

## COHORT PROFILE

# Cohort Profile: The Gateshead Millennium Study

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## How did the study come about?

The Gateshead Millennium Baby Study (GMBS) originated from the observation that slower than expected weight gain in infancy, traditionally known as failure to thrive, but more recently as 'weight faltering', had never been satisfactorily explained. There were methodological problems associated with much previous research. The first was the use of attained weight criteria to identify slow weight gain in infancy, which confounds poor postnatal weight gain with poor prenatal weight gain. The second was the use of referred samples of children, leading to selection biases. The third was the use of retrospective accounts from parents after poor weight gain had already been identified. The GMBS was thus originally designed to investigate the antecedents of weight faltering in a population-based prospective study that addressed the main methodological problems of previous research.

## What does it cover?

The original GMBS set out to examine infant feeding behaviour and relate it to subsequent weight gain and weight faltering. It also investigated risk factors for iron deficiency in infancy. Relevant maternal characteristics including feeding style, eating attitudes and depression were also examined. More recently, the title of the study has been changed to Gateshead Millennium Study (GMS) to reflect the age of the

cohort. The study has continued to focus on feeding and growth, with three additional areas of interest emerging.

First, it investigated aspects of developmental psychopathology using measurements principally taken at 5–6 years of age. A recent UK prevalence survey in 5–19-year-olds reported that mental health disorders are common, affecting ~8%, and that sub-threshold symptoms were even more common.<sup>1</sup> Eating disorders comprise an important social and medical problem developing during late childhood. Accurate figures on the prevalence of eating disorders have not been easy to establish. Those in a recent comprehensive review suggest a prevalence of 0.28% for anorexia nervosa, 1% for bulimia nervosa, 1.5% for night-eating syndrome and 2.3% for binge-eating disorder.<sup>2–4</sup> A much higher proportion of young women report less specifically diagnosable problems such as occasional binge eating or self-induced vomiting or score high on tests of abnormal eating attitudes.<sup>5</sup> There is also evidence that sub-threshold eating disorders are commonly associated with depression in adolescents, and there is a strong link between restrictive eating and aggression, attempted suicide and substance misuse.<sup>6,7</sup> Most longitudinal studies of disordered eating have started in the teenage years, but the strongest predictor of later disordered eating in these studies has always been disordered eating at the start of the study.<sup>8</sup> There is some evidence for continuity between earlier feeding problems and later eating disorder symptoms<sup>9</sup> and we are examining this systematically in this study.

The GMS also investigated children's emotional and behavioural development, and social communication skills. A topic of particular interest has been the development and prevalence of repetitive behaviours, which are key behaviours in autistic spectrum disorder but are also found in typically developing children. These repetitive behaviours can range from repetitive motor mannerisms and intense special interests or hobbies to more unusual sensory interests in the sight, taste, sound, smell or texture of objects or people.<sup>10</sup> The GMS provided an opportunity to investigate prospectively the relationship between various symptoms of psychopathology in typically developing children, and to identify early risk and protective factors for both eating problems and mental health disorders.

The second new area of interest was the high and rising rates of childhood obesity.<sup>11–13</sup> It was known that body mass index (BMI; weight/height<sup>2</sup>) tracks through later childhood into adulthood<sup>14</sup> and that teenage and adult obesity are associated with increased health risks.<sup>15–18</sup> It was also suggested that low birth weight and subsequent underweight in infancy are related to an increased risk of a number of chronic diseases in adulthood, including obesity.<sup>19</sup> However, detailed normative data are scarce and little was known about how lean and fat mass vary between individual children and how far early weight gain is associated with early childhood fatness. In addition, risk factors for early adiposity, such as dietary intake, physical activity and sedentary behaviour, needed to be investigated. Finally, there was the potential for intervention to reduce new cases of obesity in childhood. Evidence suggested that family-based interventions offered potential for success in prevention of obesity,<sup>20</sup> yet little information is available on what the content and approach of interventions should be and which would be acceptable to families. The GMS was able to investigate these issues when the cohort was aged 6–8 years.

The third new area of interest was the mechanisms by which early life exposures may influence health in later life. It has been postulated that nutrition during pregnancy as well as early feeding behaviours may alter mitotically heritable markings on DNA, so called epigenetic markings, which can influence body composition and other phenotypic characteristics in children through altering gene expression.<sup>21,22</sup> Epigenetics provide a biologically plausible mechanism to explain developmental programming and this area is currently the focus of much research activity. The GMS was able to investigate the association between early life exposure and epigenetic patterns in childhood when the cohort was aged 6–8 years.

## Who is in the sample?

The GMBS recruited participants shortly after birth in Gateshead, an urban district in north east England.

All infants born to mothers resident in Gateshead in 34 pre-specified weeks between June 1999 and May 2000 were eligible. From the 1252 eligible mothers, 1011 mothers joined the study; 116 (12%) were <20 years of age, 518 (51%) were >20 and <30 years and 377 (37%) were ≥30 years. A total of 1029 infants was recruited (18 sets of twins). Full details of recruitment are reported elsewhere.<sup>23</sup> The current GMS sample consists of any traceable survivor of the original cohort whose family have not asked to be withdrawn.

## How often have they been followed up?

The cohort was recruited by study researchers and baseline data were collected in an interview shortly after the baby was born. This was followed up by data collected by midwives at hospital discharge and 6 days, and by health visitors at 10 days and 3 months. Parents were sent postal questionnaires at 6 weeks, and at 4, 8 and 12 months. Families were invited to a clinic appointment at 13 months where the child and mother were measured for height and weight. A case-control study of children who failed to thrive had two lunchtime meals directly observed at 13–21 months. There were further parent completed postal questionnaires at 30 months and 5–6 years. A data sweep at age 6–8 years collected information from parents at home visits, and for the first time since 13 months, children participated directly at school and/or home visits. At the 6–8-year data sweep parents were followed up with qualitative focus groups and one-to-one interviews. At 8–10 years, data were collected from parents by post, and from children directly at school.

## What has been measured?

Descriptions of the data collected are shown in Table 1.

Throughout infancy and early childhood, detailed information was collected using questionnaires completed by the child's carer, usually the mother. Characteristics assessed included growth, feeding behaviour, temperament, illness and social behaviour in children. Information about parent characteristics including eating attitudes and depression was also collected. The GMBS mothers were given a special edition of the Personal Child Health Record (PCHR), which is issued routinely to all new mothers. The special edition PCHR included extra forms for health staff and parents to record details about the child on the study's behalf; in particular, mothers were asked to get their baby weighed regularly and to transcribe the weights onto the questionnaires they received and send them to the study office. The children and parents were also measured directly

**Table 1** Summary of data collected since birth ( $n = 1029$  children)

Cohort age	Where	By whom	Number of participants (%)	Data collected
After birth	Hospital/home	Mother	1029 (100%)	Birth weight Milk feeding behaviour <sup>a</sup> Mode of milk feeding Socio-economic status <sup>b</sup>
Day 3	Hospital	Midwife	633 (62%)	Feeding ratings <sup>b</sup>
Day 6	Hospital/home	Midwife	801 (78%)	Feeding ratings <sup>b</sup>
Day 10	Home	Health visitor	944 (92%)	Feeding ratings <sup>b</sup>
6 weeks	Home	Parent	832 (80%)	Milk feeding behaviour <sup>a</sup> Cessation of breast feeding, weaning etc. <sup>a</sup> Illness <sup>b</sup> Infant temperament <sup>40,c</sup> Weights (from PCHR)
3 months	Home	Health visitor	792 (77%)	Feeding ratings <sup>b</sup> Maternal depression <sup>41</sup>
4 months	Home	Parent	762 (74%)	Milk feeding behaviour <sup>a</sup> Cessation of breast feeding, weaning etc. <sup>a</sup> Illness <sup>b</sup> Accidents <sup>b</sup> Adverse family life events <sup>42,43</sup> Weights (from PCHR)
8 months	Home	Parent	675 (65%)	Solid feeding behaviour <sup>a</sup> Cessation of breast feeding, weaning etc. <sup>a</sup> Illness <sup>b</sup> Accidents <sup>b</sup> Infant temperament <sup>40</sup> Weights (from PCHR)
12 months	Home	Parent	636 (61%)	Solid feeding behaviour <sup>a</sup> Cessation of breast feeding General behaviour <sup>b</sup> Illness <sup>b</sup> Accidents <sup>b</sup> Maternal eating behaviour <sup>44</sup> Maternal childhood <sup>45</sup> Weights (from PCHR)
13 months	Clinic	Study nurse	847 (82%)	Child's height and weight (measured) Blood for full blood count, ferritin, zinc protoporphyrin Mother's height and weight (measured)
30 months	Home	Parent	492 (47%)	General feeding <sup>b</sup> Food preferences <sup>46,47</sup> Drinks <sup>b</sup> General behaviour <sup>b</sup> Repetitive Behaviour Questionnaire <sup>48,49</sup> Difficulties with child <sup>b</sup>

(continued)

Table 1 Continued

Cohort age	Where	By whom	Number of participants (%)	Data collected
				Illness <sup>b</sup>
4–5 years	School	School nurse	724 (70%)	Weights (from PCHR)
5–6 years	Home	Parent	506 (49%)	Child's height and weight (measured)
				Child's height and weight
				Mother's height and weight
				Child's appetite, mealtimes, problems <sup>b</sup>
				General child health and education <sup>b</sup>
				Mother's approach to feeding her child <sup>50</sup>
				Child's eating behaviour <sup>51</sup>
				Repetitive behaviour questionnaire <sup>48,49</sup>
				Common symptoms of psychopathology <sup>52</sup>
				Social communication problems <sup>53</sup>
				Parental employment (self-coded method) <sup>54</sup>
				Socio-economic status <sup>b</sup>
6–8 years	Home	Parent	617 (60%)	Child's eating behaviour <sup>b</sup>
				Child's risk factors for eating disorders <sup>55</sup>
				Child's food environment <sup>56</sup>
				Child physical activity environment <sup>d</sup>
				Parental concern about child's obesity in adulthood <sup>57</sup>
				Parental perception of child's body shape <sup>58,59</sup>
				Parental perception of child's activity <sup>60 e</sup>
				Parent's attitudes and knowledge about food <sup>61–63</sup>
				Maternal eating behaviour <sup>44</sup>
				Parent's physical activity <sup>64</sup>
				Parent food frequency <sup>65</sup>
				Family health status <sup>b</sup>
				Parental employment (self-coded method) <sup>54</sup>
				Socio-economic status <sup>b</sup>
				Parents' body measurements; height, weight, waist, hip, bioelectrical impedance
			488 (47%)	DNA biomarkers (saliva sample)
6–8 years	School	Teacher	576 (56%)	Common symptoms of psychopathology <sup>52</sup>
6–8 years	School	Child	619 (60%)	Attitudes and knowledge about food <sup>62</sup>
				Restrained eating <sup>66</sup>
				Body image <sup>59</sup>
				Habitual physical activity (accelerometry) <sup>67</sup>
				Habitual sedentary behaviour (accelerometry) <sup>67</sup>
				Body measurements; height, weight, waist, skinfolds (biceps, triceps, subscapular and supra-iliac), bone frame (knee, wrist, shoulders, hips and elbow) and bioelectrical impedance
			543 (53%)	DNA biomarkers (saliva sample)
6–8 years	Home and school	Parents and observers	486 (47%)	Child's food intake over 4 days <sup>68</sup>

(continued)

Table 1 Continued

Cohort age	Where	By whom	Number of participants (%)	Data collected
6–8 years	Community premises	Parents and Interviewers (Qualitative study)	38	Parent focus groups on childhood obesity
			16	Parent one-to-one interviews on childhood obesity
8–10 years	Home	Parent	495 (48%)	Child's sedentary opportunities in the home <sup>69</sup>
8–10 years	School	Child	590 (57%)	Habitual physical activity (accelerometry) <sup>67</sup> Habitual sedentary behaviour (accelerometry) <sup>67</sup> Sports activity and how they feel physically <sup>70,71</sup> Sedentary opportunities in the home <sup>69</sup> Eating patterns <sup>72</sup> and appetite <sup>a</sup> Body image <sup>59</sup> Body measurements; height, weight, waist, and bioelectrical impedance

<sup>a</sup>Influenced by previous work<sup>73</sup> or developed for the GMS.

<sup>b</sup>Items developed for the GMS.

<sup>c</sup>Items relevant to 6-week infants used.

<sup>d</sup>Non-validated, based on previous work.

<sup>e</sup>Interviewer led.

at clinics run by study nurses at 13 months. School-entry child height and weight measurements were retrieved from National Health Service (NHS) records.

When the children were aged 5–6 years, a postal questionnaire collected information about the child's eating behaviour and maternal approach to feeding their child. Information was also collected on the child's social communication skills, repetitive behaviours and common symptoms related to psychopathology, especially anxiety, emotional and conduct-related symptoms.

When the children were aged 6–8 years, information collected by parental questionnaire included the child's eating behaviour, the child's food and physical activity environment, parental eating characteristics and food intake, and socio-economic status. The children completed questionnaires on their food knowledge and eating behaviour. The child's dietary intake was observed, and physical activity levels and sedentary behaviour were measured using accelerometry. The children's and mothers' anthropometric measurements were taken, as well as saliva samples for the purposes of DNA extraction and subsequent epigenetic analysis. After the quantitative data collection had finished, for parents who expressed an interest, views on childhood obesity were sought using focus groups and one-to-one interviews to explore knowledge, perceptions of childhood obesity and potential strategies for intervention.

A data sweep when the children were 8–10 years old took direct measures of children's habitual physical

activity and sedentary behaviour (using accelerometry) and anthropometric measurements. Additionally, questionnaire data were collected from the children on their home environment, sports club activities and eating attitudes, and from parents on the children's home environment.

## What is attrition like?

The children have received a birthday card in the mail every year since birth with a letter including a reply slip for parents to return if they no longer wish to participate in the research. Unless parents have let the study know that they would prefer not to be contacted again, every effort is made to trace, contact and recruit their child for follow-up data sweeps regardless of whether they remain in the area of birth or have relocated. At the start of the 8–10-year data sweep, two children were known to have died and the parents of 161 children had asked to leave the study, leaving a sample of 866 children eligible to be contacted.

Non-participation for individual data sweeps has been substantial, but different families have participated in different data sweeps and consequently the study has retraced and collected data from 697 families over the past 3 years.

The original sample was comparable with the northern region of England in terms of socio-economic deprivation apart from slight under-representation of the most affluent quintile, assessed using the Townsend deprivation index from the 1991 census

**Table 2** Socio-economic characteristics of mothers (based on data collected at birth)

	Baseline <i>n</i> = 1011		12 months <i>n</i> = 624		13-month health check <i>n</i> = 830		30 months <i>n</i> = 482		5–6 years <i>n</i> = 495		6–8 years <i>n</i> = 605		8–10 years <i>n</i> = 576	
	<i>N</i>	%	<i>N</i>	%	<i>N</i>	%	<i>N</i>	%	<i>N</i>	%	<i>N</i>	%	<i>N</i>	%
Townsend quintile <sup>a</sup>														
1 (most affluent)	156	15	129	21	137	17	110	23	102	21	109	18	103	18
2	204	20	146	23	178	21	111	23	113	23	129	21	124	22
3	227	23	140	22	189	23	107	22	115	23	135	22	128	22
4	226	22	121	19	177	21	88	18	85	17	118	20	114	20
5 (least affluent)	192	19	83	13	143	17	61	13	75	15	108	18	101	18
Missing	6	1	5	1	6	1	5	1	5	1	6	1	6	1
Qualification														
A levels or above	243	24	186	30	213	26	150	31	159	32	175	29	167	29
GCSEs or equivalent	495	49	325	52	415	50	255	53	246	50	295	49	273	47
NVQs or none	194	19	83	13	144	17	55	11	61	12	98	16	99	17
Missing	79	8	30	5	58	7	22	5	29	6	37	6	37	6

Percentages do not add up to 100 in all cases due to rounding.

<sup>a</sup>Based on Townsend deprivation index from 1991 census, using enumeration districts as the unit of analysis with the northern region of England as the population for comparison for the calculation of the quintiles.

(Table 2). Overall, non-participation has been higher in the least affluent families than in the most affluent. Thus, only 15% of families were in the most affluent quintile at birth, but 70% of them participated at 6–8 years; 19% were in the least affluent quintile but only 56% participated at 6–8 years. This means that by 6–8 years, the distribution across all the deprivation quintiles was fairly even (Table 2) and the current sample is representative of the north of England. Non-participation patterns according to maternal qualification are similar to the Townsend deprivation index, with non-participation being higher in less educated mothers, particularly for postal data sweeps (Table 2).

Tracing and tracking of the GMS children is ongoing and they are being flagged with the UK National Health Service Central Register.

## What has it found? Key findings and publications

### Weight loss, weight gain and feeding in the first year of life

Postnatal weight loss was less than previous studies have shown. At 5 days, the mean weight loss was 50 g, only just over 1% below birth weight, and 3% of babies were 10% below, none showing any signs of serious illness. One-third had already regained their birth weight.<sup>24</sup> More frequent feeding in the first week was related to higher weight gain at 6 weeks of age for breast-fed babies, but not for bottle-fed babies. Babies who were fed by both breast and

bottle were less likely to continue to be fed by breast at 6 weeks of age than those who received only breast milk.<sup>25,26</sup>

Nearly one-quarter of the babies started eating solids before 3 months of age. Characteristics associated with early weaning were fast weight gain to 6 weeks, lower socio-economic status, parents' perceptions that their baby was hungry, and being bottle fed. Babies weaned before 3 months, compared with those weaned after 4 months of age, had increased risk of diarrhoea.<sup>27</sup>

Appetite at 6 weeks and 12 months was positively related to weight gain to 12 months, and encouraging a child to eat was associated with poorer weight gain. Children's appetite appeared to be related to how well or poorly they ate and grew.<sup>28</sup>

Mothers' characteristics such as their eating behaviour, mood and social characteristics were not strongly associated with children's weight gain over the first year. Postnatal depression was associated with slower weight gain and increased rates of weight faltering in the infants up to 4 months, especially if they came from deprived families, but by 12 months they were no different from the remainder of the cohort.<sup>29</sup>

Data from this cohort as well as the Avon Longitudinal Study of Parents and Children (ALSPAC) have been used to assess how the growth of UK infants compares to newly published WHO standards. Analysis showed that in both cohorts infants were heavier than infants in the WHO growth study from about the age of 6 months but showed very similar linear growth.<sup>30</sup>

### **Mealtime energy intake and feeding behaviour**

Video observations were used to identify types of feeding behaviour in children aged 13–21 months. Two meals were observed for each of 30 children who had shown weight faltering in the first year and 57 controls. Energy intake and weight of food eaten were also measured. The children who gained less weight were offered and accepted food at the same rate as children with normal weight gain but had a lower energy intake.<sup>31</sup>

### **Diagnosis of borderline iron deficiency**

This therapeutic trial included 462 infants whose parents agreed to have blood taken and were successfully bled during the 13-month assessment. It explored how successful five different blood markers were at identifying iron deficiency, as indicated by a clear response to treatment. Low total and mean cell haemoglobins proved good predictors of a response to treatment, but about half the children who responded had haemoglobins within the normal range. The three other markers were only associated with a response when two or more were abnormal. Using the above definition, 13% of the children tested could be defined as truly iron deficient. These children did not generally show differences in social factors or growth, apart from a moderate association with breast feeding for over 4 months and a greatly increased risk for a small minority of children from ultra orthodox Jewish families.<sup>32</sup>

### **Eating behaviour and repetitive behaviours in toddlers and young children**

Eating problems were perceived as common in toddlers and the majority were associated with normal growth, although weight faltering was more common in such children. Excessive milk consumption may have been a cause of low appetite at meal times, but was not associated with poor growth.<sup>33</sup>

Repetitive behaviours are an essential part of the diagnosis of autism but are also commonly seen in typically developing children. Repetitive behaviours data from this cohort, pooled with data from another local cohort, showed that 2-year-old children frequently engage in a range of different types of repetitive behaviours (with boys showing higher scores than girls). These behaviours can be summarized within four subscales: unusual sensory interests; repetitive motor movements; rigidity/adherence to routine; and preoccupations with restricted patterns of interests. These study results support the proposal that repetitive behaviours measured on subscales that closely resemble the repetitive behaviour subtypes within the International Classification of Diseases-10 criteria for autism, represent a continuum of functioning that extends to the typically developing child population.<sup>10</sup> Subsequent analysis of new pooled data looking at the continuity of repetitive behaviours from

2 to 6 years shows that the predominant repetitive behaviours change over time and that although the total rates of repetitive behaviours reduce over time, they do not disappear.<sup>34</sup>

### **Surveillance of physical activity in the UK**

Public health surveillance of physical activity in children in the UK has depended on a parent-reported physical activity questionnaire that has not been validated. Physical activity measured objectively using accelerometry in 6–7-year olds showed that levels of habitual physical activity in children are likely to be substantially lower than those reported in UK Health Surveys.<sup>35</sup>

### **Perceptions of childhood adiposity**

Parents' ability to identify whether their child was overweight was limited when compared with current standards for overweight or obesity. Parents neither used nor trusted current standards of childhood overweight and instead used alternative approaches that heavily relied on extreme cases as a reference point.<sup>36,37</sup>

## **What are the main strengths and weaknesses?**

Gateshead has a stable population, but even so, maintaining up-to-date contact details and keeping the families involved has been difficult. Direct contact has achieved higher participation than postal contact. For example, 636 families returned postal questionnaires at 12 months whereas 847 attended a clinic run by study nurses at 13 months. Using direct contact for retracing and data collection, the study has managed to maintain a cohort of approximately 700 children.

Gateshead has a higher rate of deprivation than the rest of the northern region of England and this was reflected in the lower proportion of the most affluent families recruited to the study. As is common for community-based studies, there has been higher rates of attrition among the most deprived families.<sup>38,39</sup> However, due to higher retention of the most affluent families compared with the least affluent families, the current sample is socially diverse and representative of the north of England.

The cohort has the benefit of a wealth of data on maternal characteristics and the children's early eating patterns, developmental psychopathology, dietary intake at 6–8 years, a comprehensive set of body composition measurements, lifestyle behaviours and physical activity at 6–8 and 8–10 years and DNA samples. It will provide crucial information for investigation of both physical and mental health. Of obvious importance is the examination of the role of fast weight gain in infancy and childhood lifestyle

behaviours in the development of later obesity and other chronic disease outcomes in later life. A cohort of this size is only adequately powered to examine variation within the normal range and between major subgroups, but since our current main area of interest, childhood obesity, is now so common, the study is likely to be adequately powered to examine important risk factors.

## Can I get hold of the data? Where can I find out more?

Most of the data are currently being actively analysed by the existing study team, but we welcome suggestions for collaboration. Potential collaborators should contact Professor Ashley Adamson at the Institute of Health and Society at Newcastle University. The study has a website at <http://research.ncl.ac.uk/gms/>.

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**Conflict of interest:** None declared.

### KEY MESSAGES

- The Gateshead Millennium Study recruited a socially diverse birth cohort in 1999/2000. The current sample is representative of the north of England.
- The cohort provides a rich dataset on children's early eating characteristics, dietary intake, physical activity and developmental psychopathology.
- The study will allow examination of the development of childhood obesity, and the development of preventative strategies.

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