Papers

Being big or growing fast: systematic review of size and growth in infancy and later obesity
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Abstract

Objectives To assess the association between infant size or growth and subsequent obesity and to determine if any association has been stable over time.

Design Systematic review.

Data sources Medline, Embase, bibliographies of included studies, contact with first authors of included studies and other experts.

Inclusion criteria Studies that assessed the relation between infant size or growth during the first two years of life and subsequent obesity.

Main outcome measure Obesity at any age after infancy.

Results 24 studies met the inclusion criteria (22 cohort and two case-control studies). Of these, 18 assessed the relation between infant size and subsequent obesity, most showing that infants who were defined as "obese" or who were at the highest end of the distribution for weight or body mass index were at increased risk of obesity. Compared with non-obese infants, in those who had been obese odds ratios or relative risks for subsequent obesity ranged from 1.35 to 9.38. Ten studies assessed the relation of infant growth with subsequent obesity and most showed that infants who grew more rapidly were at increased risk of obesity. Compared with other infants, in infants with rapid growth odds ratios and relative risks of later obesity ranged from 1.17 to 5.70. Associations were consistent for obesity at different ages and for people born over a period from 1927 to 1994.

Conclusions Infants who are at the highest end of the distribution for weight or body mass index or who grow rapidly during infancy are at increased risk of subsequent obesity.

Introduction

Levels of overweight and obesity have increased markedly during the past decade in all age groups. The UK government has set a target to halt the year on year increase in obesity in children aged ≤11 by 2010 as part of an overall strategy to tackle the rising prevalence of obesity in the population. Given the lack of evidence of effective treatments, action to achieve this target must focus mainly on prevention. It is not clear, however, how early in life prevention could begin.

Observational evidence suggests that faster growth during childhood is associated with an increased risk of obesity in later life, suggesting that interventions aimed at modifying childhood growth could prevent adult obesity. Recent studies in the US and Finland have shown that patterns of growth during infancy may be associated with both childhood and adult obesity, suggesting the potential for intervention during infancy. The precise patterns of growth leading to obesity are unclear and both infant size and infant growth have been implicated.

We carried out a systematic review to assess the association between infant growth and subsequent obesity and to establish whether groups of infants with particular patterns of growth are at greater risk. We considered both size and growth because each is important in understanding the growth status of an infant—for example, an infant may be small but be growing rapidly. Given secular trends in children's growth, we also assessed whether any associations identified in the past are likely to apply to infants now.

Methods

This research was part of a wider review of scientific evidence on infant growth and health and wellbeing throughout the life course, which was carried out alongside a review of lay perspectives on infant size and growth, supplemented by individual and focus group interviews (J Baird et al, Defining optimal infant growth for lifetime health: a systematic review of lay and scientific literature (unpublished report)).

We sought studies that described the relation between any aspect of infant growth or size and the development of overweight or obesity at any later age. Studies of infant size were eligible for inclusion if they reported at least one measurement of infant size between 3 months and 2 years. We included studies of infant growth if they reported at least two measurements of size up to 2 years, of which at least one was between 3 months and 2 years.

The outcomes we considered were overweight or obesity. We did not specify a definition of obesity as studies may have been published before currently accepted definitions were introduced. We did not impose any limits in relation to language, study timing, or setting.

We searched Medline and Embase from their start dates to June 2005 and hand searched the bibliographies of all included studies. We also contacted first authors of included studies and other experts to identify further published or unpublished analyses.

We followed the methods recommended by the Centre for Reviews and Dissemination. Study quality was assessed by using a checklist and summarised as to whether there was a low, medium, or high risk of bias for study results. The confounding factors we considered important in the relation between infant size or growth and obesity were socioeconomic status, parental size, and method of infant feeding.
Papers

Our approach to synthesis was mainly narrative but we explored the potential for meta-analysis according to standard procedures.10

Results

We identified 27,949 references. Screening of abstracts and reference lists identified 24 studies that met our inclusion criteria. All 24 studies were observational (22 cohort studies and two case-control). All but two studies were based in developed countries.

