National Institute for Health and Care Excellence

Final

Faltering Growth – recognition and management

Full Guideline

Clinical Guideline (NG75)

Methods, evidence and recommendations

September 2017

Final

Developed by the National Guideline Alliance, hosted by the Royal College of Obstetricians and Gynaecologists

Disclaimer

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

Local commissioners and/or providers have a responsibility to enable the guideline to be applied when individual health professionals and their patients or service users wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.

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Contents

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ISBN 978-1-4731-2693-0

ISBN 978-1-4731-2693-0

ISBN 978-1-4731-2693-0

1 Introduction

The term 'faltering growth' (previously called ‘failure to thrive’) is widely used to refer to a slower rate of weight gain in childhood than expected for age and sex. The term faltering growth is preferred as periods of slow growth may represent temporary variation from the expected pattern and the word ‘failure’ may be seen as pejorative. Various definitions of faltering growth have been used in the past, meaning estimates of prevalence in the UK vary widely.

The World Health Organization (WHO) has produced growth standards, based on longitudinal studies of healthy breastfed infants. These standards, along with UK term and preterm infant growth data, have been incorporated into UK WHO growth charts for monitoring growth in UK children. A child’s weight, length or height and head circumference can be plotted on these charts to provide a visual representation of growth over time. Epidemiological data suggest that healthy children usually progress relatively consistently along a growth centile.

New-born infants normally lose weight in the first days of life. Persisting or large weight losses can cause concern in parents, carers and health professionals about ineffective establishment of feeding. In older children, faltering growth can occur when nutritional intake does not meet a child's specific energy requirements. Undernutrition presents as a relatively slow weight gain, demonstrated by a fall across weight centiles on the growth chart.

Children with faltering growth may be identified by routine growth monitoring or by parental or health professional concern. Standard management is usually community based, with support and advice provided to increase energy intake and manage challenging feeding behaviour. Some children will be referred to paediatric dietitians or paediatricians for further assessment and management.

Certain health conditions predispose children to faltering growth (for example, cystic fibrosis or coeliac disease). Specific treatment for these conditions can improve or restore expected rates of weight gain. In children with no specific cause for faltering growth, simple interventions to increase nutritional intake may be effective in improving weight gain. Faltering growth in early childhood may be associated with persisting problems with appetite and feeding.

The cause of faltering growth in the absence of a specific underlying health condition is likely to be complex and multifactorial. In the past, child neglect or socioeconomic and educational disadvantage were often considered to be likely contributors. While neglected children may be undernourished, neglect is an uncommon explanation for faltering growth. Similarly, significant associations with socioeconomic or educational factors have not been demonstrated.

There is variation across the UK in care provided for infants, children and families where concerns are raised about early weight loss or faltering growth. There is cultural and socioeconomic variation in starting and continuing breastfeeding, the approach to introducing complementary solid food and choice of foods, feeding behaviour and parental acceptance of feeding support and advice.

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1.1 Guideline Committee membership, National Guideline Alliance (NGA) staff and acknowledgements

Table 1: Guideline Committee members

Name	Role
Gordon Allan	General Practitioner
Shel Banks	Lay member
Rachel Bryant-Waugh	Consultant Clinical Psychologist
Anne Marie Frohock	Paediatric Dietitian
Annalou Louw	Speech and language therapist
Russell Peek (Chair)	Consultant Paediatrician
Denise Pemberton	Feeding Lead for Maternity and Neonatal Services
Rachel Pidcock	Lay member
Caroline Roberts	Specialist Health Visitor, Growth and Nutrition
Alison Spiro	Specialist Health Visitor in Infant Feeding
Charlotte Wright	Community Paediatrician
Expert advisers	
Shirley Paddock	Nursery Care Professional

Table 2: NGA Staff

Name	Role
Alexander Bates	Senior Health Economist
Zosia Beckles	Information Scientist (until March 2016)
Nathan Bromham	Senior Systematic Reviewer (from August 2016)
Anne Carty	Project Manager (until September 2016)
Katharina Dworzynski	Guideline Lead
Linyun Fou	Systematic Reviewer (from August 2016)
Eva Gonzalez-Viana	Systematic Reviewer (from February 2016)
Lianne Gwillim	Project Manager (from September 2016)
Stephen Murphy	Clinical Advisor
Amir Omidvari	Research fellow (from January 2016 to March 2016)
Timothy Reeves	Information Scientist (from March 2016)
Valentina Ricci	Senior Systematic Reviewer (until August 2016)

Acknowledgements

Additional support was received from Annabel Flint, Hugo Pedder and Katie Webster.

1.2 Other versions of the guideline

National Institute for Health and Care Excellence (NICE) produce a number of versions of this guideline:

- The ‘short guideline’ lists the recommendations, context and recommendations for research
- NICE Pathways brings together all connected NICE guidance.

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1.3 Schedule for updating the guideline

For the most up-to-date information about guideline reviews, please see the latest version of the NICE guidelines manual available from the NICE website.

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2 Development of the guideline

2.1 What is a NICE clinical guideline?

NICE clinical guidelines are recommendations for the care of individuals in specific clinical conditions or circumstances within the NHS – from prevention and self-care through primary and secondary care to more specialised services. We base our clinical guidelines on the best available research evidence, with the aim of improving the quality of healthcare. We use predetermined and systematic methods to identify and evaluate the evidence relating to specific review questions.

NICE clinical guidelines can:

- provide recommendations for the treatment and care of people by healthcare professionals
- be used to develop standards to assess the clinical practice of individual healthcare professionals
- be used in the education and training of healthcare professionals
- help patients to make informed decisions
- improve communication between patients and healthcare professionals.

While guidelines assist the practice of healthcare professionals, they do not replace their knowledge and skills.

- We produce our guidelines using the following steps:
- The guideline topic is referred to NICE from the Department of Health.
- Stakeholders register an interest in the guideline and are consulted throughout the development process.
- The scope is prepared by the NGA.
- The NGA establishes a Guideline Committee.
- A draft guideline is produced after the group assesses the available evidence and makes recommendations.
- There is a consultation on the draft guideline.
- The final guideline is produced.

The NGA and NICE produce a number of versions of this guideline:

- The ‘full guideline’ contains all the recommendations, together with details of the methods used and the underpinning evidence.
- The ‘short guideline’ lists the recommendations, context and recommendations for research.
- ‘Information for the public’ is written using suitable language for people without specialist medical knowledge.
- NICE Pathways brings together all connected NICE guidance.

2.2 Remit

NICE received the remit for this guideline from the Department of Health. It commissioned the NGA to produce the guideline.

The remit for this guideline is to develop a clinical guideline on the recognition and management of faltering growth in children. The scope was drafted by the NGA in collaboration with NICE and then revised and finalised based on stakeholder consultation

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comments (for the scope of the guideline please refer to Appendix A and the stakeholder list in Appendix B).

2.3 Who developed this guideline?

A multidisciplinary Guideline Committee comprising healthcare professionals and researchers as well as lay members developed this guideline (see the list of group members and acknowledgements).

NICE funds the NGA and thus supported the development of this guideline. The Guideline Committee was convened by the NGA and chaired by Russell Peek in accordance with guidance from NICE.

The group met every 4 to 6 weeks during the development of the guideline. At the start of the guideline development process all group members declared interests including consultancies, fee-paid work, shareholdings, fellowships and support from the healthcare industry. At all subsequent group meetings, members declared arising conflicts of interest.

Members were either required to withdraw completely or for part of the discussion if their declared interest made it appropriate. The details of declared interests and the actions taken are shown in Appendix C.

Staff from the NGA provided methodological support and guidance for the development process. The team working on the guideline included a guideline lead, a project manager, systematic reviewers, health economists, a statistician and information scientists. They undertook systematic searches of the literature, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate and drafted the guideline in collaboration with the group.

2.4 What this guideline covers

2.4.1 Groups that will be covered

- Infants and preschool children in whom growth concerns have been raised, through either routine monitoring (defined in recommendation 17 of the NICE guideline on maternal and child nutrition) or professional or parental concern.
- The following subgroups have been identified as needing specific consideration:
  - infants and preschool children who
  - were born prematurely
  - were born with intrauterine growth restriction (IUGR)
  - with a specific disorder known to cause faltering growth, but only with regard to recognition of growth thresholds for concern

2.4.2 Key clinical issues that will be covered

1. Recognition of faltering growth, including defining growth thresholds for concern (including, early weight loss after birth).
2. Identification of risk factors for faltering growth.
3. Assessment of infants and preschool children with faltering growth. This includes identifying possible causes of faltering growth and, in the absence of any other symptoms or signs, deciding on appropriate investigations.
4. Growth monitoring in infants and preschool children with suspected or confirmed faltering growth.
5. Referral to secondary care.
6. Interventions to manage faltering growth, including:

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- breastfeeding support
- support for other types of feeding
- dietary advice and supplementation
- family support.

7. Design of services for the management of faltering growth.
8. Information and support for parents and carers of infants and preschool children with suspected or confirmed faltering growth.

2.5 What this guideline does not cover

2.5.1 Clinical issues that will not be covered

1. Specialist management of specific disorders causing faltering growth, for example coeliac disease.

2.6 Relationship between the guideline and other NICE guidance

2.6.1 Related NICE guidance

NICE is currently developing the following guidance that is closely related to this guideline:

- Developmental follow-up of children and young people born preterm. NICE Guideline, publication expected August (2017).
- Child abuse and neglect. NICE Guideline. Publication expected September (2017).
- Child maltreatment: when to suspect maltreatment in under 18s. NICE Guideline CG89 (2009).
- Coeliac disease: recognition, assessment and management. NICE Guideline NG20 (2015).
- Postnatal care up to 8 weeks after birth. NICE Guideline CG37 (2015).
- Maternal and child nutrition. NICE Guideline PH11 (2014).

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3 Guideline development methodology

This chapter sets out in detail the methods used to review the evidence and to generate the recommendations that are presented in subsequent chapters. This guidance was developed in accordance with the methods outlined in the NICE guidelines manual 2014.

3.1 Developing the review questions and protocols

The 14 review questions developed for this guideline were based on the key areas identified in the guideline scope. They were drafted by the NGA, and refined and validated by the Guideline Committee.

The review questions were based on the following frameworks:

- intervention reviews – using population, intervention, comparison and outcome (a PICO framework)
- reviews of diagnostic test or clinical prediction model accuracy – using population, diagnostic test (index tests), reference standard and target condition
- qualitative reviews – using population, area of interest and themes of interest
- prognostic reviews – using population, presence or absence of a risk factor, and outcome.

Full literature searches, critical appraisals and evidence reviews were completed for all review questions.

3.2 Searching for evidence

3.2.1 Clinical literature searches

Systematic literature searches were undertaken to identify all published clinical evidence relevant to each review question.

Databases were searched using medical subject headings, free-text terms and study type filters where appropriate. Special consideration was given to search terms relating to early weight loss following birth to ensure that relevant studies were captured. Relevant search terms such as hypernatremia and dehydration were used in the searches as well as figures for the percentage of weight change that might cause concern. Where possible, searches were restricted to retrieve articles published in English. All searches were conducted in the following databases: Medline, Embase, Health Technology Assessments (HTA), Cochrane Central Register of Controlled Trials (CCTR), Cochrane Database of Systematic Reviews (CDSR), and Database of Abstracts of Reviews of Effects (DARE). Where relevant to specific review questions the following additional databases were also searched: PsycInfo, AMED (Allied and Complementary Medicine) and CINAHL (Cumulative Index to Nursing and Allied Health Literature). All searches were updated on 20th January 2017. Any studies added to the databases after this date (including those published prior to this date but not yet indexed) were not considered relevant for inclusion.

Search strategies were quality assured by cross-checking reference lists of relevant papers, analysing search strategies from other systematic reviews and asking Guideline Committee members to highlight key studies. All search strategies were also quality assured by an Information Scientist who was not involved in the development of the search. Details of the search strategies, including study type filters that were applied and databases that were searched, can be found in Appendix E.

All references suggested by stakeholders at the time of the scope consultation were considered for inclusion. During the scoping stage, searches were conducted for guidelines, health technology assessments, systematic reviews, economic evaluations and reports on

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biomedical databases and websites of organisations relevant to the topic. Formal searching for grey literature, unpublished literature and electronic, ahead-of-print publications was not routinely undertaken.

3.2.2 Health economics literature searches

Systematic literature searches were also undertaken to identify relevant published health economic evidence. A broad search was conducted to identify health economic evidence relating to faltering growth in the following databases: NHS Economic Evaluation Database (NHS EED) and Health Technology Assessment (HTA). A broad search was also conducted to identify health economic evidence relating to faltering growth in the following databases with an economic search filter applied: Medline, Cochrane Central Register of Controlled Trials (CCTR) and Embase. Where possible, the search was restricted to articles published in English and studies published in languages other than English were not eligible for inclusion.

The search strategies for the health economic literature search are included in Appendix E. All searches were updated on 20th January 2017. Any studies added to the databases after this date (including those published prior to this date but not yet indexed) were not included unless specifically stated in the text.

3.3 Reviewing research evidence

3.3.1 Types of studies and inclusion and exclusion criteria

For most intervention reviews in this guideline, parallel randomised controlled trials (RCTs) were prioritised because they are considered the most robust type of study design that could produce an unbiased estimate of the intervention effects.

For diagnostic, clinical prediction rule or prevalence reviews, cross-sectional, retrospective or prospective cohort studies were considered for inclusion. For prognostic reviews, prospective and retrospective cohort and case-control studies were included.

For qualitative reviews, studies using focus groups, or structured or semi-structured interviews were considered for inclusion. Survey data or other types of questionnaires were only included if they provided analysis from open-ended questions, but not if they reported descriptive quantitative data only.

Where data from observational studies were included, the Committee agreed that the results for each outcome should be presented separately for each study and meta-analysis was not conducted.

The evidence was reviewed following the steps shown schematically in Figure 1:

- Potentially relevant studies were identified for each review question from the relevant search results by reviewing titles and abstracts. Full papers were then obtained.
- Full papers were reviewed against pre-specified inclusion and exclusion criteria to identify studies that addressed the review question in the appropriate population, as outlined in the review protocols (review protocols are included in Appendix D).
- Relevant studies were critically appraised using the appropriate checklist as specified in the NICE guidelines manual.
- Key information was extracted on the study's methods, according to the factors specified in the protocols and results. These were presented in summary tables (in each review chapter) and evidence tables (in Appendix G).

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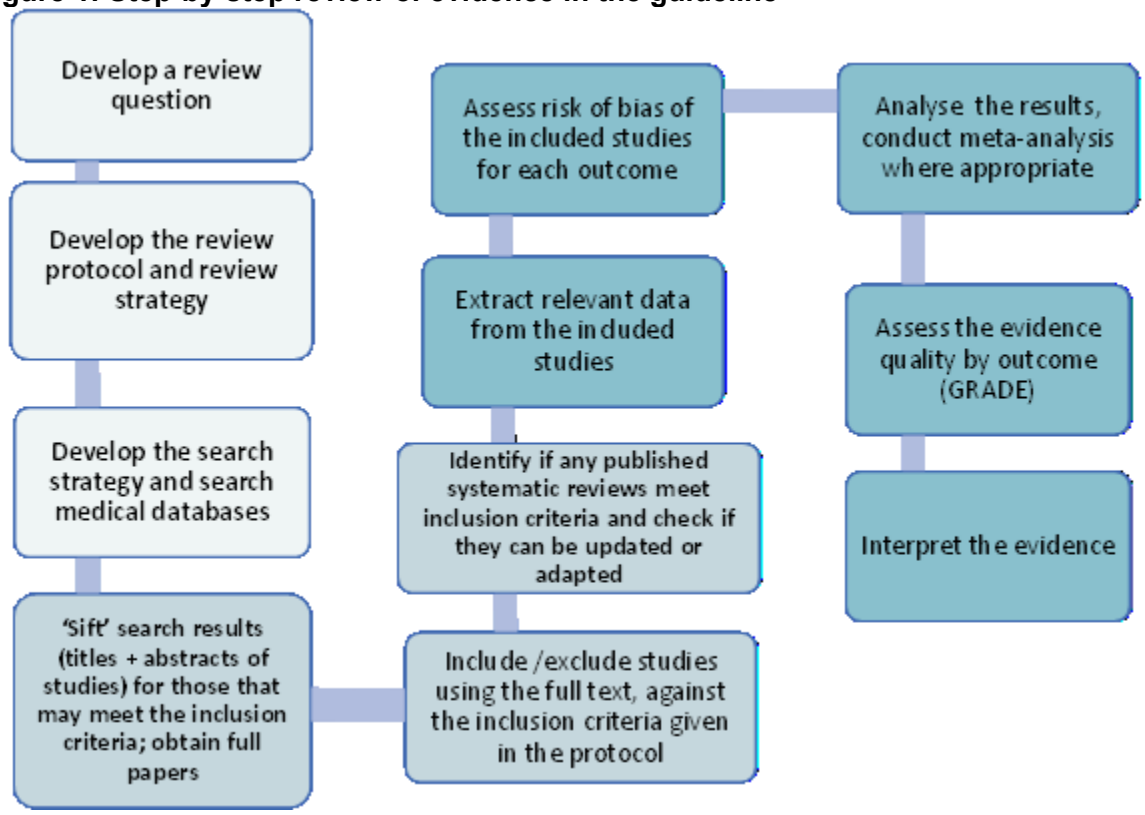
- Summaries of evidence were generated by outcome (included in the relevant review chapters) and were presented in Committee meetings (details of how the evidence was appraised is described in Section 3.5 below):
  - Randomised studies: meta-analysis was carried out where appropriate and results were reported in GRADE profiles (for intervention reviews).
  - Observational studies of interventions: data were presented as a range of values in GRADE profiles.
  - Prognostic studies: data were presented as a range of values, usually in terms of the relative effect as reported by the authors.
  - Prevalence studies: data were presented as a range of values, in terms of the absolute prevalence as reported by the authors.
  - Diagnostic or clinical prediction rule studies: data were presented as measures of diagnostic test accuracy (sensitivity and specificity) and were presented in modified GRADE profiles.

For quality assurance of study identification, a 10% sample of the study searches were double checked by a second reviewer for the following review questions: normal weight loss in the early days of life, weight loss in the early days of life associated with adverse outcomes, thresholds for faltering growth, risk factors for faltering growth, non-nutritional interventions, monitoring and referral.

Any disagreements in study selection were resolved by discussion between the two reviewers.

All drafts of reviews were checked by a second reviewer.

Figure 1: Step-by-step review of evidence in the guideline



3.3.1.1 Specific inclusions and exclusions

The definitions of the faltering growth condition varied widely between studies. Often cases were only very loosely classified. The Committee therefore decided to include any study

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referring to a 'faltering growth' population of children even when it was unlikely that the definition would be specific enough to accurately identify all children generally considered to show faltering growth. The definitions were then extracted and the applicability of this was then taken into consideration when the evidence was discussed.

Infants showing early weight loss in the first days of life were treated as a separate group. For this group of infants the term 'faltering growth' would not usually be used. We therefore widened the search for this group to include terms such as 'feeding problem ', 'weight losses and others.

Throughout this guideline only evidence from high income countries (http://data.worldbank.org/income-level/high-income) was considered for inclusion. It was agreed that the reasons and interventions for faltering growth in middle and low income countries would not be generalisable to the NHS setting.

3.4 Method of combining clinical studies

When planning reviews (protocols), the following approaches for data synthesis were discussed and agreed with Committee.

3.4.1 Data synthesis for intervention reviews

It was planned to conduct meta-analyses where possible to combine the results of studies for each review question using Cochrane Review Manager (RevMan5) software.

Fixed-effects (Mantel–Haenszel 1959) techniques were used to calculate risk ratios (relative risk) for binary outcomes, such as rate of adverse events or rate of people with symptom improvements (Mantel–Haenszel 1959).

For continuous outcomes, measures of central tendency (mean) and variation (standard deviation) are required for meta-analysis. Data for continuous outcomes (such as level of pain on a visual analogue scale [VAS]) were analysed using an inverse variance method for pooling weighted mean differences. A generic inverse variance option in RevMan5 is used if any studies reported solely the summary statistics and 95% confidence interval (95% CI) or standard error. However, in cases where standard deviations were not reported per intervention group, the standard error (SE) for the mean difference is calculated from other reported statistics (p values or 95% CIs): meta-analysis was then undertaken for the mean difference and SE using the generic inverse variance method in RevMan5. When the only evidence was based on studies summarising results by presenting medians (and interquartile ranges) or only p values were given, this information was assessed in terms of the study's sample size and was included in the GRADE tables without calculating the relative or absolute effects. Consequently, aspects of quality assessment, such as imprecision of effect, could not be assessed for evidence of this type. However, the limited reporting of this outcome was classified as a risk of bias in study limitations.

Stratified analyses were predefined for some review questions at the protocol stage when the Committee identified that these strata are different in terms of biological and clinical characteristics and the interventions were expected to have a different effect.

Statistical heterogeneity was assessed by visually examining the forest plots, and by considering the chi-squared test for significance at $p<0.1$ or an I-squared inconsistency statistic (with an I-squared value of more than 50% indicating considerable heterogeneity). Where considerable heterogeneity was present, predefined subgroup analyses were performed.

Assessments of potential differences in effect between subgroups were based on the chi-squared tests for heterogeneity statistics between subgroups. If no sensitivity analysis was found to completely resolve statistical heterogeneity, then a random-effects (DerSimonian

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and Laird) model was employed to provide a more conservative estimate of the effect – (DerSimonian and Laird 1986).

3.4.2 Data synthesis for predictive accuracy reviews

Weight loss and length/height thresholds can be used as a clinical prediction rule to help identify whether an infant with weight loss in the early days of life or a child with faltering growth is at increased risk of adverse outcomes. For studies using weight or length thresholds as predictors of adverse outcomes, results were summarised as sensitivity, specificity and likelihood ratios. Predictive accuracy data were not pooled but presented as ranges.

3.4.3 Data synthesis for prognostic reviews

Identification of risk factors for faltering growth could aid early identification and management strategies. Odds ratios (ORs) or risk ratios (RRs) with their 95% confidence intervals (95% CIs) for the effect of the pre-specified thresholds on the adverse outcome of interest, were extracted from the papers when reported. For this topic, we looked for studies that took into account possible key confounders (such as age, duration of follow-up and interventions for faltering growth) as reported in multivariable analyses. These studies were typically cohort studies and for his reason the prognostic data were not pooled but ranges were reported.

3.4.4 Data synthesis for prevalence reviews

In rare cases faltering growth is associated with an undiagnosed new clinical symptoms order and the appropriate testing strategy will depend on the prevalence of such disorders. For this topic we sought studies which had investigated cohorts of children with faltering growth and reported the prevalence of undiagnosed underlying disorders. It was agreed with the Committee that any reported prevalence values for each underlying disorder would not be pooled but reported as a range of percentages. This was due to the possible heterogeneous nature of individual cohorts that may report such prevalence rates.

3.4.5 Data synthesis for normal weight loss in the early days of life

For the review of normal weight loss in the early days of life the 50th, 95th and 97.5th centiles of the maximum weight loss compared to birth weight were extracted from cohort studies. The commonest timing of this lowest weight point (nadir) was also noted for each cohort as well as time to return to birth weight. It was agreed with the Committee that these data would not be pooled but reported as a ranges. This was due to the possible heterogeneous nature of individual cohorts.

3.5 Appraising the quality of evidence

For intervention reviews, the evidence for outcomes from the included RCTs and observational studies were evaluated and presented using GRADE, which was developed by the international GRADE working group. For prognostic and prevalence reviews the quality of evidence was summarised on a per-study basis for each reported risk-factor or prevalence estimate.

The software developed by the GRADE working group (GRADEpro) was used to assess the quality of each outcome, taking into account individual study quality factors and the meta-analysis results. The clinical/economic evidence profile tables include details of the quality assessment and pooled outcome data, where appropriate, an absolute measure of intervention effect and the summary of quality of evidence for that outcome. In this table, the columns for intervention and control indicate summary measures of effect and measures of dispersion (such as mean and standard deviation or median and range) for continuous

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outcomes and frequency of events (n/N: the sum across studies of the number of patients with events divided by sum of the number of completers) for binary outcomes. Reporting or publication bias was only taken into consideration in the quality assessment and included in the clinical evidence profile tables if it was apparent.

The selection of outcomes for each review question was decided when each review protocol was discussed with the Guideline Committee. However, given the nature of most of the review questions included in this guideline many of which were not intervention reviews the categorisation of outcomes as critical and important did not follow the standard GRADE approach but could be related to which particular risk factor was important, whether sensitivity or specificity would be given more weight, or the outcome maximal weight loss in the early days was divided into three critical outcomes (what percentage of weight loss, when it occurred and when weight would be regained). The outcomes were selected by the Committee for a review question as critical for decision-making in a specific context and recorded in the relevant review protocol.

The evidence for each outcome in interventional reviews was examined separately for the quality elements listed and defined in Table 3. Each element was graded using the quality levels listed in Table 4.

The main criteria considered in the rating of these elements are discussed below. Footnotes were used to describe reasons for grading a quality element as having serious or very serious limitations. The ratings for each component were summed to obtain an overall assessment for each outcome (Table 5).

The GRADE toolbox is designed for intervention reviews of RCTs and observational studies. For diagnostic accuracy, prognostic and prevalence reviews the evidence was assessed per study level.

Table 3: Description of quality elements in GRADE (see details in sections 3.5.1.1 to 3.5.1.4)

Quality element	Description
Risk of bias (study limitations)	Limitations in the study design and implementation may bias the estimates of the treatment effect. High risk of bias for the majority of the evidence decreases confidence in the estimate of the effect.
Inconsistency	Inconsistency refers to an unexplained heterogeneity of results or findings.
Indirectness	Indirectness refers to differences in study population, intervention, comparator and outcomes between the available evidence and the review question, such that the effect estimate is changed. This can also related to applicability or generalisability of findings.
Imprecision	Results are imprecise when studies include relatively few patients and few events and thus have wide confidence intervals around the estimate of the effect. Imprecision occurs when the confidence interval is wide and crosses the minimally clinically important threshold.
Publication bias	Publication bias is a systematic underestimate or an overestimate of the underlying beneficial

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Quality element	Description
	or harmful effect due to the selective publication of studies.

Table 4: Levels of quality elements in GRADE level

Levels of quality elements in GRADE level	Description
None	There are no serious issues with the evidence.
Serious	The issues are serious enough to downgrade the outcome evidence by 1 level.
Very serious	The issues are serious enough to downgrade the outcome evidence by 2 levels.

Table 5: Overall quality of outcome evidence in GRADE level

Overall quality of outcome evidence in GRADE level	Description
High	Further research is very unlikely to change our confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low	Any estimate of effect is very uncertain.

3.5.1 Grading the quality of clinical evidence

After results were pooled, the overall quality of evidence for each outcome was considered. The following procedure was adopted when using the GRADE approach:

- A quality rating was assigned based on the study design. For intervention reviews RCTs start as high, observational studies as moderate and uncontrolled case series as low or very low.
- The rating was then downgraded for the specified criteria: risk of bias (study limitations); inconsistency; indirectness; imprecision; and publication bias. These criteria are detailed below. Evidence from observational studies (which had not previously been downgraded) was upgraded if there was a large magnitude of effect or a dose-response gradient, and if all plausible confounding would reduce a demonstrated effect or suggest a spurious effect when results showed no effect. Each quality element considered to have 'serious' or 'very serious' risk of bias was rated down by 1 or 2 points respectively.
- The downgraded/upgraded ratings were then summed and the overall quality rating was revised. For example, all RCTs started as high and the overall quality became moderate, low or very low if 1, 2 or 3 points were deducted respectively.
- The reasons or criteria used for downgrading were specified in the footnotes.

The details of the criteria used for each of the main quality elements are discussed further in section 3.5.1.1 below.

GRADE quality assessment was not performed for the reviews of prevalence, normal weight loss in the early days of life or for prognostic reviews not involving predictive accuracy. In these cases the quality of evidence was informed by the assessment of risk of bias.

ISBN 978-1-4731-2693-0

3.5.1.1 Risk of bias

3.5.1.1.1 Intervention studies

Bias can be defined as anything that causes a consistent deviation from the truth. Bias can be perceived as a systematic error that could lead to over or underestimation of the effect.

The risk of bias for a given study and outcome is associated with the risk of over- or underestimation of the true effect.

The sources of risk of bias are listed in Table 6.

A study with a poor methodological design would lead to high risk of bias. However, the bias is considered individually for each outcomes and subjectively reported outcomes will be more prone to be affect by risk of bias than objective outcomes.

