, Srinivasan SR *et al.* (2008) The contribution of childhood obesity to adult carotid intima-media thickness: the Bogalusa Heart Study. *Int J Obes* **32**, 749–756.
40. Lauer RM, Lee J & Clarke WR (1988) Factors affecting the relationship between childhood and adult cholesterol levels – the Muscatine Study. *Pediatrics* **82**, 309–318.
41. Salonen MK, Kajantie E, Osmond C *et al.* (2009) Role of childhood growth on the risk of metabolic syndrome in obese men and women. *Diabetes Metab* **35**, 94–100.
42. Freedman DS, Khan LK, Serdula MK *et al.* (2004) Inter-relationships among childhood BMI, childhood height, and adult obesity: the Bogalusa Heart Study. *Int J Obes* **28**, 10–16.
43. Martin RM, Holly JMP, Smith GD *et al.* (2006) Associations of adiposity from childhood into adulthood with insulin resistance and the insulin-like growth factor system: 65-year follow-up of the Boyd Orr cohort. *J Clin Endocrinol Metab* **91**, 3287–3295.
44. Thearle MSBJC, Knowler WC & Krakoff J (2009) Childhood predictors of adult acute insulin response and insulin action. *Diab Care* **32**, 938–943.
45. Eriksson JG, Forsen T, Tuomilehto J *et al.* (1999) Catch-up growth in childhood and death from coronary heart disease: longitudinal study. *BMJ* **318**, 427–431.
46. Lawlor DA & Leon DA (2005) Association of body mass index and obesity measured in early childhood with risk of coronary heart disease and stroke in middle age – findings from the Aberdeen children of the 1950s prospective cohort study. *Circulation* **111**, 1891–1896.
47. Lawlor DA, Martin RM, Gunnell D *et al.* (2006) 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 studies. *Am J Clin Nutr* **83**, 767–773.
48. Bjorge T, Engeland A, Tverdal A *et al.* (2008) Body mass index in adolescence in relation to cause-specific mortality: a follow-up of 230,000 Norwegian adolescents. *Am J Epidemiol* **168**, 30–37.
49. Kirkwood B & Sterne J (2003) *Medical Statistics*, 2nd ed. London, UK: Blackwell.
50. Kaufman JS, Maclehose RF & Kaufman S (2004) A further critique of the analytic strategy of adjusting for covariates to identify biologic mediation. *Epidemiol Perspect Innov* **1**, 4.
51. Tu YK, West R, Ellison GTH *et al.* (2005) Why evidence for the fetal origins of adult disease might be a statistical artifact: the "reversal paradox" for the relation between birth weight and blood pressure in later life. *Am J Epidemiol* **161**, 27–32.
52. Bonora E, Kiechl S, Willeit J *et al.* (1998) Prevalence of insulin resistance in metabolic disorders – The Bruneck Study. *Diabetes* **47**, 1643–1649.
53. Wildman RP, Muntner P, Reynolds K *et al.* (2008) The obese without cardiometabolic risk factor clustering and the normal weight with cardiometabolic risk factor clustering: prevalence and correlates of 2 phenotypes among the US population (NHANES 1999–2004). *Arch Intern Med* **168**, 1617–1624.
54. Brochu M, Tchernof A, Dionne IJ *et al.* (2001) What are the physical characteristics associated with a normal metabolic profile despite a high level of obesity in postmenopausal women? *J Clin Endocrinol Metab* **86**, 1020–1025.
55. Muscelli E, Camastra S, Gastaldelli A *et al.* (1998) Influence of duration of obesity on the insulin resistance of obese non-diabetic patients. *Int J Obes Relat Metab Disord* **22**, 262–267.
56. Lundgren M, Svensson M, Lindmark S *et al.* (2007) Fat cell enlargement is an independent marker of insulin resistance and 'hyperleptinaemia'. *Diabetologia* **50**, 625–633.
57. Weyer C, Foley JE, Bogardus C *et al.* (2000) Enlarged subcutaneous abdominal adipocyte size, but not obesity itself, predicts type II diabetes independent of insulin resistance. *Diabetologia* **43**, 1498–1506.
58. Salans LB, Cushman SW & Weismann RE (1973) Studies of human adipose tissue. Adipose cell size and number in nonobese and obese patients. *J Clin Invest* **52**, 929–941.
59. Ford ES (2003) C-reactive protein concentration and cardiovascular disease risk factors in children: findings from the National Health and Nutrition Examination Survey 1999–2000. *Circulation* **108**, 1053–1058.
60. Weiss R, Dziura J, Burgert TS *et al.* (2004) Obesity and the metabolic syndrome in children and adolescents. *N Engl J Med* **350**, 2362–2374.
61. Bell LM, Byrne S, Thompson A *et al.* (2007) Increasing body mass index z-score is continuously associated with complications of overweight in children, even in the healthy weight range. *J Clin Endocrinol Metab* **92**, 517–522.
62. Weiss R, Taksali SE, Dufour S *et al.* (2005) The 'obese insulin-sensitive' adolescent: importance of adiponectin and lipid partitioning. *J Clin Endocrinol Metab* **90**, 3731–3737.
63. Galgani JE, Moro C & Ravussin E (2008) Metabolic flexibility and insulin resistance. *Am J Physiol Endocrinol Metab* **295**, E1009–1017.
64. McCarthy HD, Samani-Radia D, Jebb SA *et al.* (2013) Skeletal muscle mass reference curves for children and adolescents. *Pediatr Obes*. DOI: 10.1111/j.2047-6310.2013.00168.
65. Puhl RM & Latner JD (2007) Stigma, obesity, and the health of the nation's children. *Psychol Bull* **133**, 557–580.
66. Lhachimi SK, Nusselder WJ, Lobstein TJ *et al.* (2013) Modelling obesity outcomes: reducing obesity risk in adulthood may have greater impact than reducing obesity prevalence in childhood. *Obes Rev* **14**, 523–531.