The Avon Longitudinal Study of Parents and Children (ALSPAC) – a resource for the study of the environmental determinants of childhood obesity

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Abstract
Childhood obesity is a major public health problem because the prevalence is increasing and because childhood obesity is associated with short- and long-term adverse consequences. By contributing to our understanding of the causes of childhood obesity epidemiological studies can help to inform preventive strategies. Prospective studies with all-of-life measures of exposures, objective measures of physical activity and more accurate measures of diet and body composition will be better able to identify modifiable environmental exposures that act cumulatively or at critical time periods across the life course. The Avon Longitudinal Study of Parents and Children (ALSPAC) recruited around 14,000 pregnant women with estimated dates of delivery between 1991 and 1992. The children have been followed up in detail ever since and now constitute probably the most intensively studied cohort of children ever recruited. Recent analyses have identified important modifiable risk factors and further analyses based on more accurate measures of diet, activity and body composition should provide further insights.


Introduction
The prevalence of childhood obesity has increased in the United Kingdom (1) as it has across Europe (2), in Australia (3) and in the United States (4). Although obese children may also have a higher risk of asthma (5, 6) and some children who are markedly obese suffer serious physical morbidity (7, 8) the most important immediate consequences are psycho-social (9, 10). Some adult disease processes begin in childhood (11). Childhood obesity has been positively associated with cardiovascular disease risk factor levels (12, 13) and more recently with carotid intima–media thickness in adulthood (14, 15). Furthermore, some studies have reported a positive association between adiposity in childhood and subsequent adult cardiovascular and all-cause mortality (16–18). In addition to the effects on health, obese children are at increased risk of becoming obese adults (19–21). Obesity in adulthood is associated with increased risk of coronary heart disease, stroke and non-insulin-dependent diabetes mellitus (22). Childhood obesity is thus an important public health problem.

Population studies of childhood obesity
Along with laboratory and clinical studies, epidemiological studies can make important contributions to our understanding of the aetiology of childhood obesity and in so doing help to formulate evidence-based approaches to prevention. Population-based studies are required that can explore the determinants of obesity in contemporary children. Obesity is a result of chronic energy imbalance (23, 24), but in free-living humans we cannot measure usual energy intake or usual energy expenditure. Such studies are therefore not seeking to identify whether this imbalance is the result of increased consumption or reduced expenditure but to describe dietary factors and patterns of physical activity that predispose to or protect against energy imbalance. Ideally such studies should have collected all-of-life data so they can examine both the cumulative effects of exposures and the effects of exposures at critical time periods. Childhood obesity is socially patterned (25), which means that better measures of confounders are needed to attempt to disentangle causal associations. More precise and objective measures of activity, diet and obesity are required to better characterise usual activity and total and regional fat mass.

The measurement of body composition in children
Obesity is a condition in which fat stores are enlarged to an extent that impairs health (26). The gold standard for assessment of body composition is cadaveric...
dissection. Other methods are indirect and require assumptions to be made (27, 28). Body mass index (BMI) is widely used to assess population levels of adiposity because it is easy to measure. Comparisons with bio-impedance measures in The Avon Longitudinal Study of Parents and Children (ALSPAC) suggest BMI is specific and moderately sensitive in identifying obese children provided appropriate cut-offs are chosen (29). However, across the normal range BMI does not distinguish well between fat and lean mass (30). This may be important as the determinants and consequences of each may be different in children as is suggested by data relating fat and lean mass to mortality in adults (31). Dual-energy X-ray absorptiometry (DXA) provides more accurate estimates of fat mass than either BMI or bio-impedance and estimates lean mass and bone mass (28, 32). DXA provides information on the regional distribution of body fat, which may be particularly important (33). Other techniques such as deuterium-labelled water may better characterise individual fat and lean mass (particularly when the individuals are very lean) but do not provide data on fat distribution (28).

The measurement of diet in children

In addition to the general challenge of characterising the complex dynamic exposure of usual diet (34, 35) there is also the well-recognised problem of under-reporting of intake in those who are overweight (36, 37). This under-reporting may be due to failure to report food consumed or modification of diet during the period of observation (38) and is associated with obesity (39). The diet of children in their early teens is more variable than that of adults or younger children (40–42). Unlike younger children, teenagers are able to complete diet records for themselves (40). The method of choice for measuring usual diet in adults is by no means clear with some investigators favouring food frequency questionnaires (43, 44) and others preferring diet diaries (45–47). A study in girls 9–10 years of age compared 3-day diet diaries, 24 h recalls and food frequency questionnaires with directly observed intake and concluded that diet diaries were the best choice (48).

The measurement of physical activity in children

Physical activity in children is sporadic. Short bursts of activity are common but longer periods of sustained activity (lasting 20 min or more) are not (49–51). Boys are more active than girls (49–51). Until recently epidemiological studies of physical activity in adults (52) and children (53) have either relied on simple questionnaire measures of physical activity or have used a proxy measure such as cardio-respiratory fitness. The inaccuracy inherent in earlier self-report questionnaires (53) and the lack of a strong association between cardio-respiratory fitness and activity level (54) have made precise estimates of the nature and size of the association between physical activity and obesity difficult (55). Improvements in self-report methods and the development of objective measures of physical activity such as heart rate monitors, accelerometers and pedometers (56) (that have been shown to be feasible for use in large field studies (52)) allow more accurate assessment of the association between physical activity and obesity. Furthermore, prospective studies in adults suggest that activity may also be an important modifier of the association between body composition and disease risk (57).

Critical time periods for the development of childhood obesity

Based on epidemiological studies Dietz (58) suggested that there were three critical time periods for the development of childhood obesity. These critical time periods were the prenatal period (59), the period in early childhood when adiposity rebound occurs (60) and adolescence (58). Further, biological studies have suggested that the growth curve of adipose tissue is maximal at birth and just before the onset of puberty (61). Dietz and Gortmaker are now less convinced that birthweight per se is important and concluded recently that the ‘relevance of each of these periods to the prevalence of adult obesity remains uncertain’ (62).

Birth dimensions and childhood obesity

Higher birthweight (a composite measure of both fat and lean mass at birth) is associated with increased BMI in later life (63) but there is also some evidence that low birthweight is associated with increased obesity (particularly central adiposity) (64). The finding in studies with measures of fat and lean mass that birthweight is more strongly associated with lean mass than fat mass (65) may explain some of the association between birthweight and BMI reported previously (59).

Exposures in utero and childhood obesity

In the Dutch Hunger Winter the offspring of women exposed to famine during the first trimester of pregnancy were more likely to become obese whereas those exposed to famine in the third trimester of pregnancy were less likely to become obese (63). These associations were not, however, observed in the follow-up of the Leningrad Siege (63). Some studies have reported that children born to smokers were subsequently fatter (63).
Infant feeding and childhood obesity

Several studies have suggested that breastfeeding may protect against subsequent obesity (66–68). However, in the 1958 cohort (68) the protective association between breastfeeding and obesity was no longer apparent after adjustment for confounding variables.

Growth, adiposity rebound and childhood obesity

After an increase in the first year of life, BMI falls until the age of about 4–6 years, after which it increases again. This increase in BMI is called adiposity rebound and an early rebound has been shown to be associated with higher BMI in adults (58, 60, 69). Adiposity rebound has not, however, been shown to be associated with a change in fat mass or later differences in fat mass (69). Patterns of growth in early childhood may nevertheless determine subsequent risk of becoming obese (70, 71). In an analysis of the ALSPAC cohort, rapid growth in the first 2 years of life was associated with obesity at age 5 (based on BMI and skinfold thickness) (70). Others have reported that high growth rates in the first 7 years of life were associated with increased BMI at age 33 (71).

Puberty and childhood obesity

The amount and proportion of fat and lean mass change through puberty. These changes are different for boys and girls (72). In boys fat mass declines from age 14 and then rises again at about age 17, while lean mass increases from about 13–14 years of age onwards (72). In girls fat mass increases from age 8 to 18, while the increase in lean mass is much less marked than in boys (72). Maturational timing has been consistently shown to be associated with obesity – those reporting early onset of puberty becoming more obese (73–76). The US National Heart, Lung and Blood Institute (NHLBI) growth and health study showed that the large difference in obesity between the black and white American girls emerged during puberty and that the early onset of menarche in the black girls in part explained their higher fat mass (77). Whether these associations with pubertal onset represent an effect of maturational timing on fat and lean mass or are an effect of fat and lean mass on maturational timing requires investigation in longitudinal studies with accurate measures of body composition before and after puberty.

Diet, physical activity and childhood obesity

Some studies have reported positive associations between obesity and sedentary activities in childhood such as watching television (78–81), while others have reported associations with certain aspects of diet such as saturated fat intake or the consumption of sweetened drinks (82). A systematic review carried out by Parsons et al. (83) concluded that the evidence that physical activity in childhood was protective against later obesity was ‘inconsistent but suggestive’ and that ‘studies investigating diet in childhood were limited and inconclusive’. A recent joint WHO/Food and Agriculture Organisation (FAO) report on diet, nutrition and the prevention of chronic diseases reviewed the evidence on diet and obesity (25). The report concluded that there was convincing evidence that regular physical activity and high intake of non-starch polysaccharide (dietary fibre) reduces risk of obesity while sedentary lifestyles, high intake of energy-dense micronutrient-poor foods increases risk of obesity (25). The report also concluded that there was evidence that home and school environments that support healthy food choices for children and breastfeeding probably reduce risk of obesity and that heavy marketing of energy-dense food and fast-food outlets, high intake of sugar-sweetened soft drinks and fruit juices and adverse socio-economic conditions (in developed countries, especially for women) probably increase risk of obesity (25).

ALSPAC

ALSPAC is a prospective study investigating the health and development of children and has been described in detail elsewhere (84) (http://www.alspac.bris.ac.uk). Briefly, 14,541 pregnant women living in one of three Bristol-based health districts in the former County of Avon with an expected delivery date between April 1991 and December 1992 were invited to take part and 85% of them accepted this invitation. These pregnancies resulted in 14,062 live births, of which 13,971 babies were still alive at 12 months.

All-of-life data collected in ALSPAC

Detailed information has been collected from pregnancy onwards using self-administered questionnaires, data extraction from medical notes, linkage to routine information systems and at an annual clinic lasting 3 h that the children have been invited to attend from the age of 7 years. Questionnaires have enquired about development, environmental exposures and health outcomes. During the last 6 months of initial recruitment a 10% sub-sample of children called ‘Children in Focus’ (CIF) was selected for detailed study. The CIF group was seen at 4, 8 and 12 months and 1.5, 2, 2.5, 3, 3.5, 4 and 5 years of age. Various physical and psychological variables were measured. Height and weight were measured at each visit. From the age of 7 years onwards all the study children have been invited for an annual assessment. The study
team are still in contact with around 11 500 children and between 7000 and 8000 attend. Physical and neurocognitive measurements have been made and psychological interviews have been used to identify a variety of behaviours and attitudes. The measures of body composition, diet and activity used in ALSPAC are described below and are summarised in Tables 1 and 2.

**Measures of body composition in ALSPAC**

Standing and sitting height were measured to the nearest millimetre with shoes and socks removed using a Holtain stadiometer (Holtain Ltd, Crymych, Pembs, UK) on the whole cohort at annual clinics at age 7+. Weight has been measured at annual clinics and leg-to-leg impedance has been measured at ages 7+, 9+, 10+ and 11+ using a Tanita THF 300GS body fat analyser and weighing scales (Tanita UK Ltd, Yewsley, Middlesex, UK). Waist circumference and hip circumference have also been measured at annual clinics. Measures of total and region fat, lean and bone mass have been made using a Lunar Prodigy DXA scanner (GE Medical Systems Lunar, Madison, WI, USA) at age 9+. The Lunar Prodigy uses a narrow-angle fan beam that results in very short acquisition times. Software options enable precise assessments of fat mass, lean mass and bone mass both overall and for the trunk, arms and legs. The scans have been visually inspected and realigned where necessary. We are currently repeating these measures at age 11+ in ALSPAC and intend to repeat these measures again at ages 13+ and 15+.

**Measures of diet in ALSPAC**

Mothers were asked to complete a food frequency questionnaire at 32 weeks of gestation and 4 years after delivery (85). This food frequency questionnaire, although based on a previously validated instrument, did not include portion size estimates and has not been formally calibrated against diet diaries or biomarker levels. Nevertheless, the estimates of dietary intake were similar to those obtained in a representative survey of diet in healthy adults (86). Detailed information on the patterns of the child’s feeding was collected for all cohort members at 4 weeks and 6, 15 and 24 months. This included specific information on breast milk and formula milk intake, early introduction of non-milk liquids and the introduction of solid foods, snacks and confectionery. For each dietary item the age at introduction of the food and the current frequency of consumption was obtained. At 36 months (87) and at 7 and 12 years of age food frequency questionnaires have been used to assess the children. Diet diaries were given to the parents of the CIF subset and to the parents of all children at age 7 and 10. Mothers and/or carers of the children were asked to record everything the child ate and drank for 3 days (1 weekend day and 2 week days) in household measures. A trained assistant went through the diet records with the mother. Diet diaries collected at age 3.5 years are already available for analysis as well as those collected at earlier ages and later diaries are being coded. The diet diaries have been analysed using Diet In Data Out (DIDO) software. DIDO is a portion size and coding package developed by the MRC Human Nutrition Research Unit in Cambridge, which reduces the level of error and the time needed for coding the diet. A similar diary is going to be used at age 13+.

**Measures of activity in ALSPAC**

During pregnancy a questionnaire containing questions about habitual physical activity was distributed (88). In addition annual questionnaires sent out in childhood have enquired about time spent watching television and time spent engaged in various activities outside the house. At age 10+ all children were asked to take away and complete a 4-day physical activity diary and then return it in a pre-paid envelope. This diary was developed in children of this age (89) and validated against accelerometers – an objective measure of physical activity (correlations between diary and accelerometer measures of activity were 0.7 or greater; A Page, unpublished data). We are currently measuring physical activity at age 11+ over a 7-day period using a uni-axial movement sensor (Actigraph model 7164; Computer Science and Applications, Manufacturing Technology Incorporated, Florida), and plan to repeat these measures at age 13+. This is an electronic motion sensor comprising a single plane (vertical) accelerometer. The monitors are small (4.5 x 3.5 x 1.0 cm) and light (about 43 g) and are worn in a custom-made pouch (or an elastic belt) around the waist (Fig. 1). Movement in a vertical plane is detected as a combined function of movement.
Figure 2 An example of the graphical output from the Actigraph (with 5 days’ recording). Note that the recording for the last of the 5 days is incomplete.

Table 1 Summary of measurements in Avon Longitudinal Study of Parents and Children (ALSPAC).

<table>
<thead>
<tr>
<th>Trimester</th>
<th>Pregnancy</th>
<th>Birth</th>
<th>Data already collected in childhood</th>
<th>Data planned</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age years</td>
<td></td>
<td></td>
<td>0m 6w 4m 8m 9m 1y 1y 18m 2y 3y 4y 5y 7y 8+y 9+y 10+y 11+y 12+y 13+y</td>
<td></td>
</tr>
<tr>
<td>Months</td>
<td>1st 2nd 3rd</td>
<td>1y 1y 18m 2y 3y 4y 5y 7y 8+y 9+y 10+y 11+y 12+y 13+y</td>
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<tr>
<td>Body composition</td>
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<td>Gestational age</td>
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<td></td>
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<td></td>
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<tr>
<td>Length/Height</td>
<td>A* A C C A C C C C C C C A A A A A A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight</td>
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<td>A A A A A A</td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Arm circ.</td>
<td>C C C C C C C C C C C A</td>
<td>A A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Waist circ.</td>
<td>C C C C C C C C C A</td>
<td>A A</td>
<td>A A</td>
<td></td>
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<tr>
<td>Hip circ.</td>
<td></td>
<td>A A</td>
<td></td>
<td>A A</td>
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<tr>
<td>Leg length</td>
<td>C A A A A</td>
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<td></td>
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<tr>
<td>Skin folds</td>
<td></td>
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<tr>
<td>Bio-impedance</td>
<td>A A A A A A</td>
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<tr>
<td>DXA</td>
<td>A A A A</td>
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<tr>
<td>Grip strength</td>
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<tr>
<td>Activity measures</td>
<td>A A</td>
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<tr>
<td>Activity question</td>
<td></td>
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<tr>
<td>TV viewing</td>
<td>A A A A A A A A A A A A</td>
<td>A A</td>
<td></td>
<td></td>
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<tr>
<td>Time outdoors</td>
<td></td>
<td>A A A A A A A A A A A A</td>
<td>A A</td>
<td></td>
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<tr>
<td>Activity Diary</td>
<td></td>
<td></td>
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<td>A**</td>
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<tr>
<td>Activity (Actigraph)</td>
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</tbody>
</table>

A = Measurement on full cohort with around 8,000 attending clinics each year, C = measurements on Children in Focus sub-group (around 1,000). Measures at 6w, 9m and 18m–2y based on routinely recorded measures. Bioimpedence leg-to-leg using Tanita scales, circ. = circumference, Actigraph = objective measurement by accelerometer, DXA = Dual X-ray absorptiometry, FFQ = food frequency questionnaire.

* = available on around half the cohort.
** = available on some of the cohort.
frequency and intensity, while an electronic filter rejects motion outside the range of normal human movement. Minute-by-minute data are stored in memory and subsequently downloaded to a computer (Fig. 2). The Actigraph has been well validated in both children and adolescents using heart rate telemetry (90), indirect calorimetry (91) and observational techniques (92). Ekelund et al. (93) assessed the Actigraph in free-living children within the European Youth Heart Study using energy expenditure measured by doubly labelled water as the criterion measure.

Recent findings from ALSPAC to date

Height and weight measures collected at age 7+ were used to identify obese children defined as children with a BMI above the 95th percentile relative to UK 1990 reference data. The association between obesity and various environmental exposures was examined. Maternal education showed a clear, inverse association with child obesity, with a 3-fold risk in the least-educated group. Birthweight (per 100 g adjusted odds ratio 1.05, 95% confidence interval (CI) 1.03–1.08) and maternal smoking in pregnancy (20+ cigarettes per day adjusted odds ratio 2.1, 95% CI 1.1–4.01) were associated with childhood obesity. Breastfeeding and late introduction of solids to infants appeared to be protective but the effect disappeared on adjustment. A history of parental obesity was a strong predictor of childhood obesity (if both parents had a BMI greater than 30 then the adjusted odds ratio was 11.42, 95% CI 5.50–23.72). Behaviours such as TV viewing and duration of sleep were associated with obesity risk. Patterns of early growth were associated with subsequent obesity risk (94).

Conclusions

Childhood obesity is an important public health problem. Epidemiological studies can make an important contribution to understanding the causes of childhood obesity. ALSPAC is a population-based study of contemporary children with all-of-life measures of exposures, objective measures of physical activity and more accurate measures of diet and body composition and is thus a valuable resource for the study of childhood obesity (Table 3). Recent analyses have identified important modifiable risk factors and further analyses based on more accurate measures of diet, activity and body composition should provide further insights.

Table 2 Summary of measurements in Avon Longitudinal Study of Parents and Children (ALSPAC) – 2.

<table>
<thead>
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<td>Age years</td>
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<td>3rd</td>
<td>0m</td>
</tr>
<tr>
<td>Months</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Dietary measures</td>
<td>FFQ</td>
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<tr>
<td>Diet records</td>
<td></td>
<td>C</td>
<td>C</td>
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<tr>
<td>Fitness measures</td>
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<tr>
<td>Socio-economic measures</td>
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<tr>
<td>Mother education</td>
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<tr>
<td>Father education</td>
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<td>Mother SE class</td>
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<tr>
<td>Father SE class</td>
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<td>Money problems</td>
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<td>Family income and food expenditure</td>
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<td>Housing</td>
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<td>Other measures</td>
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</table>

A = Measurement on full cohort (n = 14,000) with around 8,000 attending clinics each year, C = measurements on Children in Focus sub-group (n = 1,000). Measures at 6w, 9m and 18m–2y based on routinely recorded measures. Biopmpenedence leg-to-leg using Tanita scales, circ. = circumference, Actigraph = objective measurement by accelerometer, D2O = Deuterium labelled water, DXA = Dual X-ray absorptiometry, FFQ = food frequency questionnaire.

Table 3 Advantages of the Avon Longitudinal Study of Parents and Children as a resource for the study of the environmental determinants of childhood obesity.

- Population-based
- Prospective
- All of life data from before birth
- Detailed measures of body composition
- Repeated measures of maternal and childhood diet
- Objective measure of physical activity
- Detailed measures of potential confounding factors
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