Table 6: Risk of bias in randomised controlled trials

Risk of bias	Explanation
Allocation concealment	Those enrolling patients are aware of the group to which the next enrolled patient will be allocated (this is a major problem in 'pseudo' or 'quasi' randomised trials with allocation by, for example, day of week, birth date, chart number).
Lack of blinding	Patient, caregivers, those recording outcomes, those adjudicating outcomes or data analysts are aware of the arm to which patients are allocated.
Incomplete accounting of patients and outcome events	Missing data not accounted for and failure of the trialists to adhere to the intention to treat principle when indicated.
Selective outcome reporting	Reporting of some outcomes and not others on the basis of the results.
Other risks of bias	For example: • stopping early for benefit observed in randomised trials, in particular in the absence of adequate stopping rules • use of unvalidated patient-reported outcomes • recruitment bias in cluster randomised trials.

3.5.1.1.2 Prognostic and clinical prediction rule studies

For prognostic and clinical prediction rule studies, quality was assessed using the Critical Appraisal Skills Programme (CASP) Clinical Prediction Tool Checklist. This checklist consists of 11 questions spread across 3 different sections – 'are the results valid?'; 'what are the results?' and 'will the results help locally/ are the findings applicable to the scenario?'.

More details about the quality assessment for prognostic studies are shown in Table 7:

Table 7: Risk of bias for prognostic factor studies

Risk of bias	Explanation
Are the results of the study valid?	In order for a study to have valid results, it should present with a well-defined rule and derived from a well-represented spectrum of patients. Likewise, the predictor variables and outcome should be evaluated blinded and the statistical methods used to validate the rule should be clearly described.
What are the results?	This section refers to whether the performance of the rule could be calculated and whether the rule is robust enough.

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Risk of bias	Explanation
Will the results help locally/ are the findings applicable to the scenario?	This domain refers to how direct are the findings in the study compared with the population it will be applied to and how applicable is the rule to a clinical setting (whether is reasonable and whether the information retrieved from it will change the management of the patient.

For prognostic reviews not involving predictive accuracy the CASP Clinical Prediction Tool Checklist was used instead of GRADE to derive an overall quality for each study (low, moderate or high) which was recorded in the summary of included studies table for each review. A study with 9 to 11 positive answers on the checklist was rated high quality, 6-8 answers moderate quality and 0 to 5 low quality.

3.5.1.1.3 Prevalence studies

For prevalence studies the risk of bias was assessed using the Joanna Briggs Institute Prevalence Critical Appraisal Tool (Munn 2014) which includes the critical issues of internal and external validity for prevalence studies as shown in Table 8.

Table 8: Risk of bias for prevalence studies

Risk of bias	Explanation
Sample representative of target population	This refers to how well the characteristics of the sample in the study match the target population of interest.
Participants recruited appropriately	This refers to whether the method of recruitment could have biased the study population by excluding a subset of participants.
Sample size adequate	Ideally the study authors should have conducted a sample size calculation to ensure they included enough participants to produce a reliable estimate of prevalence.
Study subjects and setting described in detail	The demographics of the study subjects and details of the setting need to be reported in sufficient detail to decide whether they are relevant to the target population and setting.
Data analysis conducted with sufficient coverage of identified sample	If a large number of participants drop out of the study then its results may be biased if the participants who drop out have a higher or lower prevalence of the condition.
Objective criteria used for measurement of condition	The condition of interest should be measured using an agreed definition.
Condition measured reliably	Those who determined whether the condition was present or absent in the study participants should do so in an unbiased way.
Appropriate statistical analysis	The methods used to should be reported in sufficient detail and should be suitable for this purpose.
Important confounders accounted for	Prevalence may be associated with confounding factors and subgroups and it is important these are taken into account in the analysis.
Subpopulations identified using objective criteria	Subpopulations of interest should be identified using agreed definitions.

For prevalence reviews the Joanna Briggs Institute Prevalence Critical Appraisal Tool was used instead of GRADE to derive an overall quality for each study (very low, low, moderate or high) which was recorded in the summary of included studies table for each review. A study with 10 positive answers on the checklist was rated high quality, 6-9 answers moderate quality and 0 to 5 low quality.

ISBN 978-1-4731-2693-0

3.5.1.1.4 Studies of normal weight loss in the early days of life

For studies of normal weight loss in the early days of life, risk of bias was assessed using the Joanna Briggs Institute Prevalence Critical Appraisal Tool (Munn 2014) as shown in Table 8. This checklist was chosen because relevant studies report the prevalence of weight loss above various thresholds.

3.5.1.1.5 Studies to identify differences in feeding and eating behaviour and practices between infants and children with or without faltering growth

For case control studies quality was assessed using the checklist for case- control studies (Appendix H in the NICE guidelines manual 2012). The checklist assesses internal validity of the study – selection of participants, assessment, confounding factors, and statistical analysis-. The different domains are rated from well covered to not applicable. See Table 9 for a summary of the different domains.

Table 9: Risk of bias for case-control studies

Risk of bias	Explanation
Selection of participants	This refers to the population the participants were taken from; participation rate, inclusion and exclusion criteria and definition of cases and controls.
Assessment	This refers to when the measures were taken and exposure status as measured in a reliable way.
Confounding factors	Ideally the study authors would have accounted for those variables that are likely to have a hidden effect on the dependent variable in the design of the study as well as analysis.
Statistical analysis	The statistical analysis used should have reported confidence intervals.

This checklist was used instead of GRADE to derive an overall quality for each study (very low, low, moderate or high) which was recorded in the summary of included studies table for each review, and used in the evidence statements.

3.5.1.2 Inconsistency

Inconsistency refers to unexplained heterogeneity of effect estimates. When estimates of the treatment effect, prognostic risk factor or diagnostic accuracy measures vary more widely between studies than would be expected due to random error alone (that is, there is heterogeneity or variability in results), this suggests true differences in underlying effects.

Heterogeneity in meta-analyses was examined; if present, sensitivity and subgroup analyses were performed as pre-specified in the protocols (appendix D).

When heterogeneity existed (chi-squared probability less than 0.1, I-squared inconsistency statistic of greater than 50%, or from visually examining forest plots), but no plausible explanation could be found (for example duration of intervention or different follow-up periods), the quality of the evidence was downgraded in GRADE by 1 or 2 levels, depending on the extent of inconsistency in the results. When outcomes are derived from a single trial, inconsistency is not an issue for downgrading the quality of evidence. However, ‘no inconsistency’ is nevertheless used to describe this quality assessment in the GRADE tables. In addition to the I-squared and chi-squared values and examination of forest plots, the decision for downgrading was dependent on factors such as whether the uncertainty about the magnitude of benefit (or harm) of the outcome showing heterogeneity would influence the overall judgment about net benefit or harm (across all outcomes).

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For diagnostic, clinical prediction rule and prognostic evidence, this was assessed visually according to the differences in point estimates and overlap in confidence intervals. For prognostic evidence this could be related to inconsistent findings across different studies for the same risk factor or on the sensitivity / specificity forest plots (looking at the overlap of confidence intervals) or the variability of study results in the summary ROC curve.

3.5.1.3 Indirectness

For quantitative reviews, directness refers to the extent to which the populations, intervention/risk factor/index test, comparisons and outcome measures are similar to those defined in the inclusion criteria for the reviews. Indirectness is important when these differences are expected to contribute to a difference in effect size, or may affect the balance of harms and benefits considered for an intervention, affect the accuracy estimate of the index test or has an impact on the prognostic effect of a risk factor.

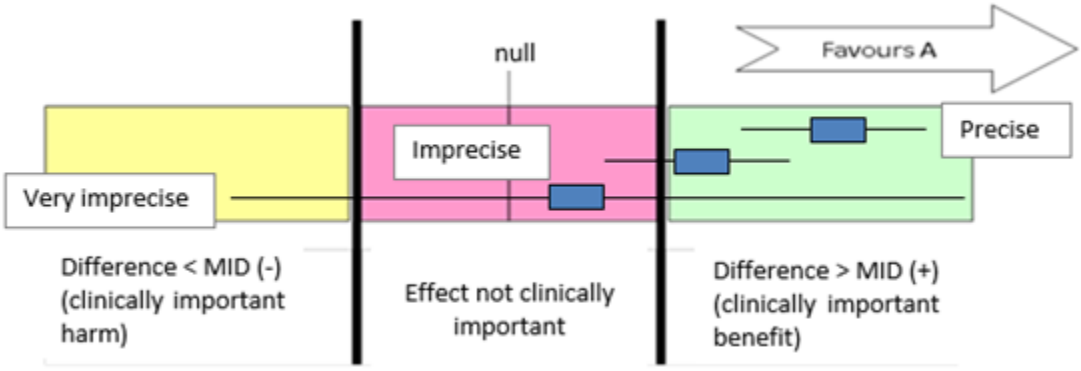
3.5.1.4 Imprecision

For intervention reviews, imprecision in guidelines concerns whether the uncertainty (confidence interval) around the effect estimate means that it is not clear whether there is a clinically important difference between interventions or not. This uncertainty is reflected in the width of the confidence interval. Imprecision occurs when this confidence interval crosses a clinical decision threshold that dictates recommending versus not recommending an intervention

The 95% confidence interval (95% CI) is defined as the range within which we can be 95% certain that the true effect lies. The larger the trial, the smaller the 95% CI and the more certain the effect estimate.

Imprecision in the evidence reviews was assessed by considering whether the width of the 95% CI of the effect estimate was relevant to decision-making, considering each outcome in isolation. This is explained in Figure 2, which considers a positive outcome for the comparison of treatment A versus treatment B. Three decision-making zones can be identified, bounded by the thresholds for clinical importance (minimal important difference, MID) for benefit and for harm. The MID for harm for a positive outcome means the threshold at which drug A is less effective than drug B by an amount that is clinically important to patients (favours B).

Figure 2: Illustration of precise and imprecise outcomes based on the confidence interval of outcomes in a forest plot



When the confidence interval of the effect estimate is wholly contained in 1 of the 3 zones (for example clinically important benefit), we are not uncertain about the size and direction of effect (whether there is a clinically important benefit, or the effect is not clinically important, or there is a clinically important harm), so there is no imprecision.

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When a wide confidence interval lies partly in each of 2 zones, it is uncertain in which zone the true value of effect estimate lies, and therefore there is uncertainty over which decision to make (based on this outcome alone). The confidence interval is consistent with 2 possible decisions and so this is considered to be imprecise in the GRADE analysis and the evidence is downgraded by 1 level ('serious imprecision').

If the confidence interval of the effect estimate crosses into 3 zones, this is considered to be very imprecise evidence because the confidence interval is consistent with 3 possible clinical decisions, and there is therefore a considerable lack of confidence in the results. The evidence is therefore downgraded by 2 levels in the GRADE analysis ('very serious imprecision').

Implicitly, assessing whether the confidence interval is in, or partially in, a clinically important zone, requires the Committee to estimate an MID or to say whether they would make different decisions for the 2 confidence limits.

The literature was searched for established MIDs for the selected outcomes in the evidence reviews, such as symptom measurement tools. In the absence of published MIDs, the Committee was asked whether they were aware of any acceptable MIDs in the clinical community. Finally, the Committee considered whether it was clinically acceptable to use the GRADE default MID to assess imprecision: for binary outcomes a 25% relative risk increase and the related relative risk reduction was used, which corresponds to clinically important thresholds for a risk ratio of 0.8 and 1.25 respectively (due to the statistical characteristic of this measure this means that this is not a symmetrical interval). This default MID for relative effect was used for all the binary outcomes in intervention reviews unless the Committee suggested a more appropriate value, such as an absolute risk difference criterion. For continuous outcomes default MIDs were also used. These use half of the median standard deviation of the control group.

For clinical prediction models (such as weight loss thresholds for concern) the Committee first considered whether sensitivity or specificity would be given more weight in the decision-making process. If one measure was given more importance than the other, then imprecision was rated on this measure. If the Committee could not agree clinically relevant thresholds of sensitivity or specificity then default values were used: less than 75% being low, 75% to 90% moderate and above 90% high sensitivity or specificity.

MIDs for prognostic factors were derived through Committee discussion of the size of the association between risk factor and outcome taking into account whether possible important confounding factors were considered in the analysis.

3.5.2 Assessing clinical significance (of intervention effects)

The Committee assessed the evidence by outcome in order to determine if there was, or potentially was, a clinically important benefit, a clinically important harm or no clinically important difference between interventions. To facilitate this, where possible, binary outcomes were converted into absolute risk differences (ARDs) using GRADEpro software: the median control group risk across studies was used to calculate the ARD and its 95% CI from the pooled risk ratio. For continuous outcomes, the mean difference between the intervention and control arm of the trial was calculated. This was then assessed in relation to the default MID (0.5 times the median control group standard deviation).

The assessment of clinical benefit or harm, or no benefit or harm, was based on the agreed MID of the effect, taking into consideration the precision around the effect estimate.

This assessment was carried out by the Committee for each critical outcome, and an evidence summary table (used in the Committee meetings, but not presented in this guideline) was produced to compile the Committee's assessments of clinical importance per

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outcome, alongside the evidence quality and the uncertainty in the effect estimate (imprecision).

3.5.3 Assessing clinical significance (of prognostic effects or clinical prediction models)

Absolute risk differences were not calculated for prognostic findings in this guideline. The Committee considered the size of the relative effects and whether this was large enough to constitute a sign or symptom predicting the outcome of interest. The usefulness of clinical prediction models, such as weight loss thresholds for concern, was judged by combining evidence about their accuracy with baseline risk to estimate the proportion who would be misclassified, taking into consideration the consequences of false positive or false negative classification.

3.5.4 Evidence statements

Evidence statements summarise the key features of the clinical evidence. The wording of the evidence statements reflects the certainty or uncertainty in the estimate of effect.

The evidence statements for intervention reviews are presented by outcome, and encompass the following key features:

- the quality of the evidence (GRADE rating)
- the number of studies and the number of participants for a particular outcome
- an indication of the direction of effect (for example, if a treatment is clinically significant [beneficial or harmful] compared with another, or whether there is no difference between the tested treatments).

The evidence statements for prognostic, prediction model or prevalence reviews include the following

- the quality of the evidence (using modified GRADE rating for prediction models, or otherwise based on the study level risk of bias)
- the number of studies and the number of participants for a particular risk factor, prediction model or prevalence estimate
- a summary of the effect size of the prognostic factor, magnitude of the prevalence estimate or accuracy of the prediction model.

3.6 Evidence of cost effectiveness

The aims of the health economic input to the guideline were to inform the Guideline Committee of potential economic issues related to the management of faltering growth to ensure that recommendations represented a cost-effective use of healthcare resources. Health economic evaluations aim to integrate data on healthcare benefits (ideally in terms of quality-adjusted life-years (QALYs)) with the costs of different care options. In addition, the health economic input aimed to identify areas of high resource impact; recommendations which – while nevertheless cost-effective – might have a large impact on CCG or Trust finances and so need special attention.

The Committee prioritised a single economic model on service delivery where it was thought that economic considerations would be particularly important in formulating recommendations and a review of the health economic literature was undertaken. There were concerns in the Committee that their recommendations might represent a high resource impact, but the economic model suggested that savings in the healthcare system offset a large part of this impact. For economic evaluations, no standard system of grading the quality of evidence exists and included papers were assessed using the economic evaluations checklist as specified in the NICE guidelines manual.

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Economic modelling was undertaken for a review question on monitoring suspected faltering growth. This was because it was thought that the Committee may want to make recommendations which were high resource impact, although the clinical evidence base did not support such recommendations. The Committee did not prioritise the health economic mode for this question as a lack of input data meant it could only function as a 'what if' analysis.

No economic analysis was undertaken for a question on interventions (nutritional or non-nutritional). While such an economic model might be valuable in deciding on the allocation of scarce NHS resources, no evidence was uncovered which might populate an economic model which meant that no model could be constructed.

No economic evaluation was undertaken for questions on risk factors, information and support, assessment, thresholds, differences between faltering growth and non-faltering growth or prevalence as it was agreed with the Committee that these reviews would focus primarily on the content and quality of information which is given to patients and clinicians respectively rather than whether the provision of such information represented a cost-effective use of NHS resources, which was thought to be clinically uncontroversial. Therefore these questions were not primarily about competing alternative uses for NHS resources and therefore were not considered suitable for economic analysis.

No economic analysis was undertaken for a question on referral to secondary care. This question was of a high health economic importance as the potential quality of life impact for misdiagnosing faltering growth and exposing a child to the potential harms of hospital is high, and potentially lifelong. However in order to perform a reasonable economic analysis on this question it would have been necessary to consider the cost-effectiveness of the treatment pathway for each possible reason to refer, some of which would be sensible referrals but – on further assessment – not turn out to be faltering growth. Some of these pathways have existing NICE guidance but some do not, which would have required de novo modelling (taking away resources from the main health economic guideline). For this question it was agreed with the Committee that health economic input would be limited to resource impact and analysis, with a full health economic evaluation being left until all possible referral pathways had been costed in other NICE Guidelines.

3.7 Developing recommendations

Over the course of the guideline development process, the Guideline Committee was presented with:

- evidence tables of the clinical and economic evidence reviewed from the literature: all evidence tables are in Appendix H
- summary of clinical and economic evidence and quality assessment (as presented in Chapters 4 to 11)
- forest plots (Appendix J)
- a description of the methods and results of the cost-effectiveness analysis undertaken for the guideline (Appendix L).

Recommendations were drafted on the basis of the group's interpretation of the available evidence, taking into account the balance of benefits, harms and costs between different courses of action. This was either done formally, in an economic model, or informally. Firstly, the net benefit over harm (clinical effectiveness) was considered, focusing on the critical outcomes, although most of the reviews in the guideline were outcome driven. When this was done informally, the group took into account the clinical benefits and harms when one intervention was compared with another. The assessment of net benefit was moderated by the importance placed on the outcomes (the group's values and preferences), and the confidence the group had in the evidence (evidence quality). Secondly, the group assessed whether the net benefit justified any differences in costs.

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When clinical and economic evidence was of poor quality, conflicting or absent, the group drafted recommendations based on their expert opinion. The considerations for making consensus-based recommendations include the balance between potential harms and benefits, the economic costs or implications compared with the economic benefits, current practices, recommendations made in other relevant guidelines, patient preferences and equality issues. The group also considered whether the uncertainty was sufficient to justify delaying making a recommendation to await further research, taking into account the potential harm of failing to make a clear recommendation.

The wording of recommendations was agreed by the group and focused on the following factors:

- the actions healthcare professionals need to take
- the information readers need to know
- the strength of the recommendation (for example the word 'offer' was used for strong recommendations and 'consider' for weak recommendations)
- the involvement of patients (and their carers if needed) in decisions about treatment and care
- consistency with NICE's standard advice on recommendations about drugs, waiting times and ineffective intervention.

The main considerations specific to each recommendation are outlined in the 'Recommendations and link to evidence' sections within each chapter.

3.7.1 Research recommendations

When areas were identified for which evidence was lacking, the group considered making recommendations for future research according to the NICE process and methods guide for research recommendations. Decisions about inclusion were based on factors such as:

- the importance to patients or the population
- national priorities
- potential impact on the NHS and future NICE guidance
- ethical and technical feasibility.

3.7.2 Validation process

This guidance is subject to a 6-week public consultation and feedback as part of the quality assurance and peer review of the document. All comments received from registered stakeholders are responded to in turn and posted on the NICE website when the pre-publication check of the full guideline occurs.

3.7.3 Updating the guideline

Following publication, and in accordance with the NICE guidelines manual, NICE will undertake a review of whether the evidence base has progressed significantly to alter the guideline recommendations and warrant an update.

ISBN 978-1-4731-2693-0

4 Weight loss in the early days of life

4.1 Normal limits of maximal weight loss

Review question: What are the normal limits of maximal weight loss in the first two weeks of life?

4.1.1 Introduction

The aim of this review was to address the topic of identifying infants with weight loss that ought to raise concerns and at which time point in the first weeks it should be measured to best capture those infants that may need an intervention. To do this the report summarised the normal range of weight loss in the first weeks of life and when weight reaches its lowest point (nadir).

For full details see review protocol in Appendix D.

4.1.2 Description of clinical evidence

Nine studies (N=171,562) were included in the review.

Most of these studies focus on the first 3 to 4 days of life only (Bertini, 2015; Davanzo 2013; Flaherman 2010, 2013, 2015; Martens 2007; Miller 2015). Two studies include weight loss measures beyond this follow-up, i.e. Macdonald 2003 up to 12 days, and Wright 2004 up to 6-8 weeks.

Due to differences in maximal weight loss, evidence was divided according to type of feeding:

- breastfed infants
- formula fed infants

as well as, mode of birth:

- vaginal birth
- caesarean birth.

It was then determined what the time to maximal weight loss was and what percentage of weight loss was reported at this time point. We then reported the 50th, 95th and 97.5th centile points at times reported in the studies.

Evidence from these studies is summarised in the clinical evidence profiles below (Table 11, Table 12, and Table 13). See also the study selection flow chart in Appendix F, summary charts in Appendix I, study evidence tables in Appendix G and exclusion list in Appendix H.

4.1.3 Summary of included studies

A summary of the included studies is presented in Table 10.

Table 10: Summary of included studies

Study, country	Sample	Follow-up	Subgroups analysed	Outcomes
Bertini (2015) Italy	N=1760 Breastfed, vaginal birth	72 hours	Male, female	Maximal weight loss (%), percentile curves, nadir time point
Davanzo (2013)	N=1003	Median 72 hours (IQR 48 – 96)	Formula fed, Breastfed exclusive,	Maximal weight loss (%)

ISBN 978-1-4731-2693-0

Study, country	Sample	Follow-up	Subgroups analysed	Outcomes
Italy			Breastfed partial, caesarean section, vaginal birth	
Flaherman (2010) USA	N=1049	39 hours	Breastfed exclusive, Breastfed partial	Maximal weight loss (%), nadir time point
Flaherman (2013) USA	N=47,687 Breastfed	Mean 48 hours (SD 24)	Breastfed exclusive, Breastfed partial	Maximal weight loss (%)
Flaherman (2015) USA	N=108,907 Breastfed	72 hours (vaginal delivery) to 96 hours (Caesarean)	Caesarean section, vaginal birth	Maximal weight loss (%), percentile curves, nadir time point, nomogram
Macdonald (2003) UK	N=971	288 hours	Formula fed, Breastfed exclusive, Breastfed partial	Maximal weight loss (%), nadir time point, time to regain birthweight
Martens (2007) Canada	N=812	Mean 59 hours (SD 30 hours)	Formula fed, Breastfed exclusive, Breastfed partial	Mean weight loss (%)
Miller (2015) USA	N=7075 Formula fed	Mean 46 hours (vaginal birth) to 72 hours (Caesarean)	Caesarean section, vaginal birth	Maximal weight loss (%), percentile curves, nadir time point, nomogram
Wright (2004) UK	N=961	Weights at birth, 5 days, 12 days and 6 - 8 weeks	-	Maximal weight loss (%)

IQR interquartile range; SD standard deviation.

4.1.4 Clinical evidence profile

The clinical evidence profiles for this review question (normal weight loss in the first two weeks) are presented in Table 11, Table 12 and Table 13. These tables summarise results for each outcome across studies. When several studies reported findings for the same outcome, results were presented as ranges of percentages, hours or days. Quality was then rated for each study.

Table 11: Summary clinical evidence profile for weight loss in exclusively breastfed infants

Weight loss in exclusively breastfed infants							
Outcomes	**Results**					**No of Participants (studies)**	**Quality of the evidence[3]**
Time of weight nadir[1]	Range 44 to 65 hours					N= 111,087 (3 studies)	Moderate for all studies[4,5]
Maximum weight loss[2]	**Birth type**	**50th centile**	**95th centile**	**97.5th centile**	**N babies**	N= 137,495 (5 studies)	Moderate for all studies[4]
	Vaginal	6.0% to 7.4%	8.8% to 10.6%	9.4%	85,193		

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Weight loss in exclusively breastfed infants							
	Caesarean	8.6%	11.7%	-	25,474		
	Not specified	5.5% to 6.6%	9.7% to 12.5%	10.6% to 13.8%	26,828		
	All combined	5.5% to 8.6%	8.8% to 12.5%	9.4% to 13.8%	137,495		
Time to return to birth weight (days)	**Birth type**	**Median**	**95th centile**	**97.5th centile**	**N babies**	N=395 (1 study)	Low[6]
	Not specified	8.3	18.7	21.0	395		

1 Mean time between birth and the lowest weight reached
2 Compared to birth weight
3 Assessed using the JBI prevalence checklist published by Munn 2014
4 Studies typically used weights routinely collected during hospital stay, detail about method of weighing was lacking, non-UK studies had potential demographic and maternity care differences to the UK population
5 Mothers and babies were often discharged before the weight nadir was reached.
6 Birth weight was not reported, method of delivery not reported. Time to regain birth weight was estimated in some infants who did not have a weight actually measured above birth weight.

Table 12: Summary clinical evidence profile for weight loss in partially breastfed infants

Weight loss in partially breastfed infants							
Outcomes	**Results**					**No of Participants (studies)**	**Quality of the evidence[3]**
Time of weight nadir[1]	Range 39 to 60 hours					N= 1118 (2 studies)	Moderate for all studies[4,5]
Maximum weight loss[2]	**Birth type**	**50th centile**	**95th centile**	**97.5th centile**	**N Babies**	N= 49,747 (5 studies)	Moderate for all studies[4]
	Vaginal	-	-	-	-		
	Caesarean	-	-	-	-		
	Not specified	5.5% to 6.3%	9.5% to 12.0%	10.2% to 13.2%	49,747		
Time to return to birth weight (days)	**Birth type**	**Median**	**95th centile**	**97.5th centile**	**N babies**	N=116 (1 study)	Low[6]
	Not specified	7.9	19.0	NR	116		

NR not reported.
1 Mean time between birth and the lowest weight reached
2 Compared to birth weight
3 Assessed using the checklist published by Munn 2014
4 Studies typically used weights routinely collected during hospital stay, detail about method of weighing was lacking, non-UK studies had potential demographic and maternity care differences to the UK population
5 Studies typically used weights routinely collected during hospital stay, mothers and babies were often discharged before the weight nadir was reached.
6 Birth weight was not reported, method of delivery not reported. Time to regain birth weight was estimated in some infants who did not have a weight actually measured above birth weight.

ISBN 978-1-4731-2693-0

Table 13: Summary clinical evidence profile for weight loss in formula fed infants

Weight loss in formula fed infants							
Outcomes	**Results**					**No of Participants (studies)**	**Quality of the evidence[3]**
Time of weight nadir[1]	Range 48 to 65 hours					N= 7471 (2 studies)	Moderate for all studies[4,5]
Maximum weight loss[2]	**Birth type**	**50th centile**	**95th centile**	**97.5th centile**	**N Babies**	N= 7915 (4 studies)	Moderate for all studies[4]
	Vaginal	2.9%	6.3%	-	4525		
	Caesarean	3.7%	6.8%	-	2550		
	Not specified	2.4% to 7.5%	7.5% to 11.6%	8.5% to 12.2%	840		
	All combined	2.4% to 7.5%	6.3% to 11.6%	8.5% to 12.2%	7915		
Time to return to birth weight (days)	**Birth type**	**Median**	**95th centile**	**97.5th centile**	**N babies**	N=389 (1 study)	Low[6]
	Not specified	6.5	14.5	16.7	389		

1 Mean time between birth and the lowest weight reached
2 Compared to birth weight
3 Assessed using the checklist published by Munn 2014
4 Studies typically used weights routinely collected during hospital stay, detail about method of weighing was lacking, non-UK studies had potential demographic and maternity care differences to the UK population
5 Studies typically used weights routinely collected during hospital stay, mothers and babies were often discharged before the weight nadir was reached.
6 Birth weight was not reported, method of delivery not reported. Time to regain birth weight was estimated in some infants who did not have a weight actually measured above birth weight.

4.1.5 Economic evidence

As this question does not concern the competing uses of NHS resources it was not prioritised for health economic analysis. No health economic evidence was identified for this topic from the overall health economic search.

4.1.6 Clinical evidence statements

The timing of maximal weight loss (the weight nadir) was reported by 6 studies including 119,676 infants. Moderate quality evidence suggested this weight nadir is typically reached between 2 and 3 days after birth, regardless of method of delivery (vaginal birth versus Caesarean section) or feeding type (exclusively breast fed, partially breast fed or formula fed).

The maximal weight loss for exclusively breast fed infants was reported by 5 studies including 137,495 infants. Moderate quality evidence indicated a mean or median maximal weight loss ranging from 5.5% to 8.6%. The 95th percentile for maximal weight loss ranged from 8.8% to 12.5%, and the 97.5th percentile ranged from 9.4% to 13.8%.

The maximal weight loss for partially breast fed infants was reported by 5 studies including 49,747 infants. Moderate quality evidence indicated a mean or median maximal weight loss

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ranging from 5.5% to 6.3%. The 95th percentile for maximal weight loss ranged from 9.5% to 12.0%, and the 97.5th percentile ranged from 10.2% to 13.2%.

The maximal weight loss for formula fed infants was reported by 4 studies including 7915 infants. Moderate quality evidence indicated a mean or median maximal weight loss ranging from 2.4% to 7.5%. The 95th percentile for maximal weight loss ranged from 6.3% to 11.6%, and the 97.5th percentile ranged from 8.5% to 12.2%.

Low quality evidence from one study including 971 infants indicated that most had returned to their birthweight by 21 days. The 97.5th percentile for time taken to return to birthweight ranged from 16.7 days for formula fed infants to 21.0 days for exclusively breastfed infants.

4.1.7 Evidence to recommendation

The Committee agreed that the reviews for normal weight loss and adverse events related to weight loss thresholds are intrinsically the linked and one cannot be considered without the other in isolation. Evidence from both was discussed together to draft recommendations and therefore rationale for these is provided in section 4.3).

4.2 Percentage birth weight loss associated with adverse outcomes

Review question: In infants under 4 weeks what percentage of weight loss is associated with adverse outcomes?

4.2.1 Introduction

This review aimed to determine the thresholds of weight loss in babies under 4 weeks that would lead to adverse events. For full details see review protocol in Appendix D.

4.2.2 Description of clinical evidence

Two studies were identified. One retrospective cohort study (N=874) from Taiwan was included in the review (Chang 2010). There were only available data for a threshold of 8% weight loss at 2 days after birth and a threshold of 11% at 3 days after birth. Evidence for these outcomes is summarised in Table 15.

One retrospective cohort study (N=1003) from Italy was also found (Davanzo 2013), although the design of the study did not directly satisfy the protocol criteria. However, it provided directly relevant data for the number of hypernatraemic infants above and below a threshold of 8% birth weight loss during the hospital stay immediately after birth. Evidence for this outcome is summarised in the clinical GRADE evidence profile below (Table 15).

See also the study selection flow chart in Appendix F, study evidence tables in Appendix G, full modified GRADE profile in Appendix J, forest plots in Appendix I and exclusion list in Appendix H.

4.2.3 Summary of included studies

A summary of the included studies is presented in Table 14.

ISBN 978-1-4731-2693-0

Table 14: Summary of included studies

Study, country	Sample	Follow-up	Subgroups analysed	Outcomes
Chang 2010 (Taiwan)	N=874 (219 infants with hyperbilirubinemia, 655 infants without) Exclusively breastfed, gestational age ≥35 weeks, birth weight >2500g	72 hours after birth	Above and below birth weight loss percentage was reported at 2 and 3 days after birth	Development of hyperbilirubinemia at 72 hours after birth
Davanzo 2013 (Italy)	N=1003 Exclusively breastfed or caesarean section, discharge age ≥36 hours	Within 2-4 days after discharge	Above and below 8% birth weight loss was reported at any time during hospital stay	Number of non-hypernatraemic infants [serum sodium concentration ≤150 mEq/L]

mEq/L milliequivalent per litre

4.2.4 Clinical evidence profile

The clinical evidence profile for this review question is presented is Table **15**.

Table 15: Summary clinical evidence profile for percent birth weight loss thresholds on 2nd and 3rd days of life to predict adverse outcomes in exclusively breastfed neonates

No of studies	N	Sensitivity [95% CI]	Specificity [95% CI]	LR+ [95% CI]	LR- [95% CI]	Quality
Weight loss of 8% or more of birth weight on day 2 of life to predict hyperbilirubinemia measured with AAP-2004 criteria						
1	874	0.47 [0.40, 0.53]	0.62 [0.59, 0.66]	1.24 [1.04, 1.47]	0.86 [0.75,0.98]	Low[1,2]
Weight loss of 11% or more of birth weight on day 3 of life to predict hyperbilirubinemia measured with AAP-2004 criteria						
1	874	0.12 [0.08, 0.17]	0.94 [0.92, 0.95]	1.90 [1.19 to 3.03]	0.94 [0.89, 0.99]	Low[1,2]
Weight loss of 8% or more of birth weight (median follow up 3 days) to predict hypernatraemia measured with sodium concentration level>145 mEq/L						
1	1001	1.00 [0.16, 1.00]	0.73 [0.70, 0.76]	3.73 [1.85, 5.20]	Cannot calculate	Very low[1,2, 3]

AAP, American Academy of Pediatrics; CI, confidence interval; mEq/L, milliequivalent per litre; LR+, positive likelihood ratio; LR-, negative likelihood ratio
[1] Downgraded one level for risk of bias – people evaluating outcomes knew the weight loss group
[2] Downgraded one level for indirectness - not 10% birth weight loss threshold (as specified in the review protocol).
3 Downgraded one level for imprecision - The judgement of precision was based on the confidence interval of sensitivity as this was considered to be the primary measure of interest. The 95% CI crosses both 75% and 90% thresholds defining moderate and high sensitivity, and the result was judged to be seriously imprecise

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4.2.5 Economic evidence

As this question does not concern the competing uses of NHS resources it was not prioritised for health economic analysis. No health economic evidence was identified for this topic from the overall health economic search.

4.2.6 Clinical evidence statements

Low quality evidence from 1 retrospective cohort study (n=874) indicates that birth weight loss thresholds of 8% at two days after birth and 11% at three days after birth have low sensitivity for hyperbilirubineamia. Most infants with hyperbilirubineamia had lost less birth weight than these threshold values and would be missed if weight loss was used as the sole criterion for selecting those at risk of hyperbilirubinaemia.

Very low quality evidence from 1 retrospective cohort study (n=1003) suggests that a percentage birth weight loss below a threshold of 8% at any time during hospital stay immediately after birth has high sensitivity for hypernatraemia, although there is uncertainty around this estimate. According to this evidence a weight loss of less than 8% during hospital stay could be useful in ruling out hypernatraemia.

4.3 Evidence to recommendations (based on evidence from sections 4.1 and 4.2)

4.3.1 Relative value placed on the outcomes considered

The aim of this review was to address the topic of identifying infants with weight loss that ought to raise concerns and at which time point in the first weeks it should be measured to best capture those infants who may need intervention.

For normal limits of maximal weight loss, the main outcomes that the Committee considered for decision- making were the average weight loss observed in newborn babies in their first two weeks of life, the variation of this weight loss and the timing of maximal weight loss. Despite the outcomes were divided between breast fed, formula fed and breastfed partially infants, the Committee decided that the pattern of weight-loss seen in breastfed babies should be used as a guide for all babies, as it is explained in section 4.3.2. The Committee also discussed that it is important to know how long it would take infants to regain weight.

For percentage of weight loss associated with adverse outcomes, no evidence was retrieved for the outcomes listed as important and critical in the protocol. However, other adverse events often seen in neonates under 4 weeks old above and below a birth weight loss threshold of 10% such as hyperbilirubinemia and hypernatremia considered a proxy and taken into consideration for decision-making. Along with these, the Committee also took into account other adverse outcomes often seen in clinical practice.

4.3.2 Consideration of clinical benefits and harms

The Committee discussed the evidence that weight loss typically reaches its lowest point by 2 to 3 days after birth and 5% of breastfed babies lose 11% or more of their birth weight. The Committee agreed that if healthcare workers were aware of usual weight loss patterns after birth that they could reassure parents and avoid unnecessary interventions for the baby. Potential harms associated with unnecessary interventions include, parental anxiety, harms due to admission to hospital and harms due to supplementary feeding.

The Committee deliberated on the different thresholds of weight loss that were reported for breastfed and bottle fed babies. The evidence indicated that bottle fed babies initially lose less weight. This is perhaps to be expected given the normal volumes of colostrum in the

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early days compared to volumes of formula milk often offered. The pattern of weight-loss seen in breastfed babies should thus be used as a guide for all babies, as breastfeeding is the physiological norm. The Committee therefore agreed to set the same recommendations for all babies.

The Committee acknowledged that weight loss is usually due to body fluid shifts in the early days of life. If this was associated with clinical evidence of dehydration it would be pathological and a reason for intervention. The Committee also discussed that infants of mothers who received intravenous fluids before delivery or before caesarean section may show larger weight loss in the early days after birth. The large cohort studies included mothers who had received intravenous fluids but separate weight loss thresholds could not be extracted for the corresponding groups of babies. The Committee recognised that a larger fluid loss would be likely for these babies in the early days, but felt that the 10% threshold should still be an initial cause for concern. Intravenous fluid during labour may then be an issue that can be discussed as part of the clinical assessment. The Committee agreed that it would be important to evaluate an infant's feeding as recommended if the weight loss was sufficient to raise some concern (more than 10%) and that the individual who observes the feeds has the relevant and appropriate expertise to do this (this could mean a health visitor or a trained person – usually with Baby Friendly Initiative accreditation). It was discussed that such expertise should not only be related to practical issues but should also include training in how to build positive relationships with mothers. Usually this assessment and observation would provide sufficient information to plan care for the infant but in some circumstances further investigations may be needed.

The infant who has lost more than 10% of their birth weight should be assessed for signs of effective feeding, milk transfer, urine and stool output. Healthcare professionals should also look for evidence of dehydration (because weight loss in the early days would usually be due to fluid loss). A related consideration is that there might be clinical evidence arising from the healthcare professional's assessment that might point to an underlying cause such as an illness or disorder that might account for the weight loss. If such a disorder or condition is identified it would then lead to onward referral to an appropriate specialist who could then consider the relevant treatment options.

In relation to the time to regain weight the Committee agreed that the 3 weeks that were reported in the evidence were a good estimate for the time when weight should have returned to birthweight and the Committee agreed that both parents and healthcare professionals should be aware of this. If a baby has lost for example 10.1% and is otherwise doing fine parents and healthcare professionals may want to monitor whether the birthweight has returned by 3 weeks and if not consider further actions if necessary (such as relevant interventions and support).

The Committee recognised that weight loss is not the only indication of an unwell baby. They believed that healthcare professionals would understand what a clinical assessment should include, but wanted to particularly raise the issue of signs of dehydrations. These could include symptoms such as vomiting or diarrhoea. They thought it was important that healthcare professionals had a clear pathway to seek advice and medical or specialist feeding assessment if there were any concerns about weight loss or an apparently unwell infant. In this pathway an individualised approach to assessment was recognised by the Committee to be important. The Committee thought that such a pathway could prevent the need for admission while an assessment is carried out and interventions and support could be provided.

4.3.3 Consideration of economic benefits and harms

Any recommendation made in this area is likely to carry an indirect cost since identifying the thresholds of normal weight loss implies that some babies might have abnormal weight loss requiring treatment; this treatment is likely to carry an economic cost even if the baby is

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perfectly healthy. The alternative, failing to identify when babies do in fact need treatment, is likely to incur a significant financial and quality of life burden as these babies are unlikely to receive appropriate management and thus might present with more significant conditions later on in their life.

Committee opinion is that the indirect effects are likely to tend towards a saving to the NHS. In their opinion having a clearly identified threshold of usual weight loss will help caregivers identify when to suspect faltering growth, and health professionals will be able to reassure parents more effectively that lesser amount of weight loss are within the expected range. There is likely to be a quality of life improvement related to this cost saving, but there is no economic evidence comparing the magnitude of this quality of life improvement with the size of the cost saving, so it is not possible to determine which factor will ultimately be more important to the NHS.

In terms of highly indirect costs, there is evidence that continued breastfeeding can reduce overall healthcare spending by making certain illnesses less likely and promoting robust health generally. As this effect is ongoing over the lifetime of the child, it is likely that relatively small investments made in breastfeeding support early will be cost-effective given the accumulation of QALYs and costs offset over the lifetime of the child.

If there is any direct resource impact associated with the first of these recommendations, it is likely to be minimal; simply informing parents of the normal limits of weight loss and answering questions they might have. Consequently the resource impact of these recommendations will not be above the NICE ‘high impact’ threshold of £1 million per recommendation. Subsequent recommendations – such as that to carry out a clinical assessment - may carry a direct cost impact but it is thought unlikely that this would be ‘high impact’ as these assessments are already carried out in the NHS and the recommendations refine under what circumstances they should be offered.

4.3.4 Quality of evidence

The quality of the evidence about the normal limits of weight loss ranged from low to moderate, using the Munn 2014 quality checklist. The included studies typically used routinely collected measurements during hospital stay and detail about the method of weighing was lacking. After vaginal birth, mothers and babies were often discharged from hospital before maximum weight loss occurred. The largest studies were carried out in the USA, with potential demographic and maternity care differences to the UK population. Consequently, the Committee noted that there were some issues regarding indirectness of the setting.

The quality of the evidence about percentage of weight loss associated with adverse outcomes was very low to low as assessed by modified GRADE.

For the domain risk of bias, the studies were assigned ‘serious risk of bias’ since the outcome assessors were aware of group allocation and the design of the studies was retrospective. However, the Committee noted that the studies were well powered and that the time between delivery and evaluation of adverse outcomes was appropriate.

No serious issues were found regarding inconsistency (heterogeneity), only single studies were included.

Some issues regarding indirectness were also identified in this review question. The Committee discussed that the participants in one of the studies did not present with the 10% birth weight loss threshold and that the study was carried out in Japan, fact that raises concerns about applicability of the study to the UK setting. Along with this, the Committee noted that one of the studies did not control for confounding variables.

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4.3.5 Other considerations

The Committee also discussed the need for consistent implementation of the recommendations into local pathways for assessment, support and referral when concerns about weight loss are raised.

It was agreed that early weight loss is not unusual and that therefore this is a distinct population in this guideline. Infants losing weight during these first few days (early days) would not be classified as having faltering growth. The Committee therefore agreed that these reviews and recommendations should be separated from the rest of the faltering growth guidance and that a preamble would be needed for this set of recommendations to highlight the difference between theses sections.

4.3.6 Key conclusions

Based on the available evidence the Committee extrapolated from indirect evidence of normal weight loss to make recommendations. Even though evidence for adverse events came from large data sets, it did not demonstrate an optimal weight loss threshold that identifies babies at risk of adverse outcomes. They therefore extrapolated from these reviews and their experience and expertise to provide a threshold (10% weight loss) that would not identify too many babies whilst capturing those where concerns would be justified. They also thought it important to highlight that commonly the birth weight is regained by 3 weeks of age.

4.4 Recommendations

Some weight loss in the first days after birth (referred to in this guideline as the early days of life) is normal and usually relates to body fluid adjustments. Sometimes there may be reason for concern about weight loss in the early days of life, which may need assessment and intervention. For this reason weight loss in the early days of life is dealt with separately in this guideline from concerns about inadequate weight gain in older infants and children, which is often related to nutritional intake.

1. **Be aware that:**
    - it is common for infants to lose some weight during the early days of life.
    - this weight loss usually stops after about 3 or 4 days of life.
    - most infants have returned to their birth weight by 3 weeks of age.

2. **If infants in the early days of life lose more than 10% of their birth weight:**
    - perform a clinical assessment, looking for evidence of dehydration, or of an illness or disorder that might account for the weight loss
    - take a detailed history to assess feeding (see NICE's guideline on postnatal care up to 8 weeks after birth)
    - consider direct observation of feeding
    - ensure observation of feeding is done by a person with appropriate training and expertise (for example, in relation to breastfeeding and bottle feeding)
    - perform further investigations only if they are indicated based on the clinical assessment.

3. **If infants lose more than 10% of their birth weight in the early days of life or they have not returned to their birth weight by 3 weeks of age, consider:**

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- referral to paediatric services if there is evidence of illness, marked weight loss, or failure to respond to feeding support (see NICE's guideline on postnatal care up to 8 weeks after birth)
- when to reassess if not referred to paediatric services.

4.5 Research recommendation

1. What is the effectiveness of feeding interventions compared to usual care/advice for breastfed neonates (up to 28 days old) with weight loss of greater than 10%?

Why this is important

Weight loss in breastfeeding infants in the first month of life can cause anxiety for parents and healthcare professionals. It can also incur costs to the NHS from admissions of the infant to hospital, with the potential for cessation of exclusive breastfeeding with its associated long-term health benefits.

Practice varies across the UK. Robust evidence about which feeding interventions improve outcomes could inform practice, potentially reducing unnecessary and costly interventions and supporting parent-infant relationships and physical and emotional health.Table 16: Research recommendation rationale

Research question	What is the effectiveness of feeding interventions compared to usual care/ advice for breastfed neonates (28 days) with weight loss of greater than 10%?
Why this is needed?	
Importance to 'patients' or the population	New parents whose babies are admitted to hospital are likely to feel emotionally upset and may feel that they have caused their babies to become unwell. Admission to hospital risks exposure to infections. Infants who have been admitted will often receive artificial supplementation, which increases their risk of long term health problems and may undermine their parents' confidence in breastfeeding.
Relevance to NICE guidance	High: The effectiveness of feeding interventions is unknown for faltering growth.
Relevance to the NHS	The most cost effective way of providing feeding support is unknown. All interventions carry a cost. Pathways for feeding support vary in different areas. Infants can be admitted to a maternity unit, neonatal unit, or a paediatric ward. Some units operate a 'rapid response system' with the infant feeding team providing intensive support in the community. Admission in these cases may be avoided.
National priorities	Exclusive breastfeeding to six months is recommended by NHS England. The National service framework for children, young people and maternity services aims for long-term and sustained improvement in children's health, and sets standards for health and social care services for children, young people and pregnant women. The Healthy Child Programme describes standards of care for screening and providing advice during pregnancy and the first 5 years of life. It includes broad recommendations on monitoring growth in infants and children.
Current evidence base	The guideline identified that there is a gap in the evidence base. The systematic review of this topic did not find any comparative effectiveness studies addressing this topic.
Equality	Recognition assessment and management of faltering growth should take into consideration parents' and carers' socioeconomic, cultural, religious and ethnic environment, and potential language barriers. Access to appropriate nutrition may also differ across socioeconomic groups. Certain groups may be

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Research question	What is the effectiveness of feeding interventions compared to usual care/ advice for breastfed neonates (28 days) with weight loss of greater than 10%?
	at greater risk of developing faltering growth, including preterm infants and children, children and infants born after intrauterine growth restriction. Those with learning-disabled parents or carers, asylum seekers, and looked-after children may find it more of a challenge to access services.
Feasibility	Study in two UK maternity units possible, preferably both UNICEF Baby-Friendly accredited. Ideally multi-centre to maximise recruitment opportunities.
Other comments	Consider stratified randomisation by unit type, e.g. in which the infant feeding team supports parents and babies at home, and comparing it to one in which babies are admitted to hospital.

Table 17: Research recommendation statements (PICO characteristics)

Criterion	Explanation
Population	Breastfed neonatal infants that have lost more than 10% of their birth weight. Specific data to consider – gestation, type of birth, mother's IV fluids
Intervention	Assessments of breastfeeds in neonates who have lost more than 10% of their birth weight, with advice given to improve attachment on the breast, hand-expressed and feed-expressed milk. Policy of Avoiding artificial milk supplements unless medically indicated.
Comparator	• Usual care
Outcome	• Number of neonates in whom excessive weight loss is prevented and the number of hospital admissions avoided. • The number of infants who have been exclusive breastfed at 6 months. • Weight, length, head circumference and arm measurements at 6 months
Study design	Randomised control trials (RCTs) which could be stratified in at least two types of setting. First, RCTs in UNICEF Baby-Friendly accredited centres. Second, RCTs in centres that do not have this accreditation.
Timeframe	3 years

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5 Faltering growth after the early days of life

5.1 Introduction

Concerns about growth in childhood are common. Parents and carers may seek advice from health professionals about weight gain or linear growth (height) in children. In other situations, parents and carers may be concerned about appetite and eating and the impact this has on their child's growth. Weight is measured routinely as part of health surveillance in young children, which may also alert health professionals to potential growth concerns.

The term 'faltering growth' is widely used to refer to slower weight gain in infants and young children than expected for age and gender. The expression 'failure to thrive' was used in the past to describe the same observation. Estimates of the prevalence of faltering growth in the United Kingdom (UK) vary, depending on the definition used.

Growth should be measured in a standardised way to provide accurate comparison with reference ranges and to monitor patterns of growth over time. The World Health Organisation (WHO) has produced growth standards, based on longitudinal studies of healthy breastfed infants. These standards, along with UK term and preterm infant growth data, have been incorporated into UK-WHO growth charts for monitoring growth in UK children. Epidemiological studies have shown that healthy children usually progress relatively consistently along a growth centile.

5.2 Thresholds for concern and measurement of weight, height or length

Review question: In infants and children with growth concern defined by one particular criterion, what are the adverse outcomes compared to children who do not have growth concern by that criterion?

5.2.1 Introduction

The aim of the current review is to explore whether current definitions (thresholds) effectively identify children with faltering growth who require intervention.

For full details see review protocol in Appendix D.

5.2.2 Description of clinical evidence

Two studies have been included in this review. Both studies reported on various measures of potential faltering growth and on adverse outcomes for children with each particular threshold definition for growth concern (Olsen 2007; Ross 2005).

One study presented the sensitivity and positive predictive values (PPV) of seven different anthropometric criteria for faltering growth in detecting "significant undernutrition" (defined as a combination of slow conditional weight gain and low body mass index [BMI]) (Olsen 2007). The sample size included in this cohort study was 5624 participants recruited from the National Birth Registry in Denmark.

One study conducted in the US aimed to identify whether a slowing in weight gain during early infancy could be used to identify children at increased risk of faltering growth at some point during the first 2 years of life (Ross 2009). The sample size for this study was 1978 healthy, term infants.

ISBN 978-1-4731-2693-0

Different definitions have been applied in the included studies to identify cases, as reported here:

- Ross 2005 identified cases by looking at undernutrition which was defined as weight for length z score of ≤-1.67.
- Olsen 2007 looked at the ability of seven clinically used criteria for 'moderate' failure to thrive to identify significant undernutrition defined as the combination of slow conditional weight gain and low BMI:
  - body mass index < 9th centile for chronological age
  - length < 9th centile for chronological age
  - weight <75% of median weight for chronological age
  - weight <80% of median weight for length
  - body mass index for chronological age <5th centile
  - length for chronological age <5th centile
  - weight deceleration crossing more than 2 major centile lines

The quality of each study was assessed using the CASP clinical prediction rule checklist. Please see the quality of the evidence section for more details.

See also the study selection flow chart in Appendix F, study evidence tables in Appendix G, and exclusion list in Appendix H.

5.2.3 Summary of included studies

A summary of the studies that were included in this review are presented in Table 18.

Table 18: Summary of included studies

Study	Sample	Objective	Definition of faltering growth	Outcomes
Olsen 2007	N=5624	To compare the prevalence and concurrence of different anthropometric criteria for FTT and test the sensitivity and positive predictive values of these in detecting children with "significant undernutrition", defined as the combination of slow conditional weight gain and low BMI.	Seven clinically used criteria applied to the cohort corresponding to 'moderate' FTT: • Weight <75% of median weight for chronological age • Weight <80% of median weight for length • Body mass index for chronological age <5th centile • Length for chronological age <5th centile • Weight deceleration crossing more than 2 major centile lines; centile lines used: 5,10,25,50,75,90,95, from birth until weight within the given age group • Conditional weight gain = lowest 5%, adjusted for	"Significant undernutrition", defined as BMI and conditional weight gain below the 5th centile

ISBN 978-1-4731-2693-0

Study	Sample	Objective	Definition of faltering growth	Outcomes
			regression towards the mean from birth until weight within the given age group • Combination of conditional weight gain and BMI below the 5th centile	
Ross 2009	N=1939 in the 4 -to-6 month time period and N=1900 in the 2-to-4 time period	To identify whether early deceleration in weight gain could be used to predict subsequent early growth childhood growth faltering.	Undernutrition was defined as weight for length <=-1.67	Change in weight-for-age and odds of becoming a case, stratified by birthweight category Sensitivity, specificity and area under the ROC curve by category of birthweight using a negative change in weight-for-age (WAZ) of ≥ -0.85

FTT failure to thrive, BMI body mass index, PPV positive predictive value, IQ intellectual quotient, UK-WHO United Kingdom- World Health Organization, GMS Gateshead Millennium Study, BMI body mass index

5.2.4 Clinical evidence profile

The clinical evidence profiles for this review question are presented in Table 20 (Olsen 2007 – 2 to 6 months), Table 21 (Olsen 2007 – 6 to 11 months), and Table 22 (diagnostic outcomes from Ross 2009).

Please see Table 19 for a definition of the Gomez and Waterlow criterion for their definitions of malnutrition. The differences in these are:

- Gomez criterion - the child's weight is compared to that of a normal child (50th percentile) of the same age. It is useful for population screening and public health evaluations.
- Waterlow criterion – refers to chronic malnutrition which could results in stunting.

Table 19: Definitions of Malnutrition (according to the Gomez and Waterlow criteria)

Classification	Definition	Grading	
Gomez criterion	Weight below % median WFA	Mild (grade 1) Moderate (grade 2) Severe (grade 3)	75%–90% WFA 60%–74% WFA <60% WFA
Waterlow criterion	z-scores (SD) below median WFH	Mild Moderate Severe	80%–90% WFH 70%–80% WFH <70% WFH

SD standard deviation; WFA weight for age; WFH weight for height.

ISBN 978-1-4731-2693-0

Table 20: Summary clinical evidence profile for accuracy of different thresholds in identifying significant undernutrition defined as the combination of slow conditional weight gain and low BMI, in infants aged 2 to 6 months.

No of studies	N	Sensitivity [95% CI]	Specificity [95% CI]	LR+ [95% CI]	LR- [95% CI]	Quality
Gomez criterion						
1	3789	0.40 [0.29, 0.52]	0.99 [0.99, 1.00]	60 [37,96]	0.60 [0.50,0.72]	moderate[1]
Waterlow criterion						
1	3789	0.29 [0.19, 0.40]	0.99 [0.99, 1.00]	53 [30,93]	0.72 [0.62,0.83]	moderate[1]
BMI < 5th centile						
1	3789	1.00 [0.95, 1.00]	0.97 [0.97, 0.98]	35 [28,41]	Cannot calculate	moderate[1]
Weight < 5th centile						
1	3789	0.68 [0.56, 0.78]	0.98 [0.97, 0.98]	32 [24,41]	0.33 [0.24, 0.46]	moderate[1]
Length < 5th centile						
1	3789	0.17 [0.09, 0.27]	0.97 [0.96, 0.97]	4.90 [2.90,8.27]	0.86 [0.78,0.95]	moderate[1]
Weight downward crossing ≥ 2 major centiles						
1	3789	0.71 [0.60, 0.81]	0.87 [0.85, 0.88]	5.32 [4.52,6.27]	0.33 [0.23,0.47]	low[1,2]
Conditional weight gain < 5th centile						
1	3789	1.00 [0.95, 1.00]	0.97 [0.97, 0.98]	37 [30,44]	Cannot calculate	moderate[1]

BMI body mass index, CI confidence interval, LR+ positive likelihood ratio, LR- negative likelihood ratio
1 Downgraded by one level due to risk of bias because it was unclear whether the predictor variables and the outcome were evaluated in a blinded fashion.
2 Downgraded by one level due to imprecision because the confidence interval of sensitivity (the primary measure of interest) crosses the 75% threshold

Table 21: Summary clinical evidence profile for accuracy of different thresholds in identifying significant undernutrition defined as the combination of slow conditional weight gain and low BMI, in infants aged 6 to 11 months.

No of studies	N	Sensitivity [95% CI]	Specificity [95% CI]	LR+ [95% CI]	LR- [95% CI]	Quality
Gomez criterion						
1	3692	0.17 [0.09, 0.28]	1.00 [0.99, 1.00]	50 [23,110]	0.84 [0.75,0.93]	moderate[1]
Waterlow criterion						
1	3692	0.17 [0.09, 0.28]	1.00 [1.00, 1.00]	76 [31,182]	0.84 [0.75,0.93]	moderate[1]
BMI < 5th centile						
1	3789	1.00 [0.95, 1.00]	0.97 [0.97, 0.98]	38 [31,45]	Cannot calculate	moderate[1]
Weight < 5th centile						
1	3789	0.76 [0.64, 0.85]	0.96 [0.96, 0.97]	21 [17,26]	0.25 [0.16,0.39]	low[1,2]
Length < 5th centile						
1	3789	0.02 [0.00, 0.08]	0.97 [0.96, 0.97]	0.44 [0.06,3.12]	1.02 [0.99,1.05]	moderate[1]

ISBN 978-1-4731-2693-0

No of studies	N	Sensitivity [95% CI]	Specificity [95% CI]	LR+ [95% CI]	LR- [95% CI]	Quality
Weight downward crossing ≥ 2 major centiles						
1	3789	0.85 [0.74, 0.92]	0.80 [0.79, 0.82]	4.29 [3.80,4.84]	0.19 [0.11,0.33]	low[1,2]
Conditional weight gain < 5th centile						
1	3789	1.00 [0.95, 1.00]	0.97 [0.96, 0.97]	31 [35,36]	Cannot calculate	moderate[1]

BMI body mass index, CI confidence interval, LR+ positive likelihood ratio, LR- negative likelihood ratio
1 Downgraded by one level due to risk of bias because it was unclear whether the predictor variables and the outcome were evaluated in a blinded fashion.
2 Downgraded by one level due to imprecision because the confidence interval of sensitivity (the primary measure of interest) crosses the 75% threshold

Table 22: Summary clinical evidence profile for accuracy of negative change in weight for age during 4 to 6 months of age (defined as weight-for-age z score change of ≥ -0.85) to predict underweight during the first 2 years of life (defined as weight-for-length ratio z score ≤-1.67)

No of studies	N	Sensitivity [95% CI]	Specificity [95% CI]	LR+ [95% CI]	LR- [95% CI]	Quality
Negative change in weight-for-age z score						
1	458	0.06 [0.04,0.09]	0.97 [0.96,–0.98]	2.00 [2.31, 124]	0.97 (0.07	moderate[1]
Negative change in weight-for-age z score, in those with birth weight < 3.0 kilograms						
1	131	0.02 [0.0,0.07]	0.98 [0.96,1.00]	1.00 [3.28, 182]	1.00 [0.07, 3.62]	moderate[1]
Negative change in weight-for-age z score in those with birth weight ≥ 3.0 kilograms						
1	327	0.07 [0.05,0.10]	0.97 [0.96,0.98]	2.33 [2.24, 120]	0.96 [0.07, 3.66]	moderate[1]

BMI body mass index, CI confidence interval, LR+ positive likelihood ratio, LR- negative likelihood ratio
1 Downgraded by one level because the prediction rule was not validated in a separate population. It was also unclear whether the predictor variables and the outcome were evaluated in a blinded fashion.

5.2.5 Economic evidence

As this question does not concern the competing uses of NHS resources it was not prioritised for health economic analysis. No health economic evidence was identified for this topic from the overall health economic search.

5.2.6 Clinical evidence statements

Moderate quality evidence from one study with 5624 participants indicates that in infants aged 2 to 11 months the Gomez criterion, the Waterlow criterion and length < 5th centile all have low sensitivity but high specificity in identifying significant undernutrition (defined as the combination of slow conditional weight gain and low BMI).

Low to moderate quality evidence from one study with 5624 participants indicates that in infants aged 2 to 6 months weight < 5th has low sensitivity and high specificity in identifying significant undernutrition, but has moderate sensitivity and high specificity in those aged 6 to 11 months.

Low quality evidence from one study with 5624 participants indicates that in infants aged 2 to 6 months weight downward crossing ≥ 2 major centiles has low sensitivity and moderate specificity in identifying significant undernutrition, but has moderate sensitivity and specificity in those aged 6 to 11 months.

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Moderate quality evidence from one study with 5624 participants indicates that in infants aged 2 to 11 months BMI < 5th centile and conditional weight gain < 5th centile both have high sensitivity and specificity in identifying significant undernutrition. This was by definition, however: the study used these parameters to define undernutrition.

Moderate quality evidence from one study with 1939 participants indicates that a shift in weight for age z score of ≥-0.85 during 4 to 6 months of age has a low sensitivity but high specificity in detecting underweight up to the age of 2 years (defined as weight for length z score ≤-1.67), regardless of the weight of the baby at the time of measurement.

5.2.7 Evidence to recommendations

5.2.7.1 Relative value placed on the outcomes considered

The aim of this review was to explore whether current definitions (thresholds) effectively identify children with faltering growth who require intervention.

The Committee identified stunted growth and cognitive development as critical outcomes for decision making and established the following important outcomes:

- persisting slow growth
- adverse events related to faltering growth such as infection
- duration of follow up for individual outcomes
- child protection instances / unrecognised underlying medical condition.

Given that no evidence was found for the critical nor the important outcomes, sensitivity and specificity of measures of potential faltering growth and adverse outcomes for children with each particular threshold definition for growth concern were retrieved in the evidence as a proxy. The Committee used the results of these studies as a starting point for their discussion, however the recommendations are based on consensus as well as on a discussion of an additional study by Wright and Garcia 2012. This study reported on the combination of weight or BMI and low absolute BMI for detecting undernutrition.

5.2.7.2 Consideration of clinical benefits and harms

The Committee acknowledged the evidence presented and used it together with their clinical expertise and awareness of the current state of services to write recommendations on how best to recognise faltering growth in infants and preschool children.

The Committee agreed that several factors have to be considered when using thresholds to recognise faltering growth, and it should not usually be based merely on a single weight measurement. Short-term fluctuations in weight are common in children due to minor illnesses or measurement or plotting error and so it is important to repeat measurements that cause concern. An infant's or child's initial weight and length centile and trajectories over time, together with the child's growth potential, have all to be considered when assessing for the presence of faltering growth. However, the Committee recognised the importance of recommending a measure that is useful, sufficiently precise and practical for health care professionals to put into practice confidently. The Committee decided to highlight the importance of measuring length or height and assessing linear growth in their recommendations in order to identify those with constitutional short or lean stature or those with growth disorders.

The Guideline Committee recommended that a BMI less than the 2nd percentile be recognised as suggesting undernutrition in a child over the age of 2 years. This was based on the advice provided by the Royal College of Paediatrics and Child Health (RCPCH) / Department of Health (DH) on the interpretation of BMI in children over the age of 2 years. That advice states that a BMI below the 2nd centile in a child over the age of 2 years is unusual and may reflect undernutrition, but may simply reflect a small build.

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5.2.7.3 Consideration of economic benefits and harms

Recognising faltering growth in infants and preschool children carries with it a clear economic benefit in being able to offer that child appropriate treatment in a timely manner. This will almost certainly improve the quality of life of that child, both in the immediate future and long-term if the treatment helps the child – for example – do better at school. It is unclear whether it carries a financial benefit to the NHS in terms of reduced future hospital appointments, but it is likely that a fuller Personal and Social Services (PSS) perspective would find the intervention represents a cost saving. If educational costs were taken into account (which is not typical for NICE Guidelines) then the reduced requirements on schools and social services might be expected to compensate for the cost of treatment.

The risks of treating are exposing a child to hospital who does not need to be there, and potentially causing anxiety to parents for no corresponding benefit to the child. In addition, there is an economic reason to prefer accurate diagnosis as treating a child who does not have Faltering Growth will incur economic cost for no benefit. The Committee took this into account when making their recommendations, suggesting that clinicians record potentially concerning growth and consider the expected height of the child given the height of the parents. Correctly identifying concerning growth should limit the economic costs of a false positive.

As the Committee intend to improve the accuracy of recognising faltering growth generally, it is unlikely that these recommendations will carry a significant cost impact, as the more accurate the recognition the lower the expected cost to the NHS. The recommendations around measurement, observation and referral will carry a direct cost to the NHS but the Committee judged that this was already taking place in an ad hoc manner throughout the country so their recommendations would bring healthcare providers in line with best practice. This should lead to a neutral resource impact.

5.2.7.4 Quality of evidence

Quality of the studies was assessed using the CASP clinical prediction rule checklist and the evidence was then appraised using an adapted GRADE approach. The protocol stated that prospective population based studies would be the most appropriate study design to address this review question. Therefore, this type of study design would initially be assigned high quality and downgraded based on potential sources of bias. The quality of the evidence was low to moderate; the Committee discussed that they had little confidence in this evidence due to the main causes of bias were uncertainty around the effect estimates of the effect related to the relatively small sample sizes of the studies.

Even though the evidence was considered, according to GRADE characteristics, to be of moderate quality, the Committee agreed that the evidence was not strong and direct enough to draw clear conclusions about the best threshold approach. They also discussed that the studies provided evidence from research settings and that this was not necessarily generalisable to wider clinical practice (for example, some measurements may not be practical in routine clinical settings).

5.2.7.5 Other considerations

In addition to the studies included for this review, the Committee discussed the contents of a paper by Wright and Garcia 2012, which although did not meet the criteria for the review, was known by the group as demonstrating a possible pathway for the recognition of faltering growth. This paper included data on the prevalence of downward centile crossings from birth to ages 4, 8 and 12 months in the Gateshead Millennium cohort, compared with the UK–WHO growth standard, broken down by centile position at birth. The Guideline Committee recognised that it is common practice to advise that concerns about faltering growth should be raised if a child crosses more than two centile spaces. The Guideline Committee

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considered this approach, but took account of the fact that children born on a lower centile are less likely to cross centile spaces than those born on a higher centile. They took account of the Millennium cohort data to make a pragmatic recommendation that there should be concern about possible faltering growth if children born below the 9th centile fell across one or more spaces, if those born above the 91st centile space fell across three or more spaces and if those born between the 9th and 91st centiles fell across two or more spaces. By adopting this approach they agreed it was less likely faltering growth would be missed in babies that are relatively light at birth and it was less likely that unnecessary concern about faltering growth would be raised about those who are relatively heavy at birth.

The Committee agreed that both length and weight measurements were essential in order to accurately identify and assess a child with faltering growth. This is because 'thinness', presenting as low weight for height, is a potential indicator of undernutrition. Children may cross centiles for weight during normal growth, but this pattern should be interpreted in light of their birthweight centile and length measurements alongside weight. The Committee acknowledged that length is not always measured, even when there is concern about weight. This is partly because it is not always an easy measurement to take accurately, especially in young infants. However, the Committee agreed that if there are concerns regarding weight, length should be quantified in order to avoid misclassification. Equally it is important to consider parental height when interpreting linear growth in a child where there are concerns about faltering growth. A recommendation was made on this.

The Committee wanted the recommendations to reflect that different methods of measuring linear growth are usually applied to children above and below 2 years old. Under 2 years, infants and children are generally measured lying down; above 2 years of age, children are generally measured when standing.

The Committee agreed that the UK WHO growth charts should be used to monitor growth in children as they combine the WHO standards with the UK preterm and birth data in breast fed children. They are readily and freely available, including online through the Royal College of Paediatrics and Child Health (http://www.rcpch.ac.uk/improving-child-health/public-health/uk-who-growth-charts/uk-who-growth-charts-0-18-years). Equally, growth measurements should be recorded in the parent or carer-held Personal Child Health Record. The Committee also recognised that there are specific standards that apply to the weighing of infants. The Committee acknowledged that there was, for instance, a report published in 2017 by the Royal College of Nursing (RCN 2017) that highlights standards and competencies for weighing infants, children and young people in acute healthcare settings.

5.2.7.6 Key conclusions

The identification of faltering growth depends on a number of different observations, including change in weight over time, length, and genetic growth potential (generally interpreted from parental height). The evidence could not clearly identify a single threshold that would reliably recognise children who have faltering growth. The Committee looked at published data on normal weight gain in children (Wright and Garcia 2012) and the associated algorithm and used this as the basis of the recommendations. The Committee concluded that their draft recommendations form a pathway that will improve recognition of faltering growth and should also be easily implemented in clinical practice.

5.2.8 Recommendations

4. **Consider using the following as thresholds for concern about faltering growth in infants and children (a centile space being the space between adjacent centile lines on the UK WHO growth charts):**
    - a fall across 1 or more weight centile spaces, if birthweight was below the 9th centile,

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- a fall across 2 or more weight centile spaces, if birthweight was between the 9th and 91st centiles,
- a fall across 3 or more weight centile spaces, if birthweight was above the 91st centile,
- when current weight is below the 2nd centile for age, whatever the birthweight.

5. **If there is concern about faltering growth (for example, based on the criteria in recommendation 4):**
    - weigh the infant or child
    - measure their length (from birth to 2 years old) or height (if aged over 2 years)
    - plot the above measurements and available previous measurements on the UK WHO growth charts to assess weight change and linear growth over time.

6. **If there are concerns about an infant's length or a child's length or height, if possible obtain the biological parents' heights and work out the mid-parental height centile. If the child's length or height centile is below the range predicted from parental heights (more than 2 centile spaces below the mid-parental centile) be aware this could suggest undernutrition or a primary growth disorder.**

7. **If there is concern about faltering growth or linear growth in a child over 2 years of age, determine the BMI centile:**
    - using the UK WHO centiles and the accompanying BMI centile 'look-up chart', **or**
    - by calculating the BMI (weight in kg/height in metres squared) and plotting this on the BMI centile chart.

    Then:
    - if the BMI is below the 2nd centile, be aware this may reflect either undernutrition or a small build
    - if the BMI is below the 0.4th centile, this suggests probable undernutrition that needs assessment and intervention.

8. **Record all growth measurements in the parent or carer-held Personal Child Health Record.**

5.3 Assessment

5.3.1 Differences in feeding and eating behaviour and practices

Review question: What are the differences in feeding and eating behaviour and practices in children with faltering growth compared to those without?

5.3.1.1 Introduction

When a child is identified in primary care as showing faltering growth, an understanding of the factors that may have contributed to the growth pattern is important in order to inform the advice offered and to decide on any further investigation, intervention or onward referral to specialist services. In some cases the factors leading to faltering growth may be clear, but in

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others it will not. Parents may fear that there is some underlying illness and struggle to understand how their child can have become undernourished. Successful feeding depends upon parents offering the right sort of foods, at a reasonable frequency, in a suitable setting and a form that the child can eat. Meanwhile successful child eating behaviour depends upon the child acquiring the necessary oromotor and fine motor skills, having a good appetite and not being exposed to adverse eating experiences.

The aim of this review was to identify possible behaviour and practices that may adversely affect feeding and eating and may thus contribute to faltering growth. This information could contribute to management strategies.

The Committee identified the following outcomes as critical for decision making:

- measurement of fluid and nutritional intake
- feeding eating and appetite behaviour and problems (e.g. refusal)
- parent-child interaction during feeding/mealtimes.

For full details see review protocol in Appendix D.

5.3.1.2 Description of clinical evidence

Six case-control studies (Drewett 2003; Kaese-Hara 2002; Wright 2000; Heptinstall 1987; Kaese-Hara 2001, and MacPhee 1996) and three nested case-control studies (McDougall 2008; Parkinson 2004 and Robertson 2011) have been included in this systematic review for assessing differences between faltering and non-faltering infants and preschool children.

Eight studies have been conducted in the UK (Drewett 2003; Black 1999; Kaese-Hara 2002; Parkinson 2004; Robertson 2011; Wright 2000; Heptinstall 1987; Kaese-Hara 2001; McDougall 2008) and one was conducted in the US (MacPhee 1996).

The sample size ranged between 23 and 127 infants and preschool children with faltering growth and all studies used a sample of children without faltering growth (but matched in age and gender) as a comparison.

Some variability has been encountered in the methods of data collection used, but most studies used observations during meals; either directly observed or videotaped. One of the studies (Wright 2000) used food diaries, whereas two studies used digital scales (Kaese-hara 2001 and Kaese-Hara 2002).

The included studies reported on the following outcomes:

- Intakes for solid foods and fluids (Drewett 2003; Heptinstall 1987; Wright 2000)
- Feeding behaviour (Drewett 2003; Parkinson 2004; McDougall 2004)
- Parent-child interactions during mealtimes (Heptinstall 1987; Robertson 2011; MacPhee 1996)
- Energy compensation characteristics (Kaese-Hara 2002)
- Hedonic response to sweet tastes (Kaese-Hara 2001)

However, the following outcomes from the review protocol have not be reported by the evidence:

- Health-related quality of life
- Parent or carer satisfaction

The variability found in the way studies reported on recognition of faltering growth is reported in Table 23:

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Table 23: definitions for faltering growth used by the studies

Study	Definition
Drewett 2003	Conditional weight gain criterion which identified the slowest gaining 5% (the 'Thrive index').
Kasese-Hara 2002	Weight gain in the slowest 5% for their age. This was established using a conditional weight gain criterion (the 'Thrive index'). Children identified as cases using this criterion are low in weight-for-age and weight-for-height in spite of normal birth weight and show poor subsequent growth to at least 8 years.
Parkinson 2004	Weight gain was assessed using the 'Thrive index'. A 'Thrive index' is change in weight (Z-score), adjusted for the child's initial weight. The score that identifies the slowest-growing 5% at different ages has been established and was used to identify cases.
Robertson 2011	Conditional weight gain ('Thrive index').
Wright 2000	Children with a 'Thrive index' of <1.3 weight SDS. This criterion identifies the slowest gaining 5% of children, whatever their initial weight centile.
MacPhee 1996	Non organic failure to thrive was defined as persistent decline or lack of weight gain since birth in the absence of organic origin.
McDougall 2008	Infants with weight gain below the 5th centile over the first 6-8 weeks
Heptinstall 1987	The child must be below the 10th population centile for height and weight at 4 years on British Standard growth charts. Additionally, in order to be considered, the children's stature had to be under the 10th centile in relation to mean parental height.
Kaese-Hara 2001	Conditional weight criterion ('Thrive index').

The quality of each study was assessed using the NICE checklist for cases-control studies. Please see the quality of the evidence section for more details.

The main reason why studies were excluded from this review was due to either cases not presenting with faltering growth or studies not presenting with a comparative or control group.

See also the forest plots in Appendix I, study evidence tables in Appendix G and the exclusion list in Appendix H.

5.3.1.3 Summary of included studies

A summary of the studies that were included in this review are presented in Table 24.

Table 24: Summary of included studies

Study	Objective	Cases	Controls	Assessment/ Methods	Outcome(s)
Drewett 2003	To compare feeding behaviour at the test meal in children who failed to thrive and appropriate controls and to examine the extent	N=27 children with failure to thrive defined as those children who presented in the slowest 5% compared with children of the same	N=27 children with normal growth. Children's age ranged between 12 and 24 months.	For each child a standard lunchtime meal was videotaped. The authors of the study developed behaviour codes to assess the mealtime behaviour. Digital scales were also used for weighing	Intakes (mass and density) of solid foods and fluids Feeding behaviour (feedself, hand, give, accept, refuse, reject).

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Study	Objective	Cases	Controls	Assessment/ Methods	Outcome(s)
	to which differences in their behaviour explained differences in their energy intake.	weight soon after birth. Children's age ranged between 12 and 24 months		food before and after the meal.	
Heptinstall 1987	To assess the nutrition and mealtime behaviours in families of growth-retarded children in compariso n with those children with normal weight gain	N=23 children with growth retardation. Children must be below the 10th population centile for height and weight at four year on British Standard growth charts. Children had a mean age of 4 years.	N=24 cases whose weight had been above the 10th centile at the last recorded health clinic attendance.	Direct observations of mother-child interactions. Mealtime observations, using an abbreviated set of codes from the scheme, expected to be specifically relevant to mealtimes. Feeding and mealtimes interview, including a food diary.	Children's nutritional intake Family attitudes to mealtimes and food Parent-child interactions during mealtimes
Kasese-Hara 2001	To investigate the possibility that failure to thrive is associated with a reduced hedonic response to sweet tasted	N=27 1-year-old children who failed to thrive in infancy diagnosed using the conditional weight criterion ('thrive index').	N=26 1-year-old children with normal growth.	Intakes of three fluids with 0.0 ml. (water), 0.2 ml. and 0.4 ml. of sucrose, each drink offered for 60 sec. with a 30 sec. interval between each.	Hedonic response to sweet tastes.
Kasese-Hara 2002	To compare the energy compensat ion characteris tics of a group of children with failure to thrive	N=27 children with weight gain in the lowest 5% for their age. Children had a mean age	N=26 children with normal weight gain. Children had a mean age of 18.3 months.	Children were given standard ad libitum test meals on 2 days in the same week, at lunchtime in their own homes. Digital scales were used for all weightings,	Energy intake

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Study	Objective	Cases	Controls	Assessment/ Methods	Outcome(s)
	with those of control children with normal weight gain. The prediction that the children who fail to thrive would show less precise energy compensation that the controls was tested.	of 17.4 months.		accurate to 0.001g. Energy contents were supplied by the manufacturers and are given in kJ per 100g.	
MacPhee 1996	To design a feeding interaction checklist to improve observation and documentation of NOFTT feeding situations. The 2 specific aims were: (a) to develop a reliable and valid tool for use in busy inpatient and outpatient settings and (b) to demonstrate the tool's usefulness in clinical practice.	N=22 mother-children dyads. Children were hospitalized and presented with non-organic failure to thrive, defined as defined as persistent decline or lack of weight gain since birth in the absence of organic origin. Children had an average age of 9.9 months.	N= 24 thriving dyads. Children had an average age of 9.85 months.	Videotaped feeding interactions. Feeding checklist Chatoor Feeding Scale	Parent-child interaction during feeding.
McDougall 2008	To identify infants with early weight	N= 74 infants with weight gain below the	N= 86 infants nearest in birth date to each case on	Structured questionnaire, focussing on	Feeding behaviour: slow feeding, weak sucking and amount of milk taken.

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Study	Objective	Cases	Controls	Assessment/ Methods	Outcome(s)
	faltering at the 6-8 week check and examine their family circumstances, feeding and behavioural development.	fifth centile over the first 6-8 weeks	the same health visitor's list	family details, feeding.	
Parkinson 2004	To examine the feeding behaviour and food intake of a cohort of children with failure to thrive	N=30 children with a weight gain below the 5th centile. Infant's age ranged between 13 and 21 months (mean 15.7, SD 1.4)	N= 57 children above the 10th percentile. Infant's age ranged between 13 and 21 months (mean 15.7, SD 1.4)	Direct observations over lunchtime meals. The video-tapes were coded for feeding behaviour using a behavioural coding inventory.	Counts of 5 feeding actions (give, accept, feed self, refuse, reject). Energy intake
Robertson 2011	To explore whether the Mellow Parenting assessment system can detect any difference in parent-child meal time interaction between children with weight faltering and normally growing children	N=30 mother-infant dyads. Infants with weight faltering were defined as those with weight gain below the 5th percentile. Infant's age ranged between 13 and 21 months.	N=29 healthy controls	Video recording Mellow parenting assessment system	Parent-child mealtime interaction
Wright 2000	To address the following hypotheses:	N=42 children with a thrive index of <1.3 weight SDS. This criterion	N=45 children identified from the district health child computer. Infants' age ranged	Standard health visitor proforma and 3 days food diary.	Energy consumption (kJ/kg) and feeding problems.

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Study	Objective	Cases	Controls	Assessment/ Methods	Outcome(s)
	Children with failure to thrive, compared with normally-growing controls would: 1. Consume less food, with less variety 2.have been weaned significantly later and show an immature feeding pattern, 3. Has higher rates of early feeding difficulty as well as less current interest in food.	identifies the slowest gaining 5% of children, whatever their initial weight centile. Infant´s age ranged between 6 and 32 months.	between 7 and 33 months.		

Sec second; ml millimetre; kJ kilocalorie; g gram; NOFTT non-organic failure to thrive; Kg kilogram.

5.3.1.4 Clinical evidence profile

The main findings reported in the evidence are summarised in Table 25 and Table 26. These tables summarise results for each outcome across studies. When several studies reported findings for the same outcome, results were presented as ranges. Quality was rated individually for each study according to risk of bias.

Table 25: Summary clinical evidence profile for differences in feeding and eating behaviour and practices between children with and without faltering growth: dichotomous outcomes

Outcome	OR [95% CI] faltering growth vs normal growth	No of Participants (studies)	Quality of evidence[1]
Parent and child mealtime interaction			
Angry confrontations	OR 3.30 [0.91, 11.93]	46 (1 study)	Low
Pressure on child to eat	OR 3.65 [0.94, 14.20]	46 (1 study)	Low
Environmental factors			

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Outcome	OR [95% CI] faltering growth vs normal growth	No of Participants (studies)	Quality of evidence[1]
Unsupervised meals	OR 4.59 [0.84, 25.16]	46 (1 study)	Low
Daily meal unpredictable	OR 9.63 [1.08, 86.18]	46 (1 study)	Low
Feeding, eating and appetite behaviour			
Infancy feeding problems	OR ranged from 3.59 [1.15, 11.18] to 4.29 [0.98, 18.72]	133 (2 studies)	Low to moderate
Child enjoys meals	OR 0.43 [0.14, 1.30]	87 (1 study)	Moderate
Mother enjoys meals	OR 0.54 [0.22, 1.32]	87 (1 study)	Moderate
Drinks from beaker	OR 0.34 [0.14, 0.82]	87 (1 study)	Moderate
Child is hungry	OR 0.12 [0.04, 0.33]	87 (1 study)	Moderate
Eats all	OR 0.41 [0.17, 0.98]	87 (1 study)	Moderate
Slow feeding at 2 months	OR 5.18 [2.31, 11.60]	160 (1 study)	Moderate
Weak sucking	OR 21.61 [2.78, 168.09	160 (1 study)	Moderate
Small quantities of milk	OR 1.69 [0.90, 3.17]	160 (1 study)	Moderate
Slow feeding after 2 months	OR 4.83 [1.69, 13.85]	160 (1 study)	Moderate
Refused breast milk after 2 months	OR 65.07 [3.86, 1098.09]	160 (1 study)	Moderate
Refused other milk after 2 months	OR 1.02 [0.51, 2.04]	160 (1 study)	Moderate

CI: Confidence interval; OR: Odds ratio
1 Assessed using checklist for case-control studies, appendix E in the NICE guidelines manual 2012

Table 26: Summary clinical evidence profile for differences in feeding and eating behaviour and practices between children with and without faltering growth: continuous outcomes

Outcomes	Mean (±SD) value with normal growth (NG)[1]	Mean (±SD) value with faltering growth (FG)[1]	Mean difference faltering growth versus normal growth[1]	No of Participants (studies)	Quality of evidence[2]
Energy intake (kJ) - measured using test meal	Mean energy intake (kJ) in the NG group ranged from 199 (±97) to 1066 (±432)	Mean energy intake (kJ) in the FG group ranged from 241 (±11) to 926 (±420)	The mean energy intake (kJ) in the FG group ranged from 378.4 lower to 42 higher than the NG group	208 (3 studies)	Low to moderate
Energy intake (kJ) - measured using food diary	Mean energy intake (kJ) in the NG group ranged from	Mean energy intake (kJ) in the FG group ranged from 536	The mean energy intake (kJ) in the faltering growth group ranged from 36 lower to 67	133 (2 studies)	Low to moderate

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Outcomes	Mean (±SD) value with normal growth (NG)[1]	Mean (±SD) value with faltering growth (FG)[1]	Mean difference faltering growth versus normal growth[1]	No of Participants (studies)	Quality of evidence[2]
	469 (±109) to 1424 (±323)	(±205) to 1388 (±356)	higher than the NG group		
Parent and child mealtime interaction - Parent Child Early Relational Assessment:	The mean parent child early relational assessment score in the NG group was 2.47 (±0.78)	The mean parent child early relational assessment score in the NG group was 2.18 (±0.81)	The mean parent child early relational assessment score in the FG group was 0.29 lower (0.5 to 0.08 lower) than the NG group	225 (1 study)	Moderate

CI Confidence interval, OR Odds ratio, SD standard deviation
1 Values are the range of means and standard deviations from the individual studies and were not pooled
2 Assessed using checklist for case-control studies, appendix E in the NICE guidelines manual 2012

5.3.1.5 Economic evidence

As this question does not investigate competing alternative used of NHS resources, it was not prioritised for HE analysis. No health economic evidence was identified for this topic from the overall health economic search.

5.3.1.6 Clinical evidence statements

Low to moderate quality evidence from three case control studies including 155 young children suggests energy intake ranges from about 380 kJ less to 42 kJ more in young children with faltering growth than in those with normal growth when measured by directly observing a test meal. This difference ranged from 36 kJ less to 67 kJ more when measured using a food diary in two other case control studies including 133 participants.

Low to moderate quality evidence from three case control studies including 358 young children indicates differences in the mealtime interaction between parents and children when comparing faltering and normal growth groups. Pressure on the child to eat and angry confrontations at mealtimes were more likely if the child had faltering growth, however both were also commonly observed in the normal growth group. Differences were also observed in maternal nurturance score, mealtime environments (unsupervised and unpredictable meals being more likely in the faltering growth group) and feeding behaviours.

Moderate quality evidence from one nested case control study including 160 young children indicates that young children with faltering growth are more frequently described as feeding slowly, as taking small quantities of milk, with weak sucking, and as refusing breast milk more than young children without faltering growth.

Although the evidence suggests differences between the mealtimes of young children with faltering and normal growth it does not indicate these differences cause faltering growth. Nor does it indicate whether interventions targeting these differences (e.g. parent and child interaction at mealtimes) will be effective.

5.3.1.7 Evidence to recommendation

The Committee agreed that the reviews for differences in feeding and approaches to the assessment of faltering growth are closely linked and they cannot be discussed in isolation. Evidence from both was considered together to draft recommendations and therefore the rationale for these is provided in section 5.3.2.7).

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5.3.2 Approaches to the assessment of faltering growth

Review question: What approaches are useful in assessing feeding and eating in faltering growth in individual children, including formal feeding observations and assessment?

5.3.2.1 Introduction

The aim of this review is to identify the most useful approaches and tools to identify mechanisms contributing to faltering growth in individual children.

The Committee identified the following outcomes as critical for decision making:

- measurement of fluid and nutritional intake
- behavioural problems (e.g. refusal).

For full details see review protocol in Appendix D.

5.3.2.2 Description of clinical evidence

One cohort study (Wright 2006) was included in this review for assessment of infants and preschool children with faltering growth. The study was conducted in the UK.

The sample size of the included study ranged between 632 and 826 children with faltering growth (depending on when the assessment was done). For more details about this study see Table 27.

Methodological limitations were assessed using the CASP clinical prediction rule checklist. Please see the quality of the evidence section for more details.

The main reason why studies were excluded from this review was due to cases not presenting with faltering growth. See Appendix H for more details about the excluded studies.

See also the study selection flow chart in Appendix F, study evidence tables in Appendix G and modified GRADE profile in Appendix J.

5.3.2.3 Summary of included studies

A summary of the study that was included in this review are presented in Table 27.

Table 27: Summary of the included study

Study	Objective	Assessment methods	Comparison	Outcome(s)
Wright 2006	To study the influences of child and maternal feeding behaviour on weight gain and failure to thrive in the first year of life	The authors of the study developed a core pool of questions. These were grouped in advance in child factors and maternal factors.	Not applicable	Feeding and eating behaviour (appetite, oromotor dysfunction, avoidant eating behaviour, maternal feeding anxiety and response to food refusal) at 6 weeks, 8 months and 12 months.

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Study	Objective	Assessment methods	Comparison	Outcome(s)
				Predictors of weight faltering to 12 months

5.3.2.4 Clinical evidence profile

The clinical evidence profiles for this review question are presented in Table 28.

Table 28: Summary clinical evidence profile for child and maternal feeding behaviour for the prediction of sustained weight faltering in the first year

No of studies	N	Sensitivity [95% CI]	Specificity [95% CI]	LR+ [95% CI]	LR- [95% CI]	Quality
Poor appetite (low appetite at 6 weeks or 12 months, or borderline appetite at both); assessed by questionnaire						
1	501	0.56 [0.35, 0.76]	0.71 [0.67, 0.75]	1.93 [1.33,2.81]	0.62 [0.40,0.97]	very low[1,2]
Low appetite at 6 weeks (versus borderline or normal appetite); assessed by questionnaire						
1	749	0.18 [0.07, 0.35]	0.98 [0.97, 0.99]	10.00 [4.06,24.65]	0.83 [0.71,0.98]	low[1]
Borderline or low appetite at 6 weeks (versus normal appetite); assessed by questionnaire						
1	749	0.55 [0.36, 0.72]	0.73 [0.69, 0.76]	2.00 [1.43,2.80]	0.62 [0.43,0.91]	low[1]
Low appetite at 12 months (versus borderline or normal appetite); assessed by questionnaire						
1	573	0.35 [0.17, 0.56]	0.88 [0.86, 0.91]	3.01 [1.69,5.35]	0.74 [0.56,0.98]	low[1]
Borderline or low appetite at 12 months (versus normal appetite); assessed by questionnaire						
1	573	0.69 [0.48, 0.86]	0.49 [0.45, 0.53]	1.36 [1.04,1.78]	0.63 [0.35,1.12]	very low[1,2]
Highly avoidant eating behaviour at 12 months (versus medium or low); assessed by questionnaire						
1	574	0.23 [0.09, 0.44]	0.91 [0.89, 0.93]	2.63 [1.24,5.59]	0.84 [0.68,1.04]	low[1]
Medium or highly avoidant eating behaviour at 12 months (versus low); assessed by questionnaire						
1	574	0.58 [0.37, 0.77]	0.70 [0.66, 0.74]	1.90 [1.34,2.71]	0.61 [0.39,0.95]	very low[1,2]
High maternal feeding anxiety at 12 months (versus borderline or normal); assessed by questionnaire						
1	574	0.54 [0.33, 0.74]	0.71 [0.67, 0.75]	1.86 [1.26,2.75]	0.65 [0.42,1.00]	low[1]
Borderline or high maternal feeding anxiety at 12 months (versus normal); assessed by questionnaire						
1	574	0.88 [0.68, 0.97]	0.25 [0.22, 0.29]	1.17 [1.00,1.38]	0.49 [0.17,1.43]	very low[1,2]
High response to food refusal at 8 months (versus medium or low); assessed by questionnaire						
1	598	0.35 [0.17, 0.56]	0.81 [0.78, 0.85]	1.83 [1.05,3.18]	0.81 [0.61,1.07]	low[1]
Medium or high response to food refusal at 8 months (versus low); assessed by questionnaire						

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No of studies	N	Sensitivity [95% CI]	Specificity [95% CI]	LR+ [95% CI]	LR- [95% CI]	Quality
1	598	0.81 [0.61, 0.93]	0.39 [0.35, 0.43]	1.32 [1.08,1.61]	0.50 [0.22,1.10]	very low[1,2]
High response to food refusal at 12 months (versus medium or low); assessed by questionnaire						
1	477	0.61 [0.39, 0.80]	0.58 [0.54, 0.63]	1.46 [1.04,2.07]	0.67 [0.40,1.12]	very low[1,2]
Medium or high response to food refusal at 12 months (versus low)); assessed by questionnaire						
1	477	0.83 [0.61, 0.95]	0.17 [0.14, 0.21]	1.00 [0.82,1.21]	1.01 [0.41,2.52]	very low[1,2]

CI confidence interval, LR+ positive likelihood ratio, LR- negative likelihood ratio
1 Downgraded by two levels due to risk of bias: it was unclear whether outcome assessors or participants were blinded to the study outcome and the feeding behaviour parameters assessed in the study were not clearly defined
2 Downgraded by one level due to imprecision because the confidence interval of sensitivity (the primary measure of interest) crosses the 75% threshold

5.3.2.5 Economic evidence

As this question does not investigate competing alternative used of NHS resources, it was not prioritised for HE analysis. No health economic evidence was identified for this topic from the overall health economic search.

5.3.2.6 Clinical evidence statements

Low to very low quality evidence came from a cohort study of a population birth cohort including 826 infants. Parents completed feeding questionnaires at six weeks, 8 months and 1 year and infants were routinely weighed. Low appetite at six weeks and highly avoidant eating behaviour had low sensitivity but high specificity for sustained weight faltering in the first year, indicating a potential association between appetite and weight faltering. Low appetite at 12 months had had low sensitivity but moderate specificity for sustained weight faltering.

5.3.2.7 Evidence to recommendations (related to both sections 5.3.1 and 5.3.2)

5.3.2.7.1 Relative value placed on the outcomes considered

The aim of this review was to identify possible behaviour and practices that may adversely affect feeding and eating and may thus contribute to faltering growth.

The majority of outcomes listed by the Committee as critical or important were retrieved by the evidence. For example, parent and child mealtime interaction, energy intake, feeding behaviour or mealtime environment. No evidence was identified for health related quality of life, measurement of fluid and nutritional intake or swallow function.

5.3.2.7.2 Consideration of clinical benefits and harms

The Committee acknowledged the multifactorial origin of faltering growth and the need to adopt an individualised approach for the assessment of this condition, appropriate for the developmental stage of each child.

The Committee discussed different factors that may influence children's eating behaviour and agreed that there are some particular aspects that healthcare professionals should explore when assessing children with faltering growth.

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The Committee discussed that these assessments would differ depending on the mode of feeding, i.e. milk fed or after the introduction of solid food. Therefore the Committee decided to separate their recommendations into two different sections, although they recognised certain aspects that are common for both groups. It was highlighted that healthcare professionals should not make assumptions, but should assess a wide range of possible contributing factors. Among these, the Committee discussed the following:

- Poor appetite, which may manifest as lack of interest in food or feeding, or absence of hunger, may lead to reduced food intake. Furthermore, the Committee agreed that is important to ask parents about the child's observed behaviour during feeding.
- Sensory sensitivities (e.g. coping with variable food textures) may be unrecognised or mislabelled as a passing phase in the child's development.
- In milk-fed infants it is important to assess feeding cues, attachment to feed and milk transfer.
- Infants with neurodevelopmental conditions may show altered feeding cues or sensitivity to latching and feeding. The Committee acknowledged that parents of children with these conditions should be offered extra support, e.g. support groups.
- Other infants may have physical conditions that may mean that they are less able to suck (e.g. cleft palate).
- Parental responsiveness (including parent-child interaction). For this factor the Committee highlighted the following:
  - Parents may not offer sufficient or appropriate food.
  - Parental food choices may not be nutritionally adequate.
  - Feeding cues in the child: It is sometimes difficult for parents to recognise whether a child is hungry, has had enough food or would want more, which can lead to reduced intake through early cessation of mealtimes.
  - This is a very complex issue, and is only present in a minority of cases, but should not be missed. The Committee wanted to make clear that neglected children may present with faltering growth, but most children with faltering growth are not neglected.
- When a child is diagnosed with faltering growth, parents often experience a sense of guilt or blame which can originate from themselves or others. Healthcare professionals will need to be aware of this and may need to provide reassurance and support.
- Feeding regime and environment: there are some specific factors that can only be identified by direct observation; such as the emotional, physical or interactional feeding environment.
- The Committee recognised the impact of the environment and atmosphere where children would have their meal. Feeding is a social activity. The Committee highlighted the importance of modelling, as parental or sibling behaviours may be copied by the child with faltering growth. To promote the positive feeding experience, there are actions that should be avoided at mealtime, such as force-feeding or confrontation.

The Committee also agreed that it was important to highlight that it may not always possible to find a cause because a range of factors which could be related to the child or the parent, could contribute to the problem. They believed that healthcare professionals should recognise in order to manage their own and the parents' expectations.

5.3.2.7.3 Consideration of economic benefits and harms

The direct cost of any recommendation in this review is likely to be very small, and potentially have zero direct economic impact. The only sources of direct cost are clinician time discussing the recommendations with parents, and as the downside cost of failing to identify potential feeding issues in faltering growth infants is likely to be high, the Committee considered that the cost-effectiveness of these recommendations was almost certain.

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As the resource impact is minimal, and potentially zero, these recommendations are unlikely to carry a substantial impact to NHS resources.

5.3.2.7.4 Quality of evidence

Six case-control studies, 3 nested case-control studies and 1 cohort study have been included in this review. The quality of the evidence ranged from low to moderate as measured by the NICE case-control checklist. The main reason for bias of the included studies were poor reporting of statistics and not controlling for confounding factors. Along with these limitations, the Committee also noted that most of the studies were underpowered and that several studies analysed outcomes from the same cohort which meant that the size of the evidence base seemed perhaps larger and more convincing than it actually was.

It was also noted that one study provided slightly inconsistent results, i.e. differences in energy intake when children were measured by direct observation (a test meal) but these differences were not observed when using a food diary.

5.3.2.7.5 Other considerations

Recommendations came from the evidence, but also from the experience and expertise of the Committee.

- Some specific details of the studies were discussed. For instance whether the videotaped meals were done in a natural or experimental environment, whether the included children in the studies had a previous history of poor eating or feeding behaviour, or the validity of the measurement scale of anxiety in one of the studies.
- Reverse causality: The Committee highlighted that is difficult to differentiate whether something is cause or effect, especially with factors such as response to food refusal. Parents may be reacting in a specific negative way because child is not eating or vice versa, i.e. the child is not eating because of parent's behaviour.
- Furthermore they discussed the issue of parental negative responses: if a parent has a negative approach, it becomes a self-fulfilling prophecy that then impacts on the child's behaviour.
- It was agreed that knowledge of the types and amounts of food that the infant or child eats would help the discussion between parents or carers and healthcare professionals. This could be facilitated by keeping a diary of what the infant or child eats which can then aid assessment and decisions about management strategies.

5.3.2.7.6 Key conclusions

The Committee concluded that any assessment needs to be tailored to individual circumstances and needs to be approached with an open mind. Having a child with faltering growth causes concerns and anxieties and healthcare professionals need to be sensitive to this. They should remain aware that most children with faltering growth are not neglected. Support and reassurance is therefore important. Different assessments will have to be applied to infants who are milk-fed and infants and children who receive solid food. The Committee agreed that direct observation of feeding and mealtime can be helpful in the assessment of faltering growth.

5.3.2.8 Recommendations (based on evidence from sections 5.3.1 and 5.3.1.7)

9. Recognise that in faltering growth:

- a range of factors may contribute to the problem, and it may not be possible to identify a clear cause
- there may be difficulties in the interaction between an infant or child and the parents or carers that may contribute to the problem, but this may not be the primary cause.

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10. **Based on the feeding history and any direct observation of feeding, consider whether any of the following are contributing to faltering growth in milk-fed infants:**
    - ineffective suckling in breastfed infants
    - ineffective bottle feeding
    - feeding patterns or routines being used
    - the feeding environment
    - feeding aversion
    - parent/carer–infant interactions
    - how parents or carers respond to the infant's feeding cues
    - physical disorders that affect feeding.

11. **Based on the feeding history and any direct observation of mealtimes, consider whether any of the following are contributing to faltering growth:**
    - mealtime arrangements and practices
    - types of foods offered
    - food aversion and avoidance
    - parent/carer–child interactions, for example responding to the child's mealtime cues
    - appetite, for example a lack of interest in eating
    - physical disorders that affect feeding.

12. **Consider asking the parents or carers of infants and children with faltering growth to keep a diary recording food intake (types and amounts) and mealtime issues (for example, settings, behaviour) to help inform management strategies and assess progress.**

5.3.3 Risk factors

Review question: What are the risk factors for faltering growth?

5.3.3.1 Introduction

The aim of this review is to determine factors that could improve recognition and identify management strategies for faltering growth.

The Committee prioritised the following as potential risk factors related to recognition of faltering growth:

Infant or preschool child variables:

- born preterm
- family history of faltering growth
- intrauterine growth restriction
- small for gestational age at birth
- neurodevelopmental delay.

Family/social factors:

- maternal mental health (including depression, eating disorders)
- parental substance misuse, including postnatal smoking
- socioeconomic status

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- parental educational status (particularly maternal)
- physical, emotional, sexual abuse and neglect (safeguarding issues).

Other potential factors:

- restricted intake (for example restricted diet)
- early weight loss (under 4 weeks of age)
- breastfeeding
- parity
- birth complications including caesarean section (neonate only)
- mother-child relationship/ attachment.

For full details see review protocol in Appendix D.

5.3.3.2 Description of clinical evidence

Ten studies have been included in this clinical review (Blair 2004; Bocca-Tjeerters 2011; Drewett, 2004; Emond 2007, Karp 1989; Kelleher 1993; O'Brien 2004; Olsen 2007; Olsen 2010; Wright 2006).

Evidence from these studies is summarised in the clinical evidence profile below (Table 31 and Table 32).

Five studies have been conducted in the UK (Blair 2004; Drewett, 2004; Emond 2007, O'Brien 2004; Wright 2006), two in the US (Karp 1989; Kelleher 1993), two in Denmark (Olsen 2007; Olsen 2010), and one in The Netherlands (Bocca-Tjeerters 2011).

Some variability has been encountered in the methods of data collection used, but most studies used self-reported questionnaires or reviews of clinical records. Two studies used a national birth registry (Olsen 2007; Olsen 2010), whereas one study relied on the use of a parent held child health record booklet (O'Brien 2004).

The following risk factors were assessed in the retrieved evidence:

- small for gestational age (Bocca-Tjeertes 2011; Kelleher 1993; Olsen 2007)
- abnormal or suspect neurological exam (Kelleher 1993)
- social class (Blair 2004; Wright 2006)
- parental education (Blair 2004; Bocca-Tjeerters 2011; Kelleher 1993)
- maternal smoking (Blair 2004; Olsen 2010; Bocca-Tjeertes 2011)
- alcohol and drugs consumption (Blair 2004)
- maternal depression (Drewett 2004; O'Brien 2004; Wright 2006)
- anxiety (O'Brien 2004)
- depression and anxiety (O'Brien 2004)
- breast-feeding duration and weak sucking (Emond 2007)
- abuse (Karp 1989)
- parity (Blair 2004; Olsen 2010)
- birth complications (Olsen 2010).

Some variability was also found in the way the studies reported on recognition of faltering growth, as reported in Table 29:

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Table 29: faltering growth definitions

Study	Definition
Blair 2004	FTT = Infants whose weight gain was below the 5th centile
Bocca-Tjeertes 2011	Growth restraint = >2SD scores below the median growth of the Dutch population
Drewett 2004	FTT=Slowest-gaining 5% of weight from birth until 9 months
Emond 2007	Cases of growth faltering were defined as those infants below the 5th centile for weight gain, corresponding to a conditional growth score of -1.645.
Karp 1989	Stunting = Height x age x sex < 5th percentile, Wasting or underweight = weight x height x sex below the 5th percentile
Kelleher 1993	Children were required to have lower than average growth velocity to meet criteria. a) who were coded by the developmental clinician during a health assessment as having FTT (infants below the 5th percentile for gestational corrected age on the National Centre for Health Statistics growth grids, and if his/her growth status put him below that recorded at the last regular assessment visit); b) whose weight was less than the 5th percentile for GCA at 2 or more points in time and; c) Whose rate of weight growth during the preceding months was less than average for gender and GCA as determined by incremental (velocity) growth curves.
O'Brien 2004	Diagnostic criteria for FTT = a fall across 2 centile channels or a fall beneath the second centile on standardized growth charts for at least 3 months (to exclude weight loss secondary to an acute illness)
Olsen 2007	1. FTT=conditional weight Gain <5% from birth until 6-11 months 2. FTT= Combination of: conditional weight gain < 5% and BMI <5th Percentile 3. FTT= crossing ≥ two major weight centiles from birth until 6-11 months
Olsen 2010	Weight faltering was defined as the slowest weight gaining 5% of all children in the cohort with an available weight.
Wright 2006	Weight faltering: For any time interval, weight gain (TI) below the 5th centile for than interval. TI: is a measure of change in weight SD over time, conditional on initial weight, to allow for regression to the mean. The TI compares a child's actual weight SD to their expected weight SD.

FTT failure to thrive; SD standard deviation; TI thrive index; CGA gestation-corrected age; BMI body mass index;

The main reason why studies were excluded from this review was due to either not adjusting for confounders or not carrying out multivariate analyses. For full details see excluded studies list in Appendix H. See also the study selection flow chart in Appendix F and evidence tables in Appendix G.

5.3.3.3 Summary of included studies

A summary of the studies that were included in this review are presented in Table 30.

Table 30: Summary of included studies

Study	Sample	Risk factor(s) studied	Adjustment for:	Quality of the study
Blair 2004	N= 11718	• Social class • Parental education • Maternal smoking	Not specified, but results reported separately for age.	Low

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Study	Sample	Risk factor(s) studied	Adjustment for:	Quality of the study
		• Alcohol consumption • Illegal drugs taken • Mother vegetarian • Mother dieting		
Bocca-Tjeertes 2011	N=1123 children, of which N=50 were growth-restricted in height and N=48 were growth-restricted in weight.	• Small for gestational age • Maternal educational level	• Gestational age • Ethnicity • Maternal education level (low versus moderate/high) • Family income (low versus moderate/high) • Smoking during pregnancy (categorical) • In vitro fertilization/intracytoplasmic sperm injection (no versus yes) • Gender • Being part of a multiple (singletons versus twins and versus triplets/quadruplets) • Breastfeeding during the first months of life (no versus yes)	Moderate
Drewett 2004	N=12,391	• Postnatal depression (as measured by the EPDS low cut-off: >12; High cut-off: >15).	• Weight gain over the first 9 months • Ordinal position of the child in the family • Crowding • Home ownership	Moderate
Emond 2007	N=11900	• Weak sucking (parent report) (birth to 8 weeks) • Breastfeeding duration (>6 months) (from 8 weeks to 9 months) (parent report)	• Time between measurement of weight from birth to 6-8 weeks	Low
Karp 1989	N=196; 53 (27%) were abused and 143 (73%) were not abused.	• Child abuse, including chronic mistreatment and neglect	• Age • Sex • Ethnicity	Low
Kelleher 1993	N=771	• Maternal education • Abnormal or suspect neurologic exam • Small for gestational age	• Abnormal or suspect neurologic exam • Birth weight • Maternal age • Maternal education	Low

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Study	Sample	Risk factor(s) studied	Adjustment for:	Quality of the study
			• Maternal height	
O'Brien 2004	N=196 index children and n=567 control mothers and children	• Postnatal depression as measured by the EPDS (cut-off= 13) • anxiety as measured by the HADS	"Logistic regression with index/control as the dependant variable was used to correct the P value for the association of depression and FG for variables that showed significant difference for index and control groups"	Low
Olsen 2007	N= 3692 children	• Gestational age • Feeding problems	• Sex • Ethnicity • Mother's age • Social level of neighbourhood • Whether parents live together • Model also includes observations concerning psychomotor development, mother-child relationship and overall development of the child	Low
Olsen 2010	N= 3638	• Mother smoking during pregnancy • Feeding problem (contemporary)	Each of the variables have been adjusted for possible confounders: • For mother smoking during pregnancy [slow starters group-birth to 2 weeks only]: sex, ethnicity, parental cohabitance, living area, mother's age • For feeding problem [slow starters group-birth to 2 weeks only]:sex, ethnicity, parental cohabitance, living area, parity, mother's age, birthweight, gestational age, congenital disorder, birth complication, smoking during pregnancy • For feeding problem [early onset (2 weeks to 4 months	Low

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Study	Sample	Risk factor(s) studied	Adjustment for:	Quality of the study
			only)]:sex, ethnicity, parental cohabitance, living area, parity, mother's age, congenital disorder, preceding and contemporary somatic illness, contemporary mother-child relationship and activity & interest. • For feeding problem [late onset (4-8 months)]: ethnicity, parental cohabitance, living area, parity, mother's age, congenital disorder, preceding and contemporary somatic illness, preceding overall development, contemporary sleeping problems and mother-child relationship.	
Wright 2006	N = 774	• Socioeconomic factors • Postnatal depression as measured by the EPDS (cut off: >12)	Unclear	Low

EPDS Edinburgh Postnatal Depression Scale; HADS Hospital Anxiety and Depression Scale; NS non-significant; SGA small for gestational age; FG faltering growth.

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5.3.3.4 Clinical evidence profile

A summary of the results by risk factor for faltering growth reported in the studies is presented in Table 31 and Table 32. The definitions for faltering growth remain the same as in Table 29 unless specified. These tables summarise results for each risk-factor across studies. Quality was assessed for each study individually based on risk of bias.

Table 31: summary of results for faltering growth risk factors

Risk factor	OR (95% CI), p-value for FTT, unless specified	Author/ Notes	Quality of evidence assessed by study with the CASP clinical prediction rule checklist
Infant or preschool child variables			
SGA	height at 4 years less than -2 SDs = 7.7 (2.9-20.4), p<0.01 weight at 4 years less than -2SDs = 9.3 (3.9-22.1),P<0.01	Boca-Tjeertes 2011	Moderate
	FTT= 2.62 (1.72,3.98), p<0.05	Kelleher 1993	Low
Prematurity	FTT = conditional weight Gain <5% from birth until 6-11 months gestational age (weeks)= 1.11 [0.96,1.27], NS FTT= Combination of: conditional weight gain < 5% and BMI <5th Percentile gestational age (weeks)= 1.15 [0.85,1.56], NS FTT= crossing ≥ two major weight centiles from birth until 6-11 months gestational age (weeks)= 1.13 [1.04,1.23], p<0.05	Olsen 2007	Low
Abnormal or suspect neurological exam	FTT= 1.82 [1.21,2.75], P <0.05	Kelleher 1993	Low

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Risk factor	OR (95% CI), p-value for FTT, unless specified	Author/ Notes	Quality of evidence assessed by study with the CASP clinical prediction rule checklist
Breast feeding duration and weak sucking	From birth to 8 weeks: weak sucking = 2.20 (1.74 to 2.78), p <0.001 From 8 weeks to 9 months: breastfeeding duration (>6 months) = 2.54 (2.01 to 3.21), p <0.001	Emond 2007	Low
Family/social factors:			
Social class	*From birth to 6-8 weeks:* FTT= 1.11 (0.87, 1.42), NS *6-8 weeks to 9 months:* FTT= 1.03 (0.79 , 1.32) , NS *Birth to 9 months:* FTT= 1.21 (0.96, 1.54),NS	Blair 2004/ Results from univariate analysis	Low
Deprivation (Townsend score)	Thrive index (birth to 6 weeks) = p 0.005	Wright 2006	Low
Parental education	*From birth to 6-8 weeks:*		

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Risk factor	OR (95% CI), p-value for FTT, unless specified	Author/ Notes	Quality of evidence assessed by study with the CASP clinical prediction rule checklist
	FTT= 1.04 (0.82, 1.32), NS *From 6-8 weeks to 9 months:* FTT= 1.09 (0.86 , 1.39),NS *From birth to 9 months:* FTT= 1.15 (0.92, 1.45), NS	Blair 2004/ Results from univariate analysis	Low
	Some college: FTT= 1.00 (ref) *< High school:*	Kelleher 1993	Low

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Risk factor	OR (95% CI), p-value for FTT, unless specified	Author/ Notes	Quality of evidence assessed by study with the CASP clinical prediction rule checklist
	FTT= 1.52 (0.86,2.69), NS *High School Graduate:* FTT= 1.51 [0.87,2.63], NS ≥ *College graduate:* FTT= 2.12 [1.09,4.13], NS		
	height at 4 y less than -2 SDs = 1.6 [0.9-2.9], NS weight at 4 y less than 2 SDs = 1.0 [0.5-1.9], NS head circumference at 1 y less than -2SDs= 5.3 (1.4-20.6), P<.05 maternal, paternal education association with weight gain =NS	Boca-Tjeertes 2011/ Results from univariate analysis	Moderate
Restricted intake	*Mother dieting* *From birth to 6-8 weeks:* FTT = 1.45 (0.85, 2.44), NS *From 6-8 weeks to 9 months:* FTT = 1.06 (0.56 , 1.96), NS *From birth to 9 months:* FTT= 1.43 (0.84, 2.41), NS	Blair 2004/ Results from univariate analysis	Low

ISBN 978-1-4731-2693-0

Risk factor	OR (95% CI), p-value for FTT, unless specified	Author/ Notes	Quality of evidence assessed by study with the CASP clinical prediction rule checklist
	Mother vegetarian *From birth to 6-8 weeks:* FTT= 1.32 (0.90, 1.94), NS *From 6-8 weeks to 9 months:* FTT= 0.98 (0.62 , 1.53), NS *From birth to 9 months:* FTT= 1.09 (0.72, 1.65), NS		
Parental substance misuse			
Maternal smoking	*1st semester of pregnancy* *From birth to 6-8 weeks:* FTT= 1.06 (0.85, 1.31), NS *From 6-8 weeks to 9 months:* FTT= 0.81 (0.64 , 1.03),NS *From birth to 9 months:* FTT= 0.96 (0.77, 1.20), NS	Blair 2004/ Results from univariate analysis; all children included in this study presented with faltering growth	Low

ISBN 978-1-4731-2693-0

Risk factor	OR (95% CI), p-value for FTT, unless specified	Author/ Notes	Quality of evidence assessed by study with the CASP clinical prediction rule checklist
	3rd semester of pregnancy *From birth to 6-8 weeks:* FTT= 1.04 (0.82, 1.31), NS *From 6-8 weeks to 9 months:* FTT = 0.83 (0.64 , 1.08),NS *From birth to 9 months:* FTT= 0.92 (0.72, 1.17), NS		
	weight faltering = 1.52 [1.06,2.18] p=0.0253	Olsen 2010	Low
	1-5 cigarettes per day: height at 4 years less than -2 SDs = 0.9 [0.3-2.7], NS weight at 4 years less than 2 SDs = 1.4 [0.5-3.6], NS head circumference at 1 year less than = 1.3 (0.2-10.4), NS *6-10 cigarettes per day:* height at 4 years less than -2 SDs = 0.6 [0.2-2.7], NS weight at 4 years less than 2 SDs = 1.9 [0.7-5.1], NS	Boca-Tjeertes/ Results from univariate analysis 2011	Moderate

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Risk factor	OR (95% CI), p-value for FTT, unless specified	Author/ Notes	Quality of evidence assessed by study with the CASP clinical prediction rule checklist
	head circumference at 1 year less than -2SDs, = 1.8 (0.2-14.6) *>10 cigarettes per day:* height at 4 years less than -2 SDs = 1.5 (0.5-4.4), NS weight at 4 years less than 2 SDs = 1.8 (0.6-5.2), NS head circumference at 1 year less than -2SDs = 2.1 (0.3-17.4), NS		
Alcohol and drugs	*Alcohol consumption* *From birth to 6-8 weeks:* FTT= 1.16 (0.68, 1.93), NS *From 6-8 weeks to 9 months:* FTT= 0.89 (0.48 , 1.62), NS *From birth to 9 months:* FTT= 1.11 (0.65, 1.88), NS *Illegal drugs taken* *From birth to 6-8 weeks:* FTT= 2.30 (1.39, 3.75) p<0.001	Blair 2004/ Results from univariate analysis; all children included in this study presented with faltering growth	Low

ISBN 978-1-4731-2693-0

Risk factor	OR (95% CI), p-value for FTT, unless specified	Author/ Notes	Quality of evidence assessed by study with the CASP clinical prediction rule checklist
	From 6-8 weeks to 9 months: FTT= 1.02 (0.49 , 2.07), NS *From birth to 9 months:* FTT= 1.41 (0.76, 2.56), NS		
Maternal mental health			
Maternal depression	*Term births, postnatal depression at 8 weeks measured by the EPDS:* EPDS >12; X^2 =0.439, P=0.51 EPDS >15; X^2 =0.030, P=0.86 *Term births, postnatal depression at 8 months measured by the EPDS:* EPDS >12; X^2 =0.020, P=0.87 EPDS >15; X^2 =.120, P=0.729 Adjusted effect of depression over a more extended period ; X^2 =1.71, P=0.192 *Preterm births, postnatal depression at 8 weeks measured by the EPDS*: EPDS >12; X^2 =.896, P=0.344	Drewett 2004/ All children included in this study presented with faltering growth	Moderate

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Risk factor	OR (95% CI), p-value for FTT, unless specified	Author/ Notes	Quality of evidence assessed by study with the CASP clinical prediction rule checklist
	EPDS >15; X^2 =1.939, P=0.164 *Preterm births, postnatal depression at 8 months measured by the EPDS :* EPDS >12; X^2 =1.744, P=0.187 EPDS >15; X^2 =.387, P=0.534 Adjusted effect of depression over a more extended period; X2 =.784, P=0.376		
	EPDS ≥9 ,(32.7% index vs.21.5% control) = 1.71 (1.16-2.53), p≤0.01 EPDS ≥13 = (14.8% index vs. 7.8% control) = 1.96 (1.13-3.38), p ≤ 0.02	O'Brien 2004/ All children included in this study presented with faltering growth	Low
Maternal depression	at 4 months, in deprived groups, depression (EPDS>12) was associated with lower TI at 4 months, in more affluent groups, depression (EPDS>12), was not associated with TI	Wright 2006	Low
Anxiety	HADS ≥8 = (24% index vs. 12.9% control) = 2.08 (1.33-3.25), p≤0.01	O'Brien 2004/ All children included in this study presented with faltering growth	Low

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Risk factor	OR (95% CI), p-value for FTT, unless specified	Author/ Notes	Quality of evidence assessed by study with the CASP clinical prediction rule checklist
Depression or anxiety	Number of women scoring EPDS ≥9 OR HADS≥8 = (35.2% index vs. 23.6% control) = 1.74 (1.19-2.54), p = 0.01	O'Brien 2004/ All children included in this study presented with faltering growth	
Abused children	Stunting (Low wgt/hgt) = 16.6 (1.9-145.0), p<0.05 Wasting (Low hgt/age) = 2.2 (0.61-7.9)	Karp 1989	Low

EPDS Edinburgh Postnatal Depression Scale; HADS Hospital Anxiety and Depression Scale; NS non-significant; FTT failure to thrive; TI Thrive Index; wgt = weight; hgt= height; FTT= failure to thrive; SD= standard deviation; SGA = small for gestational age; OR Odds ratio

Table 32: Summary of results for early weight loss risk factors

Risk factor	OR (95%), p-value for FTT, unless specified	Author	Quality of evidence assessed by study with the CASP clinical prediction rule checklist
Parity	*From birth to 6-8 weeks:* FTT= 1.13 (0.91,1.42) NS	Blair 2004	Low
	Weight faltering = Slow starters (0-2 weeks only) 0.75 (0.35,1.57), NS Weight faltering = Very early onset (0-2 weeks and later)	Olsen 2010	Low

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Risk factor	OR (95%), p-value for FTT, unless specified	Author	Quality of evidence assessed by study with the CASP clinical prediction rule checklist
	0.80 (0.40,1.70),NS		
Birth complications	Weight faltering = Slow starters (0-2 weeks only) 0.92 [0.51,1.69]NS Weight faltering = Very early onset (0-2 weeks and later) 1.70 [0.59,4.89]NS	Olsen 2010	Moderate

FTT failure to thrive, NS non-significant, OR odds ratio

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5.3.3.5 Economic evidence

As this topic does not deal with competing uses of resources the topic was not prioritised for health economic analysis and no economic evidence was identified.

5.3.3.6 Clinical evidence statements

Prematurity

Low quality evidence from one study with 3629 participants showed that there was a significant association between 'failure to thrive' defined as crossing ≥ two major weight centiles from birth until 6-11 months and decreased gestational age at birth.

Family history of faltering growth

No evidence was retrieved for this risk factor.

Intrauterine growth restriction

No evidence was retrieved for this risk factor.

Small for gestational age

Moderate quality evidence from two studies comprising a total of 1894 participants showed that there was an association between 'small for gestational age' babies and risk of persisting small stature. An association was found between low height and weight at 4 years and being born small for gestational age.

Neurodevelopmental and developmental delay

Low quality evidence from one study with 771 participants showed that there was a significantly increased risk of failure to thrive when abnormal or suspect neurological exam was present.

Breast feeding duration and weak sucking

Low quality evidence from one study with 12428 participants showed that there was a significant association between weak sucking difficulties at 4 weeks and growth faltering and between breastfeeding duration (>6 months) and weight faltering.

Depression

There was inconsistent evidence for this risk factor with moderate quality evidence from one study with 12391 participants showing no significant association between maternal postnatal depression as measured by the Edinburgh Postnatal Depression Scale (EPDS) (EPDS scale > 12 and >15) and faltering growth in the baby. However, low quality evidence from another study with 774 participants showed a significant association between maternal depression (EPDS >12) and thrive index at 4 months, but only in deprived groups. Further low quality evidence from a third study with 196 participants showed an association between faltering growth and maternal depression as measured by the EPDS (EPDS scale ≥9 and ≥13).

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Anxiety

Low quality evidence from one study with 196 participants showed an association between faltering growth and maternal anxiety as measured by the Hospital Anxiety and Depression Scale (HADS) (HADS ≥ 8).

Parental substance misuse

Maternal smoking

Low to moderate quality evidence from two studies comprising a total of 12841 participants showed that there was no significant association between maternal smoking and failure to thrive, weight, height, or head circumference.

Low quality evidence from one study with 3638 participants showed that there was an association between weight faltering and mother smoking during pregnancy.

Alcohol consumption

Low quality evidence from one study with 11718 participants showed that there was no significant association between parental alcohol consumption and failure to thrive.

Illegal drugs use

Low quality evidence from one study with 11718 participants showed that there was an association between failure to thrive (from birth to 6-8 weeks) and parent reported use of illegal drugs. However, the association was not significant for failure to thrive between 6-8 weeks and 9 months and at 9 months.

Socioeconomic status

Low quality evidence from one study with 11718 participants showed there was no significant association between failure to thrive and social class. However, moderate quality evidence from another study with 774 participants showed there was a significant association between deprivation (Townsend score) and thrive index.

Parental educational status (particularly maternal)

Low to moderate quality evidence from three studies comprising a total of 12612 participants showed no significant association between parental education and failure to thrive. No association was found with height, weight, and weight gain as well. A significant association was showed between head circumference at 1 year and lower maternal education.

Physical, emotional, sexual abuse and neglect (safeguarding issues)

Low quality evidence from one study with 196 participants showed an association between stunting (low weight/height) and child abuse, but no association was found for wasting (low height/age) in the same population.

Restricted intake (for example restricted diet)

Low quality evidence from one study with 11718 participants showed that there was no significant association between mother dieting and failure to thrive for the baby. Similarly, the same study showed no significant association between mother being vegetarian and increased risk of failure to thrive for the baby.

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Risk factors related to early weight loss (under 4 weeks)

Parity

Low quality evidence from two studies comprising a total of 15356 participants showed that there was no significant association between parity and faltering growth.

Birth complications including caesarean section (neonate only)

Moderate quality evidence from one with 3638 participants showed that there was no significant association between birth complications and faltering growth.

Mother-child relationship/ attachment

No evidence was retrieved for this risk factor.

5.3.3.7 Evidence to recommendations

5.3.3.7.1 Relative value placed on the outcomes considered

The aim of this review was to determine factors that could improve recognition and identify management strategies for faltering growth. The Committee identified the following as critical outcomes for decision making based on the impact of the risk factor:

- Improved recognition
- Measurement of growth

The different risk factors were grouped into those related to infant or preschool children as well as those related to the family and social factors. Overall, evidence was identified for all the risk factors classified as critical or important, with the exception of family history of faltering growth; birth complications, including caesarean section; and mother-child attachment. The Committee placed more importance on factors related to infant or preschool children, such as small for gestational age or neurodevelopmental delay than to family and social factors.

5.3.3.7.2 Consideration of clinical benefits and harms

The Committee considered the evidence presented and agreed that the evidence for risk factors for faltering growth is heterogeneous. Studies varied widely, for example, in measurement and recognition of faltering growth, definition of risk factors and setting in which the study was conducted.

The Committee was aware that the evidence presented used different definitions for the population of interest, and considered this when drafting the recommendations.

The Committee discussed and agreed, based on the evidence and on their expertise, that there are two independent risk factors that should be recognised: neurodevelopmental concerns and prematurity. The term ‘neurodevelopmental concern’ replicates the wording used in the literature, and reflects clinical concern about neurological abnormality on examination rather than a proven delay or disorder. With regards to prematurity, the study that covered this specific condition presented with mixed results. However, the Committee recognised that babies born prematurely do follow different growth patterns than non-preterm babies. This difference in growth may have lasting effects becoming a cause or a contributory factor associated with faltering growth.

The Committee considered the evidence presented on socioeconomic status. The consensus opinion was not to make any recommendation about socioeconomic status as a risk factor for faltering growth, given the heterogeneity of definitions and findings reported in

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the evidence presented. Socioeconomic status may be interrelated to other potential risk factors that were explored (for example maternal education and poverty).

The Committee noted that, based on their experience and some evidence, there may be no association between deprivation and faltering growth. If there is an association it may not be a direct linear relationship, but may be 'U-shaped' with an increased incidence at either end of the socioeconomic spectrum.

The evidence on maternal mental health problems as a risk factor for faltering growth was mixed and inconsistent. Based on the Committee's experience it was decided by consensus to make a recommendation that a maternal mental health problem may be a risk factor. However, the Committee was not in complete agreement about the validity of the tools used in the studies to assess maternal depression or anxiety.

The Committee wanted to explore characteristics commonly thought of as risk factors for faltering growth. The group agreed that the evidence was convincing enough to suggest that low maternal education is not a risk factor for faltering growth. They also discussed that smoking is commonly recognised as a cause of IUGR. However there was no association found between smoking and faltering growth in the evidence review.

The Committee is aware that the majority of children with faltering growth are not being abused or neglected. However, families may have needs for additional support. In families with safeguarding concerns children's growth should be monitored to look for evidence of weight faltering.

The Committee acknowledged the evidence about breastfeeding (> 6 months) and weak sucking. They agreed that it is not certain whether the infants included in this study were exclusive breastfeeding, predominant breastfeeding or continuing breastfeeding while solid foods were being introduced. Likewise, they discussed that the study may be subject to high risk of bias, and that may be subject to reverse causality. For these reasons, the Committee decided not to make recommendations about this specific study.

5.3.3.7.3 Quality of evidence

The quality of the included studies ranged from low to moderate as assessed by the CASP clinical prediction rule checklist. For prognostic risk factor reviews, observational studies such as prospective cohort studies would be the most appropriate study designs for addressing this question, which therefore would initially be assigned high quality and downgraded based on potential sources of bias. The main sources of bias were the use of non-validated clinical prediction rules for measuring the risk factors and insufficient data about the confounders the study adjusted for. Additionally, one of the studies was likely to present with selection bias as participants were referred to the study from a specific source in a systematic manner, whereas other studies presented more robust evidence as they used population based cohorts (i.e. Avon Longitudinal Study of Parents and Children [ALSPAC], The Gateshead Millennium Baby Study and The Copenhagen County Child Cohort). The Committee agreed that the low quality of the evidence for the association between risk factors and faltering growth lowered their confidence in the findings and would therefore mean that they would be unable to make a strong recommendations.

5.3.3.7.4 Consideration of economic benefits and harms

This topic does not carry a direct health economic impact; while it is clear that a child with faltering growth will cost more overall than an otherwise healthy child, most of these risk factors are not preventable and therefore the cost of subsequent weight faltering is an inevitable cost to the NHS. In some cases the possible cause of faltering is preventable – for example in rare situations where the cause is neglect – but in these cases the NHS / PSS are already trying to prevent the underlying risk factor and so there is no change in practice implied by these recommendations. Additionally the evidence in some of these causes is

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quite weak, while it is known that preventing the cause is extremely difficult and expensive, making the possibility of radical intervention in these areas unsupported on health economic grounds.

However there may be an indirect economic impact if the information allows clinicians to make diagnoses of faltering growth more quickly and confidently. In this case the recommendations will likely carry a small cost of an increased number of referrals, but then a subsequent cost and QALY benefit as babies and children have their faltering growth better managed. As there is no evidence on the numbers of clinicians already following one or more of the Committee's recommendations, the indirect effects cannot be calculated.

Finally there may be a highly indirect social and economic benefit of excluding maternal education as a risk factor if clinicians were mistakenly referring on this basis (or partially on this basis). This will have similar indirect effects to the above – if there are no subsequent benefits to the referral it will limit the initial cost – but may also have a benefit of reducing anxiety to mothers with low education of approaching healthcare professionals for advice, which might have 'externality' effects in other areas.

This topic is highly unlikely to carry a significant resource impact.

5.3.3.7.5 Other considerations

The Committee recognised that being small for gestational age (SGA) at birth was associated with smaller stature later in childhood. However, SGA was not reported in the evidence as independent risk factor. The papers reporting on SGA and faltering growth did not use widely accepted measures for faltering growth or failure to thrive. Many infants born small for gestational age would be expected to demonstrate some 'catch-up' growth in childhood, but may remain small compared to the general population.

5.3.3.7.6 Key conclusions

Guided by the evidence and the experience and expertise of the Committee, it was decided to group recommendations on risk factors into those that were clearly related to the recognition of faltering growth (neurodevelopmental concerns, and prematurity) others where evidence was mixed or inconsistent but the Committee could agree on a possible association with faltering growth (postnatal depression and anxiety), and a factor (maternal education) that they wanted to highlight as not being linked to faltering growth.

5.3.3.8 Recommendations

13. Be aware that the following factors may be associated with faltering growth:

- preterm birth
- neurodevelopmental concerns
- maternal postnatal depression or anxiety.

5.3.4 Prevalence of specific causative conditions

Review question: What is the prevalence of the specific causative conditions (and of no causative condition) identified in infants and preschool children who present with faltering growth who have no other symptoms or signs pointing to such a condition?

5.3.4.1 Introduction

The objective of this review as to determine what investigations and or referrals, if any, are appropriate in primary care settings.

The Committee identified the following outcome as critical for decision making:

ISBN 978-1-4731-2693-0

- Percentage/ proportion of children of specific causative conditions with the specific organic disorder and with no identified specific organic disorder.

For full details see review protocol in Appendix D.

5.3.4.2 Description of clinical evidence

Four studies from three different cohorts were identified on prevalence of specific causative conditions in faltering growth (Berwick 1982, Sills 1978, Wright 1998, and Wright 1996). Two of the studies were carried out in the USA and the other two in the UK and identified the prevalence of specific structural causes of faltering growth, including partial intestinal obstruction, tuberculosis, neurological cause, urinary tract infections, coeliac disease and hypercalcaemia. Two of the studies grouped the causes by organic and nonorganic. The sample sizes ranged from 122 to 229 and variable percentage of children presented with a specific structural disease, with numbers ranging from 10% to 18% of the population included.

Evidence was not found on the following outcomes: on other outcomes listed in the review protocol: hypothyroidism and chronic renal disease.

It is important to note that the generalisability of the included studies may be limited due to the small sample size and, for one of the studies, only hospitalised children were selected to participate, which may indicate that only severe cases were included.

See the study selection flow chart in Appendix F, evidence tables in Appendix G and exclusion list in Appendix H.

5.3.4.3 Summary of included studies

A summary of the studies that were included in this review are presented in Table 33.

Table 33: Summary of included studies

Study	Objective	Definition for faltering growth	Outcomes	Limitations
Berwick 1982	To assess the diagnostic yield of children in the infant-toddler age group who are admitted to hospital to investigate the cause of FTT of obscure origin.	Failure to thrive´ was defined as those children whose weight lies consistently below the 3rd centile for age, or whose growth is rapidly crossing centiles downwards.	Specific structural causes of faltering growth (N=122): • partial intestinal obstruction (N=3) • tuberculosis (N=1) • neurological cause (N=2) • coeliac disease (N=2) • hypercalcaemia (N=1) • others (N=3)	Overall quality of the study: low
Sills 1978	To assess whether laboratory tests provide additional diagnostic information to clinical examination in	Failure to thrive´ was defined as those children whose weight lies consistently below the 3rd centile for age,	Cause of faltering growth (N=185) • organic (N=34) • nonorganic (N=106) • undetermined N=(45)	Overall quality of the study: low – children may have had signs or symptoms of underlying conditions.

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Study	Objective	Definition for faltering growth	Outcomes	Limitations
	children admitted to hospital for diagnostic evaluation of FFT.	or whose growth is rapidly crossing centiles downwards.	The usefulness of laboratory tests was also reported.	
Wright 1998, 1996	Children with FG were identified via population screening for recruitment to an RCT. As part of the trial most were assessed by a paediatrician.	Second weight SD score fall of at least 1.26 from baseline weight, after adjustment for regression to the mean.	Cause of faltering growth (N=229) • solely organic (N=10) • partly organic(N=27)	Overall quality of the study: low – children may have had signs or symptoms of underlying conditions.

FTT failure to thrive; FG faltering growth; SD standard deviation

5.3.4.4 Clinical evidence profile

The clinical evidence profile for this review question is presented in Table 34. This table summarises the prevalence of each condition across studies. Quality was assessed individually for each study based on the risk of bias.

Table 34: Summary clinical evidence profile

Prevalence of specific conditions in infants and preschool children who present with faltering growth and no other symptoms or signs			
Condition	**Prevalence**	**No of Participants (studies)**	**Quality of the evidence by study[1]**
Partial intestinal obstruction: pyloric stenosis (N=2) or malrotation (N=1))	3/122 (2.5%)	122 (1 study)	Low[2,3]
Urinary tract infection	3/122 (2.5%)	122 (1 study)	Low[2,3]
Tuberculosis	1/122 (0.8%)	122 (1 study)	Low[2,3]
Neurological: Leigh´s disease (N=1) or cerebral palsy (N=1)	2/122 (1.6%)	122 (1 study)	Low[2,3]
Coeliac disease	2/122 (1.6%)	122 (1 study)	Low[2,3]
Hypercalcaemia	1/122 (0.8%)	122 (1 study)	Low[2,3]
No specific structural cause of FTT: unexplained (N=41), social-environmental (N=39), functional GI (N=26), not FTT (N=4)	110/122 (9%)	122 (1 study)	Low[2,3]

FTT failure to thrive; GI gastrointestinal
1 Methodological limitations assessed using the JBI Munn 2014 Checklist
2 Participants were admitted to hospital with FTT and may represent more severe cases of faltering growth
3 Unclear how participants were selected for inclusion

5.3.4.5 Economic evidence

As this question does not concern the competing uses of NHS resources it was not prioritised for health economic analysis. No health economic evidence was identified for this topic from the overall health economic search.

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5.3.4.6 Clinical evidence statements

Low quality evidence came from one cross sectional study including 122 young children admitted to hospital with failure to thrive of no obvious cause. Specific structural causes were identified in 12/122 cases (9.8%). These conditions included: partial intestinal obstruction (2.5% of cases), urinary tract infection (2.5%), tuberculosis (0.8%), neurological causes (1.6%), coeliac disease (1.6%) and hypercalcaemia (0.8%).

No evidence was found about the prevalence of hypothyroidism and chronic renal disease in this population.

Low quality evidence from one cross sectional study of 185 young children admitted to hospital for investigation of failure to thrive (but who may have had signs or symptoms of underlying organic disease) indicated that while organic disease was diagnosed as the underlying cause in 18% of children, in all cases the combination of history and physical examination indicated the likely final diagnosis rather than laboratory studies alone.

Low quality evidence from one cohort study including 229 young children with faltering growth (but who may have had signs or symptoms of underlying organic disease) indicated that in 4% of cases an underlying organic condition was the likely sole cause of faltering growth and in 12% of cases an underlying organic condition was a contributory factor to faltering growth. In most cases these organic conditions had already been diagnosed before study entry, however a previously undiagnosed organic condition was identified in 2% of the subset of children routinely assessed as part of the study.

5.3.4.7 Evidence to recommendations

5.3.4.7.1 Relative value placed on the outcomes considered

The main aim of this review was to identify the prevalence of specific causative and non-causative conditions in infants and preschool children who present with faltering growth but have no other symptoms or signs of such condition.

The Committee identified the prevalence/proportion of children with coeliac disease, urinary tract infections, hypothyroidism or chronic renal disease and no other identified causative condition as important outcomes. The Committee anticipated that the largest proportion of children would not have a particular causative condition. The only evidence was retrieved for the prevalence of coeliac disease and urinary tract infections, and the Committee debated whether other non-reported prioritised conditions should also feature in their recommendations

5.3.4.7.2 Consideration of clinical benefits and harms

The Committee considered the benefits and harms of testing and assessment of infants and children with faltering growth. There are benefits to correctly identifying treatable causative conditions. Recognising that such underlying conditions are rare, the Committee highlighted the potential harms of invasive investigations and false positive results. In addition repeated testing can raise anxiety and delay appropriate intervention.

The evidence indicated that the prevalence of underlying conditions (without signs and symptoms) was very low in infants and preschool children with faltering growth.

Based on their experience, the Committee thought that an individualised clinical and neuro developmental history and full physical examination was essential to establish whether there were any signs or symptoms of underlying conditions. This assessment should also take into account social circumstances that may impact on their growth. Even though socio-economic factors did not show a specific association with faltering growth (see section 5.3.3) they considered that other social factors may affect nutrition or adherence to advice. For this reason they recommended that clinicians should be aware that if a child appears well and

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there are no suggestive symptoms or signs further investigation is unlikely to reveal an unrecognised cause.

The Committee considered that (based on their experience) an underlying causative condition would be more likely in children who present with sustained faltering growth not responding to initial intervention, and that further tests or assessments could be justified in this scenario. For this reason, they recommended clinical judgement should be used in these cases when deciding on further investigation.

Although unlikely, some children with faltering growth could have an underlying causative condition without other signs and symptoms. Not testing could result in a potential harmful delay in diagnosis and treatment for these children. To mitigate this harm the Committee recommended that clinicians should think about undertaking further investigations for a child with sustained faltering growth, or if new symptoms or signs emerge during follow-up. The Committee agreed that if there were signs or symptoms or sustained faltering growth (or if new symptoms or signs are reported in future contact with the family), then further investigations for conditions such as hypothyroidism and chronic renal disease or others may be indicated according to the types of symptoms or signs based on clinical judgement.

The Committee, however, recommended screening for urinary tract infection due to the low harms associated with the test. The Committee also recommended to consider assessment for coeliac disease and cow's milk protein allergy in line with existing NICE guidance.

5.3.4.7.3 Consideration of economic benefits and harms

No cost-effectiveness evidence was found for this question. The Committee considered that avoidance of futile testing could lead to cost savings, and potentially prevent parental anxiety. However they added that performing necessary and clinically important tests could help resolve the underlying condition and this might additionally reduce parental anxiety – both of which would have an important health economic impact.

The cost of the tests the Committee considered is low, especially when undertaken at the same time. Similarly the Committee judge some tests are routinely performed which are of limited clinical benefit in the absence of other signs and symptoms, which the Committee wished to prevent. Consequently there is no way to tell whether these recommendations will lead to a net cost or saving for the NHS, but regardless of the direction of effect the overall magnitude is likely to be small and there is unlikely to be a significant resource impact.

5.3.4.7.4 Quality of evidence

Four studies from 3 different cohorts were included in this review. The quality of the evidence was assessed by the Joanna Briggs Institute Checklist for Prevalence Studies and the main sources of bias were lack of valid methods for identification of the condition and lack of information with regards to the method used for sampling the participants of the study. Other issues noted by the Committee included indirectness – the participants were admitted to hospital with 'Failure to Thrive' and it was unclear how participants were selected for inclusion. Two of the studies included children who may have had signs or symptoms of underlying organic disease.

5.3.4.7.5 Other considerations

It was discussed that in current practice children presenting with signs of faltering growth are investigated with many different tests. The Committee noted that this is often carried out in an attempt to reassure the parents or to be seen as being thorough. However, the available evidence indicates that these tests are unlikely to reveal any causative conditions in the absence of other clinical features.

The Committee also acknowledged that the detailed feeding or eating history as well as direct observation of feeding or meal times needs to be tailored to the individual infant or

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child taking into account a broad range of other factors, e.g. age, severity of weight loss, but also other factors such as social circumstances and the food choices that are made in the family. The Committee agreed that a comprehensive list of all possible factors cannot be listed and that clinical judgement is needed to apply an individualised approach to this.

5.3.4.7.6 Key conclusions

Based on the available evidence and the experience and expertise of the Committee it was concluded that infants and children initially presenting with faltering growth and no signs and symptoms of a particular underlying causative condition are unlikely to need further tests because they are unlikely to find an unrecognised condition.

5.3.4.8 Recommendations

14. If there is concern about faltering growth:

- perform a clinical, developmental and social assessment
- take a detailed feeding or eating history
- consider direct observation of feeding or meal times
- consider investigating for:
  - urinary tract infection (follow the principles of assessment in NICE's guideline on urinary tract infection in under 16s)
  - coeliac disease, if the diet has included gluten-containing foods (follow the principles of assessment in NICE's guideline on coeliac disease)
- perform further investigations only if they are indicated based on the clinical assessment.

15. Be aware that investigations (other than those recommended in 14) are unlikely to reveal an underlying disorder in a child with faltering growth who appears well with no other clinical concerns.

16. If a child with faltering growth develops new clinical symptoms or signs after the initial assessment, reconsider whether investigations are needed.

5.3.4.9 Research recommendations

Are routine investigations for underlying medical or behavioural conditions effective and cost-effective in children with faltering growth?

Why this is important

Concern about growth in young children is common. Parents and health professionals often worry that there is an underlying reason for slow growth that has been missed or could be easily treated to improve growth. Children may be offered blood tests or other investigations looking for unrecognised illness.

The limited evidence available at the moment is inconclusive therefore further research is needed. This research recommendation aims to find out how commonly children with faltering growth have unrecognised medical problems.

This information would help families and health professionals to plan care for children with faltering growth, particularly in deciding whether tests should be offered to look for unrecognised illness.

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Table 35: Research recommendation rationale

Research question	Are routine investigations for underlying medical or behavioural conditions effective and cost-effective in children with faltering growth?
Why this is needed	
Importance to 'patients' or the population	Concern about growth in young children is common. Parents and health professionals often worry that there is an underlying reason for slow growth that has been missed or could be easily treated to improve growth. Children may be offered blood tests or other investigations looking for unrecognised illness. The limited evidence available at the moment suggests that children are unlikely to have an underlying causative condition for faltering growth without other signs or indications. This research recommendation aims to find out how commonly children with faltering growth have unrecognised medical problems. This information would help families and health professionals to plan care for children with faltering growth, particularly in deciding whether tests should be offered to look for unrecognised illness.
Relevance to NICE guidance	NICE guidance prioritises evidence based investigations to identify health problems and therefore guide effective intervention to improve health and wellbeing. An accurate understanding of the likely and possible aetiology of faltering growth is important to guide initial assessment and management.
Relevance to the NHS	Prioritise effective investigation and treatment to minimise waste of limited resources.
National priorities	The National Service Framework for children, young people and maternity services aims for long-term and sustained improvement in children's health, and sets standards for health and social care services for children, young people and pregnant women. The Healthy Child Programme describes standards of care for screening and providing advice during pregnancy and the first 5 years of life. It includes broad recommendations on monitoring growth in infants and children.
Current evidence base	Extremely limited data specifically looking at the prevalence of medical or behaviour conditions in a population of children presenting with faltering growth.
Equality	Recognition assessment and management of faltering growth should take into consideration parents' and carers' socioeconomic, cultural, religious and ethnic environment, and potential language barriers. Access to appropriate nutrition may also differ across socioeconomic groups. Certain groups may be at greater risk of developing faltering growth, including preterm infants and children, children and infants born after intrauterine growth restriction. Those with learning-disabled parents or carers, asylum seekers, and looked-after children may find it more of a challenge to access services.
Feasibility	A large cohort of children with faltering growth would be required given the expected low incidence of underlying medical conditions.
Other comments	There is a gap in the evidence base. However it may be difficult to address this since large number are required.

Table 36: Research recommendation statement (diagnostic accuracy study characteristics)

Criterion	Explanation
Population	Infants after the first days of life and pre-school children with faltering growth, as defined by the thresholds in this guideline (see recommendation 4) without obvious signs or symptoms of an underlying condition (following clinical and neuro developmental history and full physical examination).
Index Test	Specific investigations as detailed in related guidelines (i.e. urine dipstick and screen for coeliac disease).

ISBN 978-1-4731-2693-0

Criterion	Explanation
Reference standard	Diagnosis of underlying medical or behavioural conditions based on additional investigations undertaken by health professionals or clinical follow up in those who do not have further investigations.
Outcome	Prevalence of underlying conditions, diagnostic accuracy of routine investigations, factors associated with increased prevalence of unsuspected underlying conditions (e.g. severity of faltering growth, signs and symptoms), subsequent diagnosis during follow up (e.g. medical condition or social communication disorder).
Study design	Prospective multi-centre cohort study (faltering growth)
Timeframe	Follow up to school age (up to 5 years)

5.4 Interventions for faltering growth

5.4.1 Breastfeeding support

Review question: What forms of breastfeeding support are effective in the management of faltering growth?

5.4.1.1 Introduction

The aim of this review is to identify effective interventions to support breastfeeding in the context of borderline or definite faltering growth.

For full details see review protocol in Appendix D.

5.4.1.2 Description of clinical evidence

No clinical study was identified for this review.

5.4.1.3 Economic evidence

Although this topic was considered important for health economic evaluation, a global evidence search did not identify any literature on this topic and consequently no evaluation could be supported.

5.4.1.4 Clinical evidence statements

No evidence was identified for any of the prioritised outcomes.

5.4.1.5 Evidence to recommendations

5.4.1.5.1 Relative value placed on the outcomes considered

The aim of this review is to identify effective interventions to support breastfeeding in the context of borderline or definite faltering growth.

The committee indicated the following as the critical outcomes for decision making:

- measures of growth
- continuation of breastfeeding
- health related quality of life.

No evidence was identified for this review and the Committee based their recommendations on consensus informed by the experience and expertise of its members as well as

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information from one Clinical Guideline (Postnatal Care, CG37) one Public Health Guideline (Maternal and Child Nutrition, PH11) and an Interventional Procedures Guideline (Division of ankyloglossia (tongue-tie) for breastfeeding, IPG149).

5.4.1.5.2 Consideration of clinical benefits and harms

The Committee acknowledged that there are many health benefits associated with breastfeeding, with positive long and short term effects on both mother and baby and that healthcare professionals should explain the benefits and support the continuation of breastfeeding wherever possible.

Where there are concerns about faltering growth it is important to carry out a breastfeeding assessment and to provide support and advice based on this assessment. Further details on assessments of faltering growth and information provision and support are provided in chapters 5.4 and 7.

Even though not directly covering the faltering growth population, the Committee considered the recommendations made in CG37 on postnatal care and PH11 on Maternal and Child Nutrition. It was discussed that faltering growth in breastfed infants is usually due to insufficient milk transfer and not lactation failure, and that requires the involvement of skilled health professionals, as stated in CG37. It was highlighted that the postnatal care guideline only covers the first 8 weeks of life. This could be a time during which concerns about faltering growth are first raised. The Committee agreed that the recommendations could continue to apply after the 8 week period. Breastfeeding should be encouraged and promoted if there are concerns about faltering growth. However, where there are growth concerns, breastmilk could be expressed and given in addition to breast feeds. Where necessary, breastmilk could be supplemented with formula milk. In these cases it is important to support the woman's choice whilst also highlighting the benefits of continued breastfeeding.

The Committee discussed the use of galactagogues (for example, domperidone, fenugreek, metoclopramide). Without evidence of effectiveness and with the possible risk of side effects, the Committee decided not to recommend them.

5.4.1.5.3 Consideration of economic benefits and harms

Breastfeeding support may have a small direct cost, associated with clinical time and follow up which could be incurred if a woman needs – for example – a discussion with her midwife about breastfeeding.

In terms of indirect costs, there is evidence that continued breastfeeding can reduce overall healthcare spending on a baby by making certain illnesses less likely and promoting robust health generally. As this effect is ongoing over the lifetime of the child, it is likely that relatively small investments made in breastfeeding support early will be cost-effective given the accumulation of QALYs and costs offset over the lifetime of the child.

None of the recommendations represent a significant resource impact from what is already typically done in the NHS.

5.4.1.5.4 Quality of evidence

No evidence was retrieved for this review.

5.4.1.5.5 Other considerations

The Committee also discussed ankyloglossia (tongue-tie) and elected not to make a specific recommendation for or against particular interventions for tongue tie. The NICE Interventional Procedure Guideline (IPG149) Division of ankyloglossia (tongue-tie) for breastfeeding featured in this discussion. The Committee's decision not to directly refer to

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tongue-tie was based on the quality of the evidence in IPG149 and the fact that no evidence related to tongue-tie in infants with faltering growth was identified. The Committee also discussed whether to directly refer to PH11, but decided not to because the guidance addresses what should be done in the 'normal population' rather than the actions to take when there are concerns about faltering growth.

5.4.1.5.6 Key conclusions

The Committee concluded that supporting and encouraging breastfeeding was an important component in the care of mothers where there are concerns about their infant's growth. Due to the lack of directly applicable evidence the Committee based their decision on other related public, clinical and interventional procedure guidance as well as on their expertise and experience. It was also highlighted and agreed by the Committee that the observation and assessment of breastfeeding as well as comprehensive information and support from a healthcare professional with the relevant expertise are important aspects in the promotion of breastfeeding, which are topics that are addressed separately in other parts of this guideline (chapters 5.3 and 7).

5.4.1.6 Recommendations

Weight loss in the early days of life

17. **Provide feeding support (see recommendations in NICE's guideline on Postnatal care up to 8 weeks after birth) if there is concern about weight loss in infants in the early days of life, for example if they have lost more than 10% of their birth weight.**

18. **Be aware that supplementary feeding with infant formula in a breastfed infant may help with weight gain, but often results in cessation of breastfeeding.**

19. **If supplementation with an infant formula is given to a breastfed infant:**
    - support the mother to continue breastfeeding
    - advise expressing breast milk to promote milk supply, and
    - feed the infant with any available breast milk before giving any infant formula.

Faltering growth after the early days of life

20. **If observation of eating or feeding is needed because of concern about faltering growth, ensure this is done by a person with appropriate training and expertise.**

21. **Provide feeding support (see recommendations in NICE's guideline on postnatal care up to 8 weeks after birth) if there is concern about faltering growth in the first weeks of life. Consider whether such feeding support might be helpful in older milk-fed infants, including those having complementary solid foods.**

22. **Be aware that while supplementary feeding with infant formula may increase weight gain in a breastfed infant if there is concern about faltering growth, it often results in cessation of breastfeeding.**

23. **If supplementation with an infant formula is given to a breastfed infant because of concern about faltering growth after the early days of life:**
    - support the mother to continue breastfeeding

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- advise expressing breast milk to promote milk supply, and
- feed the infant with any available breast milk before giving any infant formula.

5.4.2 Dietary advice and supplementation

Review question: What is the effectiveness of providing dietary advice or supplementation to families or carers in the management of infants and preschool children with suspected or confirmed faltering growth when compared to no intervention or compared to advice on feeding practices other than breastfeeding, or family support?

5.4.2.1 Introduction

Faltering growth results from a nutritional intake below that needed to support growth. Health professionals often offer advice aimed at increasing or supplementing energy intake in children where there are concerns about faltering growth.

The aim of this review is to identify what interventions are clinically and cost effective for improving nutritional status in children with concerns regarding possible or actual faltering growth.

5.4.2.2 Description of clinical evidence

Four parallel randomised controlled trials were included in this evidence review on the effectiveness of nutritional interventions for faltering growth (Alarcon 2003; Clarke 2007; Fewtrell 2001; Panahi 2010).

Evidence from these studies is summarised in the clinical GRADE evidence profile below (Table 38, Table 39, Table 40, and Table 41). For full details, please see the full GRADE profiles in Appendix J. See also the review protocol in Appendix D, forest plots in Appendix I, study evidence tables in Appendix G and the exclusion list in Appendix H.

With regards to the population studied, one trial included children with faltering growth due to what they described as picky-eater behaviour defined as refusal of all or certain type of food (Alarcon 2003); one trial included infants with faltering growth, defined as poor growth (Clarke 2007); one looked at term infants with weight below the 10th centile (Fewtrell 2001); and finally one study included children with mild or moderate nonorganic failure to thrive (Panahi 2010).

Sample size ranged from 23 to 299 infants and children.

The included studies compared the effectiveness of several nutritional interventions:

- nutritional supplementation in addition to counselling versus counselling alone (Alarcon 2003)
- nutrient-dense formula versus either energy supplemented formula (Clarke 2007), or standard term formula (Fewtrell 2001)
- supplementary bovine colostrum in addition to routine treatments versus routine treatments alone (Panahi 2010).

Growth measurements, including weight and length gain, were the most reported outcomes (Alarcon 2003; Clarke 2007; Fewtrell 2001; Panahi 2010); most studies reported on adverse effects, but none presented statistical analysis.

No data was found for the following other outcomes listed in the review protocol:

- health-related quality of life

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- parent or carer satisfaction
- adherence to interventions
- cognition and neurodevelopment.

5.4.2.3 Summary of included studies

A summary of the studies that were included in this review are presented in Table 37.

Table 37: Summary of included studies

Study	Population	Intervention	Comparison	Outcomes	Other
Alarcon 2003	92 subjects aged 36 to 60 months who had picky-eater behaviour (defined as refusal of all or certain types of food) and evidence of FG (below the 25th percentile in weight for height)	Nutritional counselling + nutritional supplement (Pediasure; a lactose-free supplement that provided 1.0 kcal/mL, with 12% of calories as protein, 43.8% as carbohydrate, and 44.8% as fat)	Nutritional counselling alone (a physician counselled parents at each visit on techniques to enhance their child's eating behaviours, and these principles were reinforced at each visit - parents were encouraged to follow 10 key points, see full text)	Weight, weight for age, height, height for age - all measured at day 30, 60, 90. Weight for height was measured as well.	Subjects were enrolled at three study sites in the Philippines and at one site in Taiwan. Not clear definition of 'faltering growth'.
Clarke 2007	49 infants with faltering growth, defined as poor growth = an infant less than the third centile for weight and height for age, and/or a weight gain that was less than 50% of expected over the 1-week period prior to recruitment.	Nutrient-dense formula[1] (4.2 kJ mL-1) for 6 weeks	Energy-supplemented formula (4.2 kJ mL-1) for 6 weeks.	Weight z-score, increase in median MUAC between the two groups.	UK based
Fewtrell 2001	299 healthy term infants with weight below the 10th centile.	Nutrient-enriched formula[2]	Standard term formula[2]	Weight, length, and occipitofrontal head circumference at 9 and 19 months.	UK based <10% is a bit of a less stringent criterion than usually used
Panahi 2010	120 children (1-10 years of age) with mild or moderate nonorganic FTT. The two groups	Routine treatments + supplementary bovine colostrum at	Routine treatments for FTT, such as parents' instructions	Height for age, and weight for age.	Study from Iran

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Study	Population	Intervention	Comparison	Outcomes	Other
	were matched for sex, age, weight, and height at the time of entry.	the dose of 40mg*kg-1*day-1 for a three month period.	regarding correct dietary programs, daily multivitamins and minerals, and zinc sulphate syrup.		

BW birth weight; EF enriched formula; FG faltering growth; FTT failure to thrive ;kg kilogram; kJ kilocalories; ml millilitre; MUAC mid upper arm circumference; mg milligram; OFC occipital-frontal circumference; TF term (standard) formula.
1 Nutrient-dense formula has more energy (up to 52% more), more protein (up to 73%) and more minerals, such as sodium, potassium, iron and zinc than energy-dense formula.
2 Nutrient-enriched formula has a higher protein content (approximately 30%) than the standard formula. In addition, the formula has more protein-to-energy ratio and contains more minerals, such as calcium (31 mg more), phosphorus (8 mg more), sodium (5 mg more) and potassium (21 mg more).

5.4.2.4 Clinical evidence profile

The clinical evidence profiles for this review question (nutritional interventions in faltering growth) are presented in Table 38, Table 39, Table 40 and Table 41.

Table 38: Summary clinical evidence profile Comparison 1: counselling + nutritional supplement versus counselling alone for faltering growth

Counselling + nutritional supplement versus counselling alone for faltering growth					
Outcomes	**Illustrative comparative risks* (95% CI)**		**Relative effect (95% CI)**	**No of Participants (studies)**	**Quality of the evidence (GRADE)**
	Assumed risk counselling alone (±SD)	**Corresponding risk Counselling + nutritional supplement**			
weight for age change from baseline Follow-up: 30 days	The mean change in weight for age at 30 days in the control group was 1.37 (±4.04)	The mean weight for age in the intervention groups was 2.48 higher (0.53 to 4.43 higher)	-	104 (1 study)	Very low[1,2]
weight for age change from baseline Follow-up: 60 days	The mean change in weight for age at 60 days in the control group was 1.49 (±4.40)	The mean weight for age in the intervention groups was 5.93 higher (3.12 to 8.74 higher)	-	104 (1 study)	Low[1]
weight for age change from baseline Follow-up: 90 days	The mean change in weight for age at 90 days in the control group was	The mean weight for age in the intervention groups was 8.03 higher (4.86 to 11.2 higher)	-	104 (1 study)	Low[1]

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Counselling + nutritional supplement versus counselling alone for faltering growth					
	of 0.96 (±4.93)				
height for age change from baseline Follow-up: 30 days	The mean change in height for age at 30 days in the control group was of 0.24 (±3.36)	The mean height for age in the intervention groups was 1.85 higher (0.31 lower to 4.01 higher)	-	104 (1 study)	Very low[1,3]
height for age change from baseline Follow-up: 60 days	The mean change in height for age at 60 days in the control group was of -0.21 (±4.24)	The mean height for age in the intervention groups was 3.17 higher (1.09 to 5.25 higher)	-	104 (1 study)	Very low[1,4]
height for age change from baseline Follow-up: 90 days	The mean change in height for age at 90 days in the control group was of -0.15 (±4.20)	The mean height for age in the intervention groups was 5.24 higher (2.82 to 7.66 higher)	-	104 (1 study)	Low[1]

CI confidence interval, SD standard deviation
1 Evidence was downgraded by 2 due to unclear allocation sequence generation, unclear allocation concealment, significant difference in baseline characteristics, incomplete outcome data were not clearly addressed, and knowledge of the allocated interventions was not adequately prevented during the study.
2 Evidence was downgraded by 1 due to serious imprecision as 95%CI crossed one default MID (± 0.5 x 4.04 = ±2.02)
3 Evidence was downgraded by 1 due to serious imprecision as 95%CI crossed one default MID (± 0.5 x 3.36 = ±1.68)
4 Evidence was downgrade by 1 due to serious imprecision as 95% CI crossed one default MID (± 0.5 x 4.24 = ±2.12)

Table 39: Summary clinical evidence profile Comparison 2: routine treatments + bovine colostrum versus routine treatments alone for faltering growth

routine treatments + bovine colostrum versus routine treatments alone for faltering growth					
Outcomes	**Illustrative comparative risks* (95% CI)**		**Relative effect (95% CI)**	**No of Participants (studies)**	**Quality of the evidence (GRADE)**
	Assumed risk routine treatments alone	**Corresponding risk Routine treatments + bovine colostrum**			
weight for age Gomez index Follow-up: 1 months	The mean weight for age was 75.2 (SD 6.67)	The mean weight for age in the intervention groups was 0.71 higher (1.68 lower to 3.1 higher)	-	120 (1 study)	Moderate[1]

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routine treatments + bovine colostrum versus routine treatments alone for faltering growth					
weight for age Gomez Index Follow-up: 2 months	The mean weight for age was 75.85 (SD 7.05)	The mean weight for age in the intervention groups was 2.73 higher (0.21 to 5.25 higher)	-	120 (1 study)	Very low[1,2]
weight for age Gomez Index Follow-up: 3 months	The mean weight for age was 77.12 (SD 8.31)	The mean weight for age in the intervention groups was 4.6 higher (1.63 to 7.57 higher)	-	120 (1 study)	Very low[1,3]
height for age Waterlow index Follow-up: 1 months	The mean height for age was 91.06 (SD 3.62)	The mean height for age in the intervention groups was 0.08 higher (1.22 lower to 1.38 higher)	-	120 (1 study)	Moderate[1]
height for age Waterlow index Follow-up: 2 months	The mean height for age was 91.55 (SD 3.87)	The mean height for age in the intervention groups was 0.55 higher (0.83 lower to 1.93 higher)	-	120 (1 study)	Moderate[1]
height for age Waterlow index Follow-up: 3 months	The mean height for age was 91.71 (SD 3.687)	The mean height for age in the intervention groups was 1.2 higher (0.19 lower to 2.59 higher)	-	120 (1 study)	Very low[1,4]

CI confidence interval, SD standard deviation
1 Evidence was downgraded by 1 due to unclear allocation concealment and knowledge of the allocated interventions was not adequately prevented during the study.
2 Evidence was downgraded by 1 due to serious imprecision as 95%CI crossed one default MID (± 0.5 x 4.05 = ±3.52)
3 Evidence was downgraded by 1 due to serious imprecision as 95% CI crossed one default MID (± 0.5 x 8.31 = ±4.15)
4 Evidence was downgraded by 1 due to serious imprecision as 95% CI crossed one default MID (± 0.5 x 3.89 = ±1.94)

Table 40: Summary clinical evidence profile Comparison 3: nutrient-dense formula versus energy-supplemented formula for faltering growth

nutrient-dense formula versus energy-supplemented formula for faltering growth					
Outcomes	**Illustrative comparative risks* (95% CI)**		**Relative effect (95% CI)**	**No of Participants (studies)**	**Quality of the evidence (GRADE)**
	Assumed risk energy-supplemented formula	**Corresponding risk Nutrient-dense formula**			
median weight gain g kg^{-1} day^{-1}	The median weight gain was 7.6 g kg^{-1} day^{-1}	The median weight gain was 7.2 g kg-1 day-1	-	49 (1 study)	Moderate[1]

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nutrient-dense formula versus energy-supplemented formula for faltering growth					
Follow-up: 6 weeks					
median change weight z-score Follow-up: 6 weeks	The mean change in weight z-score was 0.49 (-0.9 lower to 2.3 higher)	The mean change in weight z-score was 0.29 (-0.6 lower to 1.5 higher)	-	49 (1 study)	Moderate[1]
median linear growth cm per week Follow-up: 6 weeks	The median linear growth was 0.60 cm week^{-1}	The median linear growth was 0.67 cm week^{-1}	-	49 (1 study)	Moderate[1]
median change in length z-score Follow-up: 6 weeks	The mean change in length z-score was -0.28 (-1.3 lower to 2.1 higher)	The mean change in length z-score was -0.18 (-1.7 lower to 1.2 higher)	-	49 (1 study)	Moderate[1]
median MUAC cm per week	The mean change in MUAC was 0.26 cm wk^{-1}	The mean change in MUAC was 0.4 cm wk^{-1}	Not estimable	49 (1 study)	Moderate[1]

CI confidence interval; MUAC mid upper arm circumference.
1 Evidence was downgraded by 1 due to unclear concealment of allocation and knowledge of the allocated interventions not clearly adequately prevented during the study.

Table 41: Summary clinical evidence profile Comparison 4: nutrient-enriched formula versus standard term formula for faltering growth

nutrient-enriched formula versus standard term formula for faltering growth					
Outcomes	**Illustrative comparative risks* (95% CI)**		**Relative effect (95% CI)**	**No of Participants (studies)**	**Quality of the evidence (GRADE)**
	Assumed risk standard term formula (±SD)	**Corresponding risk Nutrient-enriched formula**			
weight (change from baseline) kg Follow-up: 9 months	The mean weight (change from baseline) in the control group was 5.66 kg (±0.21)	The mean weight (change from baseline) in the intervention groups was 0.21 higher (0.02 lower to 0.44 higher)	-	247 (1 study)	High
weight (change from baseline) g Follow-up: 18 months	The mean weight (change from baseline) in the control	The mean weight (change from baseline) in the intervention groups was 0.25 higher (0.03 lower to 0.53 higher)	-	240 (1 study)	Moderate[1]

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nutrient-enriched formula versus standard term formula for faltering growth					
	group was 7.52 g (±0.21)				
weight g Follow-up: 9-18 months	The mean weight in the control group was 1.95 g (±0.61)	The mean weight in the intervention groups was 0.1 lower (0.26 lower to 0.06 higher)	-	240 (1 study)	High
length (change from baseline) cm Follow-up: 9 months	The mean length (change from baseline) was 22.2 cm (±1.4)	The mean length (change from baseline) in the intervention group was 1.1 higher (0.4 to 1.8 higher)	-	247 (1 study)	Moderate[2]
length (change from baseline) cm Follow-up: 18 months	The mean length (change from baseline) was 32 cm (±1.4)	The mean length (change from baseline) in the intervention groups was 1 higher (0.23 to 1.77 higher)	-	240 (1 study)	Moderate[3]
length cm Follow-up: 9-18 months	The mean weight in the control group was 9.84 cm (±1.94)	The mean length in the intervention groups was 0.33 lower (0.87 lower to 0.21 higher)	-	240 (1 study)	High
OFC (change from baseline) cm Follow-up: 9 months	The mean OFC (change from baseline) was 12 cm (± 0.8)	The mean ofc (change from baseline) in the intervention groups was 0.5 higher (0.1 to 0.9 higher)	-	247 (1 study)	Moderate[4]
OFC (change from baseline) cm Follow-up: 18 months	The mean OFC (change from baseline) was 14 cm (± 0.8)	The mean ofc (change from baseline) in the intervention groups was 0.6 higher (0.18 to 1.02 higher)	-	240 (1 study)	Moderate[5]
OFC cm Follow-up: 9-18 months	The mean OFC was 2.36 cm (±0.80)	The mean ofc in the intervention groups was 0.01 lower (0.2 lower to 0.18 higher)	-	240 (1 study)	High

CI confidence interval; ofc occipital frontal circumference.
1 Evidence was downgraded by 1 due to serious imprecision as 95%CI crossed one default MID (± 0.5 x 1.13 = ±0.13)
2 Evidence was downgraded by 1 due to serious imprecision as 95% CI crossed one default MID (± 0.5 x 3 = ±1.5)
3 Evidence was downgraded by 1 due to serious imprecision as 95% CI crossed one default (± 0.5 x 3.2 = ±0.64)
4 Evidence was downgraded by 1 due to serious imprecision as 95% CI crossed one default (± 0.5 x 1.8 = ±0.9)
5 Evidence was downgraded by 1 due to serious imprecision as 95% CI crossed one default (± 0.5 x 1.8 = ±0.9)

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5.4.2.5 Economic evidence

No health economic evidence was identified for this topic from the overall health economic search, however some costing information was available for consideration by the Committee.

5.4.2.5.1 Oral liquid nutritional supplementation

There are many oral liquid nutritional supplementation products on the market. Some of these are 'artificial' in the sense of being created by a pharmaceutical company to offer a measured dose of a particular nutrient, while others are 'natural' in the sense of being available as a food product in the supermarket or other retailer. Table 42 gives indicative costs for some examples of such 'artificial' supplements.

Table 42: Indicative costs of 'artificial' oral supplements

Oral supplement	Type of nutrient	Quantity (typical dose, ml)	Price	kcal / 100ml	kcal / £
Pro-Cal® powder	Protein, fat and carbohydrate	100 (when 15g sachet dissolved for preparation)	£5.11 for 8 sachets, £0.64 per sachet	100 (when 15g sachet dissolved for preparation)	156.3
Pro-Cal® shot	Protein, fat and carbohydrate	30	£9.58 for 6 shots, £1.60 per shot	330	61.9
PaediaSure®	Carbohydrate	200	£3.25	100	61.5
PaediaSure® Fibre	Fibre and carbohydrate	200	£4.05	100	49.4
PaediaSure® Peptide	Protein and carbohydrate	200	£5.73	100	34.9
PaediaSure® Plus	Carbohydrate	200	£4.35	150	69.0
PaediaSure® Plus Fibre	Fibre and carbohydrate	200	£4.15	150	72.3
PaediaSure® Plus Juice	Carbohydrate	200	£4.85	150	61.9
Similac® High Energy	Carbohydrate	200	£3.39	100	59.0
SMA PRO® High Energy	Carbohydrate	250	£3.95	91	57.6

(a) These products are intended to be representative of the market only, and not a guide to which supplements to offer. Some are unsuitable for children under three years and most are unsuitable for children under one year.
(b) Nutritional information taken from respective manufacturer's product pages accessed 06/07/17. Costs taken as cheapest price for that product from online retailer, http://www.nutridrinks.co.uk, accessed 06/07/17 with exception of Pro-Cal powder taken from MIMS online, http://www.mims.co.uk, accessed 06/07/17. This source used as no standard NHS costing.

The cost of supplements will also depend on the frequency those supplements are administered. If they were used to substitute rather than complement diet at home, the cost could be substantial, but the Committee do not recommend this. In general, oral supplementation with 'artificial' products is cheap, but not as cheap as 'natural' alternatives.

It might be appropriate to supplement a child's diet with a 'natural' product, such as switching from semi-skimmed to full fat milk. This would not normally incur a cost to the NHS as typically food would be bought out of a family's personal budget, however for completeness Table 43 gives some indicative costs should the NHS pay the difference between a lower energy-density food and a higher. These costs are not substantial, although switching from

ISBN 978-1-4731-2693-0

frying food in oil to frying in butter could be considered more expensive than some 'artificial' supplements if fried food is to be eaten regularly.

Table 43: Indicative costs of 'natural' oral supplements

Lower density foodstuff	Price	Higher density foodstuff	Price	Difference
Single cream 300ml	£0.85	Double cream 300ml	£0.95	£0.10
500g low fat natural yoghurt	£0.90	500g full-fat Greek yoghurt	£1.00	£0.10
1 l vegetable oil	£1.15	1 kg butter	£4.36	£3.21

Source: www.tesco.com, retrieved 28/02/17

5.4.2.5.2 Tube feeding

Tube feeding would be regarded as a more extreme (and costly) intervention to oral supplementation. There are a variety of methods of tube feeding an infant, however the costs associated with long-term nutritional supplementation via gastrostomy or nasogastric tube feeding are outside the scope of NHS Reference Costs. As an estimate of these costs, currency codes related to endoscopic insertions from NHS Reference Costs are presented in Table 44 as a proxy.

Table 44: Cost of tube feeding procedures

Procedure	Cost
Endoscopic Insertion of Gastrostomy Tube, 18 years and under, elective inpatient	£2,104
Endoscopic Insertion of Gastrostomy Tube, 18 years and under, day case	£1,108

(a) Source: NHS Reference Costs 2014/15

5.4.2.6 Clinical evidence statements

5.4.2.6.1 Nutritional supplementation in addition to counselling versus counselling alone

Very low to low quality evidence from 1 randomised controlled study with 104 participants found that there is a clinically significant beneficial effect of counselling and nutritional supplementation on weight for age compared with supplementation alone at day 30, 60 and 90.

Low to very low quality evidence from 1 randomised controlled study with 104 participants found that there may be a clinically significant beneficial effect of counselling and nutritional supplementation on height for age compared with supplementation alone at day 30 but there is uncertainty around the estimate. The same evidence however showed that there is a clinically significant beneficial effect of counselling and nutritional supplementation on height for age compared with supplementation alone at day 60 and 90.

5.4.2.6.2 Supplementary bovine colostrum in addition to routine treatments versus routine treatments alone

Moderate to low quality evidence from 1 randomised controlled study with 120 participants found that there is no clinically significant difference in weight for age between bovine colostrum compared with routine treatments alone at 1 and 2 months. The same evidence however showed a clinically significant beneficial effect of bovine colostrum on weight for age compared to routine treatments alone at 3 months.

ISBN 978-1-4731-2693-0

Moderate to low quality evidence from 1 randomised controlled study with 120 participants found that there is no clinically significant difference in height for age between bovine colostrum compared with routine treatments alone at 1, 2 and 3 months.

5.4.2.6.3 Nutrient-dense formula versus either energy supplemented formula

Moderate evidence from 1 randomised controlled study with 49 participants found that there is no significant difference in median weight gain between nutrient-dense formula and energy-supplemented formula at 6 weeks.

Moderate evidence from 1 randomised controlled study with 49 participants found that there is no significant difference in linear growth between nutrient-dense formula and energy-supplemented formula at 6 weeks.

Moderate evidence from 1 randomised controlled study with 49 participants found that there is no significant difference in median MUAC between nutrient-dense formula and energy-supplemented formula at 6 weeks.

5.4.2.6.4 Nutrient-dense formula standard term formula

High to moderate quality evidence from 1 randomised controlled study with 299 participants found that there is no clinically significant difference in weight change from baseline between nutrient-enriched formula and standard term formula at 9 months; however, the same evidence found that there may be a clinically significant beneficial effect of nutrient-enriched formula on weight change from baseline compared with standard term formula at 18 months, but there is uncertainty around the estimate. When looking at weight change between 9 and 18 months, there is no clinically significant difference between nutrient-enriched formula and standard term formula.

High to moderate quality evidence from 1 randomised controlled study with 299 participants found that there is no clinically significant difference between length change from baseline with nutrient-enriched formula or standard term formula at 9 months; however, there is a clinically significant beneficial effect of nutrient-enriched formula compared with standard term formula on length change from baseline to 18 months. When looking at change in length between 9 and 18 months, there is no clinically significant difference between nutrient-enriched formula and standard term formula.

High to moderate quality evidence from 1 randomised controlled study with 299 participants found that there is no clinically significant difference between the occipital frontal circumference with nutrient-enriched formula or standard term formula at 9, 18 months and between 9 and 18 months.

5.4.2.7 Evidence to recommendations

5.4.2.7.1 Relative value placed on the outcomes considered

The aim of this review is to identify what interventions are clinically and cost effective for improving nutritional status in children with concerns regarding possible or actual faltering growth. No evidence was identified for health related quality of life, parent/carer satisfaction, adherence to interventions or adverse effects related to interventions on cognition and neurodevelopment. Therefore, the only outcomes the Committee could rely for decision-making from the outcomes retrieved by the evidence were measurements of growth.

5.4.2.7.2 Consideration of clinical benefits and harms

The Committee agreed that the first line approach that should be considered when assessing the needs of a child with faltering growth is to look at the nutritional content of the food he or she eats. They discussed that the main objective of this would be to review the child's daily intake and to enhance the energy and nutrient density of their normal diet, if required. These

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adjustments should be appropriate for the child's age and should be reviewed on a regular basis. Along with this approach, the Committee agreed on other factors that should be considered and discussed with the parents of the child. For instance, usual liquid intake should be reviewed, as drinking too much milk or too many energy-dense drinks, may be supressing the child's appetite and therefore, stopping the child from eating food at regular times.

The Committee discussed recommending a trial of nutritional supplementation for those cases in which assessing feeding practices was not possible (i.e. child refusing oral intake; family poverty) or did not have an adequate effect. It was agreed that nutritional supplementation should be considered on a case by case basis, reviewed at least monthly and should be stopped at the first sign of seeing no benefit or undesirable effect.

During the assessment for nutritional supplementations, there are several factors that should be reviewed regularly (depending on the severity of faltering growth), including weight gain and growth; impact on developmentally appropriate oral intake; adherence to treatment and planned cessation.

Finally, the Committee agreed that enteral tube feeding should be reserved and considered for severe faltering growth with the aim to discontinue this as soon as possible. They noted that this should only be initiated if there are serious concerns about weight gain, if a multidisciplinary assessment identified that this is needed and if all other intervention options have been unsuccessful in leading to improvement. They left the type of multidisciplinary assessment intentionally vague, as in 'appropriate', to allow clinical judgement based on the circumstance of the individual infant or child. They therefore agreed tube feeding is not usually necessary and if considered should be based on a multi-disciplinary assessment and approach and should include consideration of the goals to indicate when tube feeding is no longer needed.

5.4.2.7.3 Consideration of economic benefits and harms

Direct interventions may carry large costs – especially the intervention of enteral tube feeding. In general dietary supplements carry a low or zero cost to the NHS depending on whether the supplements are 'artificial' or not – for example bovine colostrum vs switching to full-fat milk. Dietary advice and support may have a small direct cost, associated with clinical time and follow up which could be generated if a parent needs to have detailed discussion with a clinician. However since most clinicians will already offer dietary advice to parents, the effect of these recommendations should only be to improve the advice given at these sessions.

In terms of indirect costs, inadequate nutrition may cause downstream costs that are difficult to capture in a conventional trial. As this effect is ongoing over the lifetime of the child, it is likely that relatively small investments made in nutritional support early will be cost-effective given the accumulation of QALYs and costs offset over the lifetime of the child – this is similar to the justification for offering breastfeeding support.

Overall since these recommendations should do nothing more than improve what is already offered by the NHS, it is thought unlikely that they will carry a significant resource impact.

5.4.2.7.4 Quality of evidence

The quality of the available evidence was of low to very low quality as assessed by GRADE and was drawn from 4 randomised controlled trials. For the domain risk of bias, the studies were assigned ´very serious risk of bias´ and the main sources of bias were: lack of information on the randomisation method used; concealment of allocation unreported or unclear, and lack of blinding of investigators.

No serious issues were found regarding inconsistency (heterogeneity) as only single studies were included in the comparisons. Some issues were raised regarding indirectness, for

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instance the Committee considered that some of the evidence presented was indirect since faltering growth was poorly defined (for example weight below the 10th centile). Other comments included the effect size of the studies, as this was also imprecise due to the small number of children that participated in these trials.

5.4.2.7.5 Other considerations

The Committee reviewed the evidence presented and used it together with their clinical experience to make recommendations on dietary advice or supplementation in children and young people with faltering growth. The Committee recognised the very heterogeneous group of children that may present with faltering growth, therefore they discussed different approaches according to degree of severity.

5.4.2.7.6 Key conclusions

Based on the clinical evidence and on their expert opinion, the Committee concluded that in a child with faltering growth, nutritional density of the diet should be considered along with a discussion about feeding practices and behavioural interventions. In situations where this approach does not have an adequate effect, nutritional supplementation should be offered, along with a referral to a paediatric dietitian. Enteral tube feeding is to be used under the supervision of a multidisciplinary team and in cases of severe faltering growth.

5.4.2.8 Recommendations

24. If necessary, based on the assessment, advise on food choices for infants and children that:

- are appropriate to the child's developmental stage in terms of quantity, type and food texture
- optimise energy and nutrient density.

25. In infants or children who need a further increase in the nutrient density of their diet beyond that achieved through advice on food choices, consider:

- short-term dietary fortification using energy-dense foods
- referral to a paediatric dietitian.

26. Advise the parents or carers of infants or children with faltering growth that drinking too many energy-dense drinks, including milk, can reduce a child's appetite for other foods.

27. Consider a trial of an oral liquid nutritional supplement for infants or children with continuing faltering growth despite other interventions (see recommendations 20, 21, 22, 24, 25, 26 and 31).

28. Regularly reassess infants and children receiving an oral nutritional supplement for faltering growth to decide if it should be continued. Take into account:

- weight change
- linear growth
- intake of other foods
- tolerance
- adherence
- the views of parents or carers.

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29. **Only consider enteral tube feeding for infants and children with faltering growth when:**
    - there are serious concerns about weight gain, **and**
    - an appropriate specialist multidisciplinary assessment for possible causes and contributory factors has been completed, **and**
    - other interventions have been tried without improvement.

30. **If enteral tube feeding is to be used in an infant or child with faltering growth, make a plan with appropriate multidisciplinary involvement for:**
    - the goals of the treatment (for example, reaching a specific weight target)
    - the strategy for its withdrawal once the goal is reached (for example, progressive reduction together with strategies to promote oral intake).

5.4.2.9 Research recommendation

Do high energy liquid feed supplements improve growth in children with faltering growth?

Why this is important

It seems logical to attempt to treat inadequate dietary intake with food of some kind, and high energy liquid dietary supplements appear to be effective when used in older adults. Although they are also widely promoted for use in children, little research on their efficacy has been done. Experimental research suggests that high energy liquid feed supplements may suppress appetite and displace normal diet, and one case series found that when high energy liquid feed supplements were withdrawn appetite improved with no impact on weight. Further research is important to establish whether their effectiveness justifies their cost and the suppressant effect on appetite.

Table 45: Research recommendation rationale

Research question	Do high energy liquid feed supplements improve growth in children with faltering growth?
Why this is needed:	
Importance to 'patients' or the population	High energy liquid nutritional supplements are widely used in children with low intake or poor weight gain but it is not clear if they are effective and they may have adverse effects on appetite, causing or exacerbating previously confirmed feeding behaviour problems.
Relevance to NICE guidance	The relevance to NICE is high. There is no clear priority for using high energy liquid feed supplements, or whether they should be used at all in children with inadequate intake or weight gain. It is also unclear whether they can cause adverse effects in such children.
Relevance to the NHS	If use of feed supplements was evidence based, there could be potential cost savings to the NHS. When supplements are used, the initial cost to the NHS of these and the additional treatment required if feeding behaviour problems are present will be offset by growth improvement. The improvements in quality of life in both the children and their families may also reduce the burden of care in primary and social care.
National priorities	The National Service Framework for children, young people and maternity services aims for long-term and sustained improvement in children's health, and sets standards for health and social care services for children, young people and pregnant women.

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Research question	Do high energy liquid feed supplements improve growth in children with faltering growth?
	The Healthy Child Programme describes standards of care for screening and providing advice during pregnancy and the first 5 years of life. It includes broad recommendations on monitoring growth in infants and children. This research would also address healthy-eating targets (as set out in the Department of Health obesity and healthy eating policy).
Current evidence base	The guideline identified that there is a gap in the evidence base. The systematic review of this topic did not find any comparative effectiveness studies addressing this topic. There are two published RCTs, both or indirect and one of low quality, the other only in a group of children with a specific condition (cystic fibrosis).
Equality	Recognition assessment and management of faltering growth should take into consideration parents' and carers' socioeconomic, cultural, religious and ethnic environment, and potential language barriers. Access to appropriate nutrition may also differ across socioeconomic groups. Certain groups may be at greater risk of developing faltering growth, including preterm infants and children, children and infants born after intrauterine growth restriction, those with learning-disabled parents or carers, asylum seekers, and looked-after children.
Feasibility	Due to the small prevalence of infants and preschool children with faltering growth this would have to be a multi-centre study to optimise recruitment.
Other comments	This might be a very heterogeneous population. It could result in difficulties in arriving at a clear case definition. A separate study would be useful for infants under 6 months of age looking at the use of high energy formula.

Table 46: Research recommendation statements (PICO characteristics)

Criterion	Explanation
Population	Infants or children aged 6-48 months with Faltering growth, where supplementary feeding is being considered, Exclusions: children with unsafe swallow, severe developmental delay (inability to eat), underlying medical condition (e.g. infection)
Intervention	High energy liquid feed supplements to supply equivalent of at least 20% of daily energy requirement
Comparator	• dietetic assessment and advice about high energy oral diets (standard practice).
Outcome	• measurements of nutritional status (weight, length or height, head circumference, mid-arm circumference): for example change in weight SD score, change in length SD score. • parental health related quality of life • satisfaction with treatment
Study design	Randomised controlled trial (RCT). Stratified (or restricted) by age: 6-12 months, 12-24 months, 24-48 months
Timeframe	3 years Some of this would depend on age: 1-6 months follow up on treatment plus 1-3 months after treatment stopped

5.4.3 Non-nutritional interventions

Review question: What is the effectiveness of providing advice on, and practical support for feeding practices other than breastfeeding to families or carers in the

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management of children with suspected or confirmed faltering growth when compared to no intervention or compared or dietary advice and supplementation?

5.4.3.1 Introduction

Where a health professional recognises that factors other than nutritional intake may be leading to faltering growth, non-nutritional measures may be proposed to improve oral energy intake. The committee sought to review evidence for non-nutritional interventions in managing faltering growth.

5.4.3.2 Description of clinical evidence

The objective of this review was to identify what non-nutritional practices and interventions are effective for improving nutritional status in children with faltering growth. For full details see review protocol in Appendix D.

One randomised controlled trial has been included in this systematic review (Turner 1994). The main aim of this study was to examine the effects of a behavioural parent training (BPT) in comparison to a standard dietary education (SDE) in energy and nutrition intake. The study included 20 participants with persistent feeding difficulties (the majority of them displayed this type of difficulties for over 12 months) and the severity of these was assessed during a structured intake interview with the children's parents.

Evidence from these are summarised in Table 47. See also the study selection flowchart in Appendix F, forest plots in Appendix I, study evidence tables in Appendix G, exclusion list in Appendix H and full GRADE profiles in Appendix J.

5.4.3.3 Summary of included studies

Table 47: Summary of the included study

Study	Intervention/ Comparison	Population	Outcomes	Comments
Turner 1994	Behavioural parent training/ standard dietary education	20 children with severe feeding difficulties	• energy intake (% RDI) • protein intake (% RDI)	Unclear sequence generation; unclear method to conceal the allocation; unclear whether the outcome assessors were blinded.

RDI reference daily intake.

5.4.3.4 Clinical evidence profile

Table 48: Summary clinical evidence profile for BPT compared to SDE for persistent feeding difficulties

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk with SDE	Corresponding risk with BPT			
Energy intake (% RDI) Mealtime Record Form	The mean energy intake (% RDI) in the control groups was 6.1	The mean energy intake (% RDI) in the intervention groups was 1.60 lower (16.64 lower to 13.44 higher)	-	20 (1 study)	very low[1,2,3]

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Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk with SDE	Corresponding risk with BPT			
Protein intake (% RDI) Mealtime Record Form	The mean protein intake (% RDI) in the control groups was -17.7	The mean protein intake (% RDI) in the intervention groups was 25 lower (54.85 lower to 4.85 higher)	-	20 (1 study)	very low[1,2,4]

CI: Confidence interval; RDI: reference daily intake
1 Generation of a randomised sequence, method used to conceal the allocation and blinding of outcome assessors has not been reported.
2 Included participants presented with severe feeding difficulties and not with faltering growth
3 Evidence was downgraded by 2 due to very serious imprecision as 95% CI crossed 2 default MIDs (23.2 x ±0.5 = ± 11.6)
4 Evidence was downgraded by 1 due to serious imprecision as 95% CI crossed 1 default MID (34.9 x ± 0.5 = ±17.1)

5.4.3.5 Economic evidence

One study of potential economic relevance was found: Karniski, 1986 entitled 'A treatment program for failure to thrive: a cost/effectiveness analysis'. This study found that the price of gaining 100g of weight in a neonate was $1635 in a hospital and $308 in a specialist Medical Placement Home.

Locating direct costing sources for the interventions in the protocol is difficult as the time, number of sessions and seniority of the clinicians involved can vary greatly depending on various factors, including the severity of the weight faltering, skill and experience of the local clinical team and availability of substituting alternatives. Estimates for these values can be found in Table 49.

Table 49 – Estimates for total cost of high health economic impact non-nutritional interventions

Intervention	Delivery	Cost
Sensory intervention (SOS)	Specialist Band 6/7 OT assessment of 1-2 hours followed by 6 hour-long groups sessions of 'messy play'	Assessment Community Occupational Therapist at £44 / hour (PSSRU Unit Costs, 2015) * 1.5 hours total = £66 Group Sessions Community Occupational Therapist at £44 / hour (PSSRU Unit Costs, 2015) * 6 sessions / 10 children per session (estimate) = £26.40 Total £92.40
Video observation of mealtime	Health visitor required for 2 hours of travel and observation	Health Visitor at £76 / hour per hour of patient visiting (PSSRU Unit Costs, 2015) * 2 = £152
Oral motor therapy	Intervention is 5 minutes / day 5 days / week for 10 weeks, but contact estimated to be once per week for 30 minutes with Specialist Band 6/7 practitioner	Non-specified Band 6 Practitioner at £125 / hour per hour of patient contact (PSSRU Unit Costs, 2015) * 10 sessions * 0.5 hours per session = £625

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These interventions therefore do not have a high cost impact in an absolute sense, but relative to other interventions that might be tried first could be considered high cost. The Committee discussed how these interventions should not generally be offered without considering less time-intensive approaches first.

5.4.3.6 Clinical evidence statements

Energy intake (% RDI)

Very low quality evidence from one randomised controlled trial with 20 participants found that there is no significant difference between the behavioural parent training and the standard dietary education for this outcome.

Protein intake (% RDI)

Very low quality evidence from one randomised controlled trial with 20 participants found that there is no significant difference between behavioural parent training and the standard dietary education for this outcome.

5.4.3.7 Evidence to recommendations

5.4.3.7.1 Relative value placed on the outcomes considered

The Committee considered measurements of growth and adverse effects of any intervention to be critical outcomes for this review topic. Other outcomes (relating to both the child with faltering growth and parents or carers), such as health related quality of life, satisfaction and adherence to interventions were also considered to be important. However, none of these outcomes were reported. The Committee discussed whether energy and protein intake were good proxy outcomes but agreed that they only provide indirect information on growth.

5.4.3.7.2 Consideration of clinical benefits and harms

The Committee acknowledged that the range of interventions in the protocol would require different levels of involvement of parents or other family members and that adherence to changes in routine are potentially challenging. The possible benefits of interventions using detailed assessment methods, need to be weighed up against the impact they may have on the day-to-day life of the family and the severity of the child's presentation. The Committee therefore elected to recommend general principles of documenting feeding behaviour, rather than specific interventions that may not be appropriate for the general population of children with faltering growth (for instance applied behavioural analysis). It was discussed that interventions need to be tailored to individual circumstances to be most beneficial for the child.

The Committee discussed feeding behaviours or practices generally regarded as unhelpful and counterproductive in the long term, such as coercive feeding, and felt that guidance about this would be useful.

5.4.3.7.3 Consideration of economic benefits and harms

The one study that was reporting costs (Karniski, 1986) looked at 'Medical Placement Home' which was not an intervention in scope or in the protocol, and it is not clear that the population was in scope either. Additionally, the study was dated, based in the US and had a small sample size (n=35). For these reasons the study was not considered by the Committee to be appropriate evidence for making recommendations.

Many interventions listed in the protocol carry a minor or even zero cost. For example offering mealtime advice might take less than a minute in the course of an ordinary appointment and so is unlikely to cost more money than it generates in QALY benefits.

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Similarly some interventions such as a feeding cup or age appropriate cutlery will represent a very small one-time cost and be unlikely to cost more money than they generate in benefits. Further, some interventions such as nursery placement or Applied Behavioural Analysis may carry a cost that is not borne by the NHS or in the form of parental disutility, and so is not relevant to the perspective of a NICE Guideline.

However some interventions that the Committee planned to look at require sustained specialist intervention, and therefore are likely to cost a great deal of money. From the protocol, these interventions include:

- Sensory interventions
- Video observation of mealtime
- Oral motor therapy

The Committee discussed how the high cost and lack of evidence of the effectiveness of these interventions made it difficult to justify their inclusion in the recommendations.

The recommendations are largely focused on low or zero cost interventions, and so this is unlikely to cause a significant resource impact on the NHS.

5.4.3.7.4 Quality of evidence

The available evidence was of very low quality according to GRADE considerations and was drawn from a single well conducted randomised controlled trial that compared different interventions for faltering growth.

For the domain risk of bias, the studies were assigned ´serious risk of bias´ as generation of randomised sequence, method used to conceal the allocation and blinding of outcome assessors was not reported. No serious issues were found regarding inconsistency (heterogeneity) since only one study was included in the review.

The Committee discussed that the low number of children who participated in the study lowered their confidence in the findings particularly related to the wide confidence intervals and the generalisability of the findings to the wider population of all infants and children with faltering growth.

5.4.3.7.5 Other considerations

The Committee based the recommendations on the presented clinical evidence as well as expert opinion and consensus.

The Committee discussed and agreed that observation of meal time behaviour can be a useful assessment tool, but as there is no direct evidence regarding feeding and meal time interventions for faltering growth, recommendations cannot be made.

The Committee was aware of research into interventions to improve feeding behaviour in infants and children. However this research did not specify either the population of children with faltering growth or measure growth as an outcome.

The Committee discussed the importance of providing individualised, developmentally and culturally appropriate information about feeding and mealtime behaviour to parents and carers.

Based on their discussion, the Committee decided to recommend some principles to be discussed between an individual with relevant expertise and parents and carers. The Committee acknowledged that, based on their experience, active meal time management has a positive impact on infant and child feeding. In some situations, the parent or carer could be directed to a mealtime behavioural management programme, composed of parenting education and support and nutritional intervention.

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The importance of a number of recommendations were explored. Family meals, for instance, offer the opportunity to model normal eating behaviour and address eating habits and the outcomes of these are listed below:

- Family meals: offer the opportunity to model normal eating behaviour and address eating habits, diet, expectations and beliefs. There should not be pressure on the child to eat and the child should not be forced/ coerced into eating. Likewise, distractions should be avoided. During the meal, families should talk about something not related with food.
- A diary can be useful to keep track of what the child is eating. This can help when parents visit healthcare professionals in order for them to assess whether the child's food intake is sufficient for their activity level, age and height for instance.
- Encourage self-feeding (for instance that children try to feed themselves rather than being spoon fed by parents)
- Allow messy play and encourage the child to feel the texture of the food
- In cases of faltering growth with attentional difficulties, the developmental stage of the child should be considered when providing advice.

The Committee agreed on making recommendations to help the parents gain an understanding of feeding behaviours that can suppress appetite. In particular the group identified intake of large volumes of fluids as potentially unhelpful feeding practices because of their potential to supress appetite for meals, and recommended advising families about these.

In addition, the group also discussed the possibility of making research recommendations to support work to improve the quality of evidence for this topic in future and in particular to provide evidence on important outcomes such as growth. Due to the very limited research evidence with inconclusive findings, the Committee agreed that it was important to bridge this gap and provide evidence to inform future updates of this guideline. They highlighted that there was a particular lack of knowledge about the effectiveness of behavioural as well as oro-motor interventions in the management of faltering growth. Oro-motor interventions are used by speech and language therapists in a sub-group of children with faltering growth identified as having possible difficulties in oro-motor functions. However, this is not backed up by evidence. Therefore two research recommendations were drafted.

5.4.3.7.6 Key conclusions

The recommendations are based on the limited evidence as well as the experience and expertise of the Committee. It is acknowledged that there are steps that can be taken to promote positive feeding and mealtime behaviours. The Committee chose to highlight general principles regarding management of feeding and eating.

5.4.3.8 Recommendations

31. When there are concerns about faltering growth, discuss the following, as individually appropriate, with the infant's or child's parents or carers:

- encouraging relaxed and enjoyable feeding and mealtimes
- eating together as a family or with other children
- encouraging young children to feed themselves
- allowing young children to be 'messy' with their food
- making sure feeds and mealtimes are not too brief or too long
- setting reasonable boundaries for mealtime behaviour while avoiding punitive approaches
- avoiding coercive feeding

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- establishing regular eating schedules (for example 3 meals and 2 snacks in a day).

5.4.3.9 Research recommendations

2. What is the effectiveness of behavioural interventions compared to usual care/advice for children with faltering growth?

Why this is important

Health visitors provide behavioural interventions for faltering growth in community settings. This is carried out with the aim to optimise the Healthy Child Programme and provide support and build relationships with parents and children. Behavioural interventions are time consuming and therefore incur costs. Evidence for the specific components of behavioural interventions are scarce and if found to be effective they could have short-term and longer-term preventative results. A standardised approach to behavioural interventions could both improve clinical practice and save costs.

Table 50: Research recommendation rationale

Research question	What is the effectiveness of behavioural interventions compared to usual care/ advice for children with faltering growth?
Why this is needed	
Importance to 'patients' or the population	A consultation does not always afford the opportunity to obtain information crucial to the choice of a specific behavioural intervention nor, more generally, to engage in an individualised assessment of the needs of a child with faltering growth. This is needed when planning individualised behavioural treatment. Observation of a meal or feed, preferably at home, may provide much of the information needed to choose an appropriate behavioural intervention, such as the quality of parent-child interaction, parental responsiveness, whether there is pressure to eat and the child or infant's feeding behaviour. Such an observation could be performed as part of universal home visits by the health visiting team. Other important information that can also inform the choice of behavioural strategies includes the meal/feed setting and length, variety of foods offered or accepted and the child's development and oro-motor skills.
Relevance to NICE guidance	High priority due to potential to minimise longer term adverse outcomes.
Relevance to the NHS	Early assessment and intervention may reduce the need for referral to secondary care in children diagnosed with faltering growth. If included as part of universal home visits, it may reduce the incidence of faltering growth by identifying issues at an early stage and planning appropriate interventions. This would could be cost effective for the NHS.
National priorities	The National service framework for children, young people and maternity services aims for long-term and sustained improvement in children's health, and sets standards for health and social care services for children, young people and pregnant women. The Healthy Child Programme describes standards of care for screening and providing advice during pregnancy and the first 5 years of life. It includes broad recommendations on monitoring growth in infants and children. This research would also address healthy-eating targets (as set out in the Department of Health obesity and healthy eating policy).
Current evidence base	The guideline identified that there is a gap in the evidence base. The systematic review of this topic did not find any comparative effectiveness studies addressing this topic.

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Research question	What is the effectiveness of behavioural interventions compared to usual care/ advice for children with faltering growth?
Equality	Recognition assessment and management of faltering growth should take into consideration parents' and carers' socioeconomic, cultural, religious and ethnic environment, and potential language barriers. Access to appropriate nutrition may also differ across socioeconomic groups. Certain groups may be at greater risk of developing faltering growth, including preterm infants and children, children and infants born after intrauterine growth restriction. Those with learning-disabled parents or carers, asylum seekers, and looked-after children may find it more of a challenge to access services.
Feasibility	Could be added to the health visitors' High Impact Areas which therefore may increase uptake of the study.
Other comments	Intervention at an early stage may help prevent parental anxiety and benefit the family's future health.

Table 51: Research recommendation statements (PICO characteristics)

Criterion	Explanation
Population	Children with faltering growth
Intervention	Structured feedback, advice and care planning following mealtime observation (e.g. eating and feeding behaviour) at home
Comparator	Usual advice/care without structured feedback
Outcome	• measurements of nutritional status (weight, length or height, head circumference, mid-arm circumference) • Child Eating Behaviour Questionnaire (CEBQ) or • Behavioral Pediatrics Feeding Assