ORIGINAL ARTICLE

What is the long term outcome for children who fail to thrive? A systematic review

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Aims: To ascertain the long term outcomes in children diagnosed as having failure to thrive (FTT).

Methods: Systematic review of cohort studies. Medline, Psychinfo, Embase, Cinahl, Web of Science, Cochrane, and DARE databases were searched for potentially relevant studies. Inclusion criteria: cohort studies or randomised controlled trials in children <2 years old with failure to thrive defined as weight <10th centile or lower centile and/or weight velocity <10th centile, with growth, development, or behaviour measured at 3 years of age or older.

Results: Thirteen studies met the inclusion criteria; eight included a comparison group, of which five included children identified in community settings. Two were randomised controlled trials. Attrition rates were 10-30%. Data from population based studies with comparison groups and which reported comparable outcomes in an appropriate form were pooled in a random effects meta-analysis. Four studies report IQ scores at follow up and the pooled standardised mean difference was -0.22 (95% CI -0.41 to -0.03). Two studies reported growth data as standard deviation scores. Their pooled weighted mean difference for weight was -1.24 SDS (95% CI -2.00 to -0.48), and for height -0.87 SDS (95% CI -1.47 to -0.28). No studies corrected for parental height, but two reported that parents of index children were shorter.

Conclusions: The IQ difference (equivalent to ~3 IQ points) is of questionable clinical significance. The height and weight differences are larger, but few children were below the 3rd centile at follow up. It is unclear to what extent observed differences reflect causal relations or confounding due to other variables. In the light of these results the aggressive approach to identification and management of failure to thrive needs reassessing.

Most child health surveillance programmes both in the West and in poor countries include the regular weighing of infants and young children, with the aim of identifying those children who are growing inappropriately slowly. A variety of cut-off points for action are used, including weight below a particular centile (which ranges from <10th to <0.4th centile) or crossing more than a certain number of centiles. Recently it has been argued that clinicians should use the new charts which identify the slowest growing children while correcting for regression to the mean.¹

A small number of children who are identified in this way will be diagnosed as having an organic illness, but over 90% will be labelled as having non-organic failure to thrive.² A number of explanations have been advanced for this phenomenon of poor growth in early life in the absence of organic disease and in the presence of adequate supplies of food. Child abuse,³ oro-motor coordination leading to feeding difficulties,^{4,5} and inadequate parenting⁶ have all been implicated, and there is a widespread assumption that this early poor growth has significant long term effects on children's growth and development.

A variety of approaches to treatment of failure to thrive have been developed, but there is inconsistent evidence that these improve outcome.⁷⁻⁹ There is furthermore a clear potential for harm in this situation: failure to thrive is often a pejorative diagnosis, and may instil significant anxiety and feelings of lack of competence within the family.¹⁰

Given that there is currently little good evidence from randomised controlled trials that interventions are beneficial in failure to thrive, along with the lack of high quality studies on the effects of growth monitoring programmes on children's health,¹¹ we aimed to systematically review

prognostic studies of children diagnosed as having failure to thrive. We attempted to identify all cohorts of children labelled as having failure to thrive, however diagnosed, that reported measures of growth or psychomotor development at 3 years of age or later, regardless of what interventions were used.

METHODS

Search strategy

Medline, Cinahl, Psychinfo, Web of Science, and Embase databases were searched for cohort studies using the key terms failure to thrive, weight faltering, growth faltering with appropriate synonyms, and mis-spellings, combined with methodological terms including risk factors, prognosis, cohort studies, and outcomes. Randomised controlled trials were also identified for data relating to long term follow up of children in these studies (for this purpose the Cochrane Controlled Trials Register and DARE libraries were also searched). A full search strategy is available from MCJR.

Titles and abstracts identified by electronic searches were examined on screen to select potentially relevant studies. In addition, reference lists of identified studies and review articles were examined. Experts in the field were contacted for unpublished data.

Inclusion criteria

Studies identified as potentially relevant by the searches were reviewed by the authors against the following inclusion criteria:

- **Population:** Children identified as failing to thrive (defined as weight below the 10th or a lower centile, and/or a

Table 1 Details of studies with a comparison group

First author	Population	Definition of FTT	Duration of follow up	Adequacy of follow up	Controls	Blinding at assessment	Potential confounders reported in the study
Population based studies							
Mitchell, 1980 ¹²	19 of 30 children with history of FTT prior to 24 months of age in a primary care clinic of 312 identified by review of notes	<80% normal wt, or FTT cited on the problem list	At 3–6 years	12 of 19 cases 16 of 19 controls	Controls matched at inception for age, maternal age, marital status, and family problems	Blinded for McCarthy Scale and behavioural questionnaire but not growth	Life events score, sex, mother's education, FTT
Corbett, 1996 ¹³	52 children identified as FTT by child health surveillance from 306 eligible children registered in 2 clinics	A fall of 2 centile lines for weight, sustained for >1 month	5 years later	48 of 52 (89%) cases and 46 of 52 (88%) controls	Next child on clinic register of same age and sex	Psychologists blind to child's status	No control for confounders
Drewett, 1999 ¹⁴	136 children with FTT identified from a birth cohort of 3418	Thrive index <5% on 2 or more occasions between ages 3–18 mth	At 7–9 years	IQ testing: 79% cases, 87% controls Growth measures: 82% cases, 91% controls	Selected from cohort for normal growth and matched for age and residential area	Psychologists blind to child's status	Maternal IQ, parental height, organic disease, maternal smoking, breast feeding, family size, birth order
Kerr, 2000 ¹⁵	92 children with FTT, of 193 children enrolled in a longitudinal study of child development and maltreatment	Weight <5th centile Age <25 mth Normal birth wt	At 6 y of age	Not clear	101 children with wt >10% matched for age, race, sex, and SES	No detail given	Maltreatment as defined by a Child Protective Services Report for neglect, sexual or physical abuse, SES, age, gender
Boddy, 2000 ¹⁶	47 children identified as FTT by the age of 12 months from a cohort of 2004 births in 1986 and still resident in the area	Weight at 12 mth at or <3rd centile and sustained for at least 3 mth	At 6 years	IQ testing: 42 of 47 cases, 42 of 47 controls Growth measures: 38 cases, 39 controls	Matched at inception for birth wt, sex, ethnicity, and residential area	Blinded for growth, unclear if blinded for IQ testing	Maternal height, maternal IQ, changes in social index
Clinical sample based studies							
Singer, 1984 ¹⁷	13 babies hospitalised at age 5–9 months for FTT	Weight <3%	At 3 years	All 13 cases, 9 of 13 organic FTT and 5 of 13 controls	Selected at inception from children attending the emergency room, but no details given. At F/U the remaining controls had higher BW, gestational age and parental education	No details given	Parental education
Drotar, 1992 ¹⁸	68 hospitalised infants aged 1–9 months, randomly assigned to 3 types of intervention	Normal birth weight decreasing to weight <5th centile Weight gain demonstrated in hospital	Age 42–48 mth	48 of 68	47 controls matched at inception for age, sex, ethnicity, social factors, mother's education	No comment on blinding of assessors	Effect of treatment group
Reif, 1995 ¹⁹	86 children diagnosed with FTT at <2 years of age either as in or outpatients	Age <2 y, weight, height <5th centile for at least 6 mth, term infants	5 years later	61 of 86 children	65 controls matched at assessment for age, sex, social setting, ethnicity (but birth wt and maternal ht were higher)	No comment on blinding of assessors	Birth weight, severity of growth delay, parental heights, parental education

reduction in weight gain velocity) in the first two years of life in either hospital or community settings

- **Outcome:** At least one outcome measured at the age of 3 years or older, relating to growth, psychomotor development, and/or behaviour
- **Study design:** Cohort studies with or without comparison groups or randomised controlled trials.

Studies were specifically excluded if all participants were children born of low birth weight (<2.5 kg), if they were conducted in countries where malnutrition is prevalent, or if

they included children identified as failing to thrive after the age of 2 years.

Data extraction

Data extracted from the studies included case definition, selection of controls, attrition rate, length of follow up, and measures of weight, height, psychomotor development, or IQ and behaviour.

In addition, we recorded whether in those studies with a control group, the outcome assessors were blind to case status, and what attempts had been made to adjust results for potential confounding variables.

Table 2 Details of studies without a comparison group

Author	Population	Definition of FTT	Duration of follow up	Adequacy of follow up
Population based studies				
Hutcheson, 1997 ²⁰	130 children who were recruited from primary care clinics to participate in an RCT of home intervention for FTT for 12 months	Age <25 mth old with weight <5th centile and weight/height <10th centile	At age 4 years	74 of 116 children who completed the trial
Wright, 1998 ⁹	229 children identified as FTT by child health surveillance, and enrolled in RCT of health visitor intervention for 7–35 months (120 intervention, 109 non-intervention)	Fall of 1.26 SD in weight using the thrive index method	At age >3 years	105/120 for intervention, 97/109 for non-intervention
Clinical sample based studies				
Kristiansson, 1987 ²¹	34 babies aged 4–18 months who had been hospitalised with NOFTT	Rate of wt gain <–2SD	At age 4 years	34 of 34 children
Drotar, 1988 ²²	88 babies aged 1–9 mth hospitalised for FTT of whom 80 consented to participate and were randomly allocated to 3 forms of intervention	Normal birth weight decreasing to weight <5th centile Weight gain demonstrated in hospital	At age 36 mth	59 of the 80 children
Sturm, 1989 ²³	Same children as above			

Data analysis

The studies were grouped as follows:

- *Population based studies* which attempted to ascertain all cases meeting prespecified criteria
- *Clinical samples* where defined entry criteria were taken to identify children who were inpatients, outpatients, or community referred children.

They were further divided according to whether or not they included a comparison group of children without failure to thrive.

The study details and results were then tabulated within these groups.

Where population based studies included an appropriate comparison group and had comparable methods of outcome assessment and reported data in a usable form, we pooled the results using a random effects meta-analysis. For estimates of weight and height differences, we included only studies that reported standard deviation scores (that is, standardised for age) and their confidence intervals, and performed a pooled weighted mean difference. For measures of psychomotor development or IQ we included studies that used any

Figure 1 (A) Meta-analysis of weight SD scores in children who had experienced failure to thrive in infancy as compared with controls. (B) Meta-analysis of height SD scores in children who had experienced failure to thrive in infancy compared with controls.

Table 3 Studies with a comparison group (data expressed as cases mean (SD) versus controls mean (SD))

Author	Growth	Intellectual	Behavioural	Comments
Population based studies				
Mitchell, 1980 ¹²	Weight: 86% normal wt v 96%, p<0.05 Height: 97% normal weight v 99%	McCarthy Scale of Children's Abilities: General Cognitive Index 87.5 v 92.5 (sd12.9), p=NS	No behavioural deficits on behavioural questionnaire	No organic disease found. Life events score was a predictor of GCI
Corbett, 1996 ¹³	Mean weight SD -0.53 (0.83) v 0.34 (1.11), p<0.001 Mean height SD: -0.5 (0.99) v 0.07 (1.29), p=0.02	WISC-R (Wechsler Preschool and Primary scale of intelligence-revised) IQ 83.6 (11.5) v 87 (11.9) (p=NS)	No difference in number of behaviour problems Child Behaviour Checklist: 33 v 34 Teachers' report form: 23 v 14	4 in care; there was a relation between severity of FTT and IQ, p=0.03
Drewett, 1999 ¹⁴	Weight: 18th centile v 56th centile Height: 21st centile v 47th centile	WISC IQ 87.6 (17.4) v 90.6 (17.1) p=NS Reading score 93.5 (16.2) v 94.5 (15.6) p=NS		FTT paternal height significantly shorter IQ difference reduced to a mean of 1.7 when maternal IQ factored in When parental height was taken into consideration the height difference between groups was marginally reduced
Kerr, 2000 ¹⁵		WISC-R 78 (13.8) to 82 (12.8) v 83.6 (12.4) to 84 (12.5) range depending on presence of maltreatment or not	Child Behavior Checklist 28.1 (22.8) to 34.9 (21.2) vs 26.7 (18.4) to 29 (20.5) range depending on presence of maltreatment or not No increase in school behaviour problems or maternal report of problems unless maltreatment also present	Overall 97% had wt for ht >95%
Boddy, 2000 ¹⁶	Weight SD -0.97 (0.92) v 0.68 (1.44) p<.001 Height SD -0.91 (1.25) v 0.27 (0.92), p<0.001	McCarthy Scale of Children's Abilities: General Cognitive Index 99.8 ± 15.9 v 103.7 ± 19.7, p=NS		FTT maternal height significantly shorter Strong correlation observed between height and maternal height
Clinical based samples				
Singer, 1984 ¹⁷		Stanford-Binet Intelligence Scale NOFTT 78.6 (13) v OFTT 67.7 (20) Controls 97.4 (25)		There was high attrition among controls FTT parental education was shorter than controls Parental education related to: IQ at age 3, p<0.02
Drotar, 1992 ¹⁸			Inc. in parental report of behavioural symptoms CBC 58.5 (10.7) v 53.2 (12.7), p<0.005 No. of children in clinical behaviour problem range 15 v 10 p=NS Deficits in behavioural organisation, ego control and resiliency	
Reif, 1995 ¹⁹	Weight centile: 18.1 (2.35) v 36 (3.0), p<0.001 Height centile: 21 (2.8) v 53.6 (2.9), p<0.01	Learning difficulties 18% v 3.1% Developmental delay 11.5% v 0%	School problems and poor achievement commoner	Overall 85% were >5% for weight, 90% were >5% for height Maternal height and birth weight were lower in cases than controls. Birth weight, maternal height, and education correlated with outcome

standardised scale and reported the group means and standard deviation. As these scales have different population means and standard deviations we calculated a pooled standardised mean difference.

RESULTS

Forty seven studies were identified from the searches as being of potential interest,^{7 9 12-56} of which 13^{9 12-23} met the inclusion criteria. Eight were cohort studies,^{12-17 19} and five were randomised controlled trials.^{9 18 20 22 23} Of these, eight included a comparison group.¹²⁻¹⁹ Study characteristics are described in table 1 for those with a comparison group and in table 2 for those without. The main results are described in table 3 for studies with, and in table 4 for studies without a comparison group. All studies without a comparison group reported results suggesting that children with failure to thrive were shorter, lighter, and

scored lower on measures of psychomotor development than population norms, with those recruited as clinical samples generally doing worse. Given the role of potential confounding variables, these studies were not analysed further.

Quality of studies (tables 1 and 3)

The definition of failure to thrive varied widely across studies with criteria ranging from weights <5th centile to <3rd centile, a fall down 2 centile lines, <80% normal weight and a low thrive index. Attrition rates were 10-30%.

In studies including a comparison group, most selected comparison groups at inception, and were matched for a variety of sociodemographic factors. Blinding was reported for developmental testing in all studies but none reported blinding of assessment of growth.

Table 4 Results of studies without a comparison group (data expressed as mean (SD))			
Author	Growth outcome	Intellectual outcome	Comments
Hutcheson, 1997 ²⁰	Intervention children: height SD -0.8 (1.0), wt for ht SD -1.7 (0.6) Non-intervention children: height SD -1.0 (1.1), wt for ht SD -1.5 (0.8)	Battelle Developmental Inventory 71.6 (17.9) to 84.9 (13.2) depending on intervention status and degree of maternal negativity	Took into account demographic and maternal psychological risk factors
Wright, 1998 ⁹	Weight SD -0.93 (intervention) v -1.29 (non-intervention), p=0.04 Height SD -0.79 (intervention) v -1.13 (non-intervention), p=0.03		Difference in height between controls and intervention not significant when adjusted for parental height
Kristiansson, 1987 ²¹	Weight >-2SD 21 children (62%) Height >-2SD 30 (88%)		2 children were in foster care and 4 had social services support
Drotar, 1988 ²²		Stanford Binet Intelligence score: mean IQ 85.4 (15) In 49% the IQ was >85, in 14% it was <70	IQ was related to maternal education, income, and onset and duration of FTT
Sturm, 1989 ²³	Weight for height: 93.6 (8.7) 7% were wasted 15% <5% for weight 5% <5% height		

Growth

Growth data were presented in a variety of forms including standard deviation scores, mean centile position, % normal weight/height, and weight for height, limiting the number of studies that could contribute to the pooled estimates. The data as presented also did not allow for analysis of differing severities of failure to thrive. All studies reported that children who had failure to thrive were lighter and shorter than comparison children at follow up.^{12-14 16 19} The majority of index children were however above the 3rd centile for both weight and height. Three studies reported that parental height was on average shorter for the cases.^{14 16 19}

Two studies reported weight and height standard deviation scores (SDS)^{13 16} and were pooled in a random effects meta-analysis. The pooled difference in weight was -1.2 SDS (95% CI -2.0 to -0.5), and in height -0.9 SDS (95% CI -1.5 to -0.3) (fig 1).

Psychomotor development

A variety of measures of psychomotor development and IQ were reported including the Wechsler Intelligence Scale for Children (WISC), McCarthy, Stanford Binet scales, or the Battelle Developmental Inventory. Measures were low overall, but no single study reported a statistically significant difference in IQ between cases and comparisons,^{12-17 19} although one clinic based study with a comparison group

reported that 18% of the sample had learning difficulties as compared with only 3% of controls.¹⁹ One study commented that when they adjusted for maternal IQ they found a reduction in differences between the groups,¹⁴ and three studies reported a relation between parental education and child's IQ.^{17 19 22}

Four studies reported differences between group means and their standard deviations and were included in the meta-analysis.^{12-14 16} The pooled standardised mean difference in developmental quotient/intelligence quotient was -0.2 (95% CI 0.4 to 0.0) (fig 2). This difference equates to a mean difference of approximately 3 IQ points on the Wechsler Intelligence Scale for children.

Behaviour

Five studies with a comparison group reported assessments of behaviour.^{12 13 15 18 19} All used informal questionnaires to teachers or parents. Only one reported an increase in school problems. Three studies^{13 15 18} reported results on the Child Behaviour Checklist,⁵⁷ of which only one¹⁸ found a difference between the groups.

DISCUSSION

Where convincing evidence of the benefit of intervention is lacking, justification of efforts to identify and treat those with the "condition" must depend on the demonstration of

*SMD standardised mean difference

Figure 2 Meta-analysis of intellectual scores in children who had experienced failure to thrive in infancy compared with controls.

What is already known on this topic

- Identification of failure to thrive by weight monitoring is a time honoured practice underpinned by the assumption that there are damaging consequences for growth and intellectual development
- Considerable stress and anxiety are often precipitated by health professionals when a child is found to be failing to thrive

deleterious effects on later outcome. The main finding of this review was the paucity of high quality follow up studies. The population studies which included comparison groups were small, none adjusted adequately for potential confounders (although a number matched on some important variables), and few reported data in a form which allowed inclusion in the meta-analyses. This relative lack of usable data reduces the precision of our estimates of the magnitude of the association between a diagnosis of failure to thrive and long term growth and cognitive development, and means that we cannot entirely exclude quite substantial effects. The heterogeneity of case definition further complicated interpretation, and the data were presented in a way that did not allow for analysis of differing levels of severity. Given this background, the pooled results need to be treated with caution.

The aim of systematic reviews is to provide an unbiased estimate of an association by including all studies meeting the inclusion criteria, whether or not they have been published. It is generally believed that location bias is likely to be a particular problem when dealing with observational studies. Although we used an exhaustive search strategy, including asking authors working in the field, we did not find unpublished studies and cannot be entirely certain that we have identified all relevant data.

Results of the included studies suggest that, on average, children identified as having failure to thrive in infancy will be shorter, lighter, and score less well on measures of psychomotor development than their peers. However, the clinical significance of these differences needs to be questioned for a number of reasons, both methodological and clinical.

Although a few of the studies attempted to control for potential confounding variables in their analyses, there is the strong likelihood that residual confounding remains. Some studies commented that "failure to thrive" parents were shorter^{14 16 19} and one study that parental education was of shorter duration,¹⁷ giving some credence to this suggestion.

On clinical grounds, the results also need to be interpreted with caution. Firstly, the pooled difference in IQ scores was relatively small and so of doubtful clinical significance. As regards growth, although the cases were on average smaller than the controls, few children were below the third centile on follow up. As no studies adjusted for parental height, and children were studied during the early primary school years, conclusions regarding final height would be premature. Lastly, some of the children may have had underlying genetic or pathophysiological reasons for poor growth which could affect growth both early in life and later, but should not lead one to conclude that the poor infant growth *caused* reduced growth in childhood.

Although severe and prolonged malnutrition clearly has profound long term effects on growth and psychomotor development,³⁸ this review provides little good evidence that the growth pattern experienced by children included in the population based studies has serious deleterious effects on subsequent growth or psychomotor development although such an effect cannot be excluded. In most of the included

What this study adds

- Failure to thrive is associated with little reduction in IQ, but some reduction in childhood weight and height, although even this may be exaggerated as studies did not adjust for confounding factors such as parental height and IQ
- There is little evidence that identifying failure to thrive is predictive of damaging consequences for growth and intellectual development

studies, children from both FTT and control groups had relatively low scores on standardised tests of cognitive function at follow up compared to population norms. This suggests that these samples may have been largely drawn from relatively disadvantaged sections of the community.

This conclusion however does not mean that there is no benefit in identifying children who are growing poorly, particularly when there are associated developmental problems or clinical signs and symptoms. Clinical experience suggests that for a small number of children this is a route to the diagnosis of important, remediable organic conditions.² A further small proportion of poorly growing children may do so as a result of neglect or the deliberate withholding of food, where poor growth can be an important marker for the need for intervention. Finally, this may be a route by which parents who are having difficulties in the management of feeding, or whose children have more general developmental problems, may access care.¹⁰

The challenge facing clinicians is how best to identify those children among the slowest growing who would benefit from investigation or intervention, without generating damaging anxiety in those that do not. Bearing in mind that there is currently little robust evidence from randomised controlled trials that intervention is associated with clear long term benefit,⁷⁻⁹ it is arguable whether screening can be justified, although it remains important that clinicians should respond appropriately to parental anxieties. Yet again, this illustrates the need for randomised controlled trials of interventions that pay careful attention to entry criteria and have adequate long term follow up.

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