We considered that 15 studies were at medium risk of bias, six at high risk, and three at low risk. Common sources of bias were insufficient description of participants, high rates of attrition, and inadequate consideration of confounding factors.

Studies of infant size

Eighteen studies assessed the relation between infant size and obesity at ages ranging from 3 to 35 years (table 1). Most focused on "infant obesity" defined in various ways or on infants at the highest end of the distribution of weight or body mass index. Year of birth of infants was 1927 to 1992. Sixteen were cohort studies, two were case-control studies, and all but one were set in developed countries.

Eleven studies described infant obesity with varying definitions based on body mass index,11–13 weight, weight for height,16–25 or skinfold thickness21 (table 1). When reporting the findings of these studies we have used the term infant obesity to describe exposure status, though we recognise that the definition of infant obesity is controversial. The seven other studies assessed infant size in terms of weight,21–24 weight for height,24,25 or body mass index21 without using a definition of infant obesity.

All studies used centile points in body mass index, skinfolds, weight for height, or a clinical definition to define obesity as an outcome. Six studies focused on obesity in childhood up to the age of 10; four of these defined obesity according to weight for height17–20,25 and two according to body mass index.21,25 Five studies focused on obesity in adolescence (9–18 years), three defining obesity by body mass index,14,15,16 and two using weight.21,25 Seven studies described adult obesity, four using body mass index to define obesity11–13,25 and three using weight or skinfold thickness measurements.16,21,24 Most of the studies in adults were of those aged 20–35 years.

Table 1 Summary data extracted from studies of infant size, ordered by year of birth

<table>
<thead>
<tr>
<th>Study</th>
<th>No of subjects, year of birth</th>
<th>Measure of infant size</th>
<th>Definition of obesity</th>
<th>Analysis</th>
<th>Size of effect</th>
<th>Risk of bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mosberg (1989)7 Stockholm, Sweden</td>
<td>27 (sex not reported), 1927-47</td>
<td>BMI at 7th centile v 50th centile</td>
<td>Weight for height SD scores at 40-50 years v reference population</td>
<td>Weight for height SD scores with obesity reported in infancy and at follow-up in adulthood</td>
<td>SD scores (SE of mean): 2.3 (0.31) on admission; 1.8 (0.46) in late childhood; 0.2 (0.28) in adulthood (40-50 years)</td>
<td>High</td>
</tr>
<tr>
<td>Guo (1984)8 USA</td>
<td>555 (50% male), 1929-60</td>
<td>BMI at 5th and 95th centile</td>
<td>Logistic regression giving odds ratio for overweight in adulthood higher BMI centile in infancy v lower one (50th, 75th centiles used)</td>
<td>Odds ratios (95% CI): 1.0 at 1 year (0.99 to 2.21) for males, 1.5 (1.01 to 2.35) for females; at 2 years 1.63 (1.04 to 2.54) for males, 1.51 (0.96 to 2.38) for females</td>
<td>Medium</td>
<td></td>
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<tr>
<td>Eriksson (2000)9 Helsinki, Finland</td>
<td>2135 male, 2380 female, 1933-44</td>
<td>Maximum lifetime risk of obesity defined as BMI &gt;30 kg/m2 at 60-70 years</td>
<td>Incidence (%) of adult obesity in each of four BMI categories at 6 months</td>
<td>Cumulative incidence (95% CI): males: 28.6 (24.1 to 33.1) in lowest 6 month group (&lt;16.3 kg/m2), 44.1 (40.0 to 48.5) in highest 6 month group (&gt;18.0 kg/m2), P&lt;0.0001 for trend; females: 27.5 (23.8 to 31.3) in lowest 6 month group (&lt;16.3 kg/m2), 36.8 (32.0 to 41.7) in highest 6 month group (&gt;18.0 kg/m2), P&lt;0.001 for trend</td>
<td>Medium</td>
<td></td>
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<tr>
<td>Head (1965)10 Washington DC; Massachusetts, USA</td>
<td>158 cases, 94 controls (all female), 1945-50</td>
<td>1 year weight (lb)</td>
<td>Cases (clinically obese) and controls (not obese) at mean age 15 years</td>
<td>Mean values for infant size reported for cases and controls, with SDs and t tests for differences</td>
<td>Mean difference in 1 year weight (lb): cases-controls 1.446 (P=0.009)</td>
<td>High</td>
</tr>
<tr>
<td>Chamney (1978)11 Rochester, USA</td>
<td>366 (sex not reported), 1945-55</td>
<td>Infant obesity: weight centile &gt;90th at 3 and 6 months</td>
<td>Weight ≥20% above mean for height and age 20-30 years</td>
<td>Contingency tables of heavy, average, and light infants and underweight, normal, overweight, and obese adults, from which relative risks of adult obesity in &quot;obese&quot; v non-obese infants were derived</td>
<td>Relative risks: 1.63 (1.14 to 2.33) for unadjusted (n=366), 1.81 (0.96 to 3.44) for neither parent overweight (n=225), 3.37 (1.69 to 6.70) for at least one parent overweight (n=110), and 2.51 (2.25 to 2.80) for combined (n=335)</td>
<td>High</td>
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<tr>
<td>Asher (1966)12 Birmingham, UK</td>
<td>137 (sex not reported); 21 cases, 24 controls, 1950</td>
<td>Infant obesity: weight &gt;90th centile at 6 months; &gt;90th centile at 1 year</td>
<td>Childhood obesity: weight &gt;90th centile at 3-5 years; weight &gt;97th centile at 5 years</td>
<td>Relative risk for child obesity in &quot;obese&quot; v non-obese infants</td>
<td>Relative risk: 2.33 (0.52 to 167) for weight &gt;90th centile at 3-5 years; 6.56 (2.90 to 14.8) for weight &gt;97th centile at 5 years</td>
<td>High</td>
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<tr>
<td>Rolland-Cachera (1987)13 France</td>
<td>164 (52% male), 1950</td>
<td>Infant obesity: BMI &gt;75th centile at 1 year</td>
<td>BMI &gt;75th centile: &gt;23.4 kg/m2 (men) or &gt;22.3kg/m2 (women) at 21 years</td>
<td>Relative risk of obesity at 21 years in &quot;obese&quot; v non-obese infants</td>
<td>Relative risk (95% CI): 2.76 (1.32 to 5.77)</td>
<td>Medium</td>
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<tr>
<td>Garn (1985)14 Tecumseh, USA</td>
<td>129 (29% male), 1957-60</td>
<td>Infant obesity at 1 or 2 years: triceps skinfold &gt;85th centile for age/sex. Same definition for subcapsular skinfold.</td>
<td>Same definitions as for infancy at 21-22 years</td>
<td>Percentage of &quot;obese&quot; infants who remained obese 20 years later, with P value for deviation from chance figure of 15% (with binomial test)</td>
<td>Percentage of obese infant (triceps) 33.3% (P&lt;0.01) at 1-2 years; 18.2% (P=0.07) at 2-22 years; percentage of obese infant (subcapsular) 33.3% (P&lt;0.01) at 1-2 years; 20.0% (P=0.66) at 2-22 years</td>
<td>Medium</td>
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<tr>
<td>Johnston (1978)15 Philadelphia, USA</td>
<td>288 (51% male), 1958-65</td>
<td>Relative weight, weight for height ≥1 SD at 1 year (high v low) v ≤1 SD at 1 year (low)</td>
<td>At 8-15 years: relative weight (predicted weight/actual weight) ≥120%, triceps skinfold &gt;90th centile for age, sex/race</td>
<td>Relative risk of obesity at ages 9-15 years, according to whether subjects had high or low relative weight or skinfold thickness at 1 year, stratified for sex</td>
<td>Relative risk (95% CI): for relative weight 3.75 (1.15 to 6.54) for males, 4.06 (2.52 to 6.35) for females; for triceps skinfold 2.97 (2.03 to 4.35) for males, 2.70 (2.14 to 4.71) for females</td>
<td>Medium</td>
</tr>
</tbody>
</table>
There was considerable consistency in study findings. Eleven studies found that infants who were heavier during infancy or were defined as obese were more likely to develop obesity in childhood,\(^1\) \(^2\) \(^4\) \(^6\) \(^11\) \(^22\) \(^28\) \(^32\) adolescence,\(^14\) \(^15\) \(^16\) \(^20\) and adulthood.\(^17\) \(^18\) \(^19\)

Six studies related infant size to obesity in childhood. Four found that infants who had been obese\(^16\) \(^24\) \(^25\) or who were in the highest end of the distribution for weight\(^16\) \(^25\) were more likely to be obese at age 5-7 years than non-obese infants, with odds ratios ranging from 1.50 to 9.38. Three of the studies were based on cohorts of children born since 1985,\(^1\) \(^6\) \(^19\) \(^22\) \(^28\) \(^32\) The fourth was of children born between 1968 and 1970, suggesting that these relations have been consistent over time.\(^1\) Of the two other studies in childhood, one study failed to show an association.\(^2\) The other study failed to show an association in the overall sample, though not significant, was consistent with the findings of the other studies.\(^1\)

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Of the seven studies in adulthood, three reported significant associations between infant size and later obesity. Two studies showed that obese infants were more likely to be obese as young adults at ages 20-30 years than non-obese infants\(^1\) \(^6\) \(^16\) and the third found that larger size at 6 months of age was associated with increased lifetime risk of obesity.\(^1\) The findings of three other studies of adults suggested a positive relation between infant size and later obesity. Two studies showed that obese infants were more likely to be obese as young adults at ages 20-30 years than non-obese infants\(^1\) \(^6\) \(^16\) and the third found that larger size at 6 months of age was associated with increased lifetime risk of obesity.\(^1\) The findings of three other studies of adults suggested a positive relation between infant size and later obesity. Two studies showed that obese infants were more likely to be obese as young adults at ages 20-30 years than non-obese infants\(^1\) \(^6\) \(^16\) and the third found that larger size at 6 months of age was associated with increased lifetime risk of obesity.\(^1\) The findings of three other studies of adults suggested a positive relation between infant size and later obesity. Two studies showed that obese infants were more likely to be obese as young adults at ages 20-30 years than non-obese infants\(^1\) \(^6\) \(^16\) and the third found that larger size at 6 months of age was associated with increased lifetime risk of obesity.\(^1\) The findings of three other studies of adults suggested a positive relation between infant size and later obesity. Two studies showed that obese infants were more likely to be obese as young adults at ages 20-30 years than non-obese infants\(^1\) \(^6\) \(^16\) and the third found that larger size at 6 months of age was associated with increased lifetime risk of obesity.\(^1\) The findings of three other studies of adults suggested a positive relation between infant size and later obesity. Two studies showed that obese infants were more likely to be obese as young adults at ages 20-30 years than non-obese infants\(^1\) \(^6\) \(^16\) and the third found that larger size at 6 months of age was associated with increased lifetime risk of obesity.\(^1\) The findings of three other studies of adults suggested a positive relation between infant size and later obesity.
life. Two studies used increase in weight for age or weight for height z scores. Six studies examined obesity in children, four with body mass index and two with weight. Of two studies of adolescents, one defined obesity according to body mass index and the other used a clinical definition. Seven of the ten studies examining infant growth found that more rapid growth in infancy was associated with greater risk of obesity at ages ranging from 4.5 to 20 years. In four studies of childhood, odds ratios of obesity in children who grew more rapidly in infancy compared with those who grew less rapidly ranged between 1.06 and 5.70. The studies of adolescents and young adults reported odds ratios of later obesity ranging from 1.41 to 5.22. The analyses in six of the seven studies were adjusted for important confounding factors, and we considered three studies to have a low risk of bias. Associations between infant growth and later obesity were consistent over time of birth ranged from 1945 to 1994. Three studies, two in children and one in adolescents, failed to show a association between infant growth and later obesity.

We could not carry out a meta-analysis of the relation between infant size or growth and later obesity because the definitions of both the exposures (infant size or growth) and outcomes (childhood or adult obesity) varied widely between studies.
Discussion

This review suggests that both size and growth during infancy are related to risk of obesity in children and adults. Most studies of infant size found that infants who were defined as "obese" or who were at the highest end of the distribution for weight or body mass index were more likely to develop obesity in childhood, adolescence, or early adulthood than other infants. The evidence relating to infant growth was also consistent across most studies reviewed. Infants who grew more rapidly (usually measured as weight gain) were more likely to be obese in childhood, adolescence, and early adulthood than other infants. There was no evidence to suggest that exposure at a particular time during infancy was critical: larger size or a rapid phase of growth at a range of intervals during the first and second year of life predisposed to later obesity. Associations were also consistent across a range of settings in developed countries; for obesity measured in childhood, adolescence, and early adulthood; and over time for people born from 1927 to 1994.

Strengths and limitations of this review

Our review used rigorous and standard methods and was supported by an expert advisory group.1 There were several challenges in interpreting the evidence. Most studies had at least a medium risk of bias in relation to the review question. Less than half of the studies of infant size took adequate account of confounding factors, though seven of the ten studies of infant growth considered most important confounders. Definitions of both the exposure (infant size or growth) and the outcome (obesity) varied between studies making meta-analysis impossible. This limits our ability to make precise conclusions about the size of the effect, though the consistency of the associations we observed between both infant size and growth and later obesity across a range of settings and time periods suggest that the association is robust.

Systematic reviews are subject to publication bias. Although we attempted to limit the impact of this through contact with first authors and experts, we did not identify any unpublished analyses. This review was part of a much larger review and so it was impractical to obtain original data from study authors to carry out secondary analyses. We therefore relied on published data from studies that were of variable quality.

Comparison with other research

Our findings amplify those of earlier systematic reviews. These found that rapid growth at different ages in childhood was associated with greater risk of later obesity.1–3 One review also found that birth weight was positively associated with adult body mass index.1 In our review odds ratios and relative risks of subsequent obesity in infants who had been obese compared with non-obese infants ranged between 1.35 and 9.38. Though not directly comparable, odds ratios tended to be lower in the studies of birth weight. For example, in a study of young Swedish men odds ratio of overweight increased from 1.07 to 1.67 going from the lowest (≤ 5th centile) to the highest (> 95th centile) birthweight group.14 In our review both large infant size and rapid infant growth were associated with later obesity. Babies who are small at birth experience rapid growth, at least in early infancy. Taken with other evidence, our review suggests that both prenatal and infant growth trajectories may be important in predicting adult obesity.

Conclusions

Infants in the highest end of the distribution for weight or body mass index and those who grow rapidly are at increased risk of obesity in childhood and adulthood. This suggests that factors during infancy or before that are related to infant growth influence the risk of later obesity. To inform public health policy aimed at reducing levels of childhood obesity, future research needs to investigate the determinants of these patterns of growth. The relation of infant growth with other health outcomes should be explored to assess whether interventions to alter infant growth to prevent obesity are likely to be associated with other benefits or harms. It will also be important to assess whether factors influencing infant growth are amenable to change, to establish which strategies might alter infant growth, and to find out whether these are acceptable to parents.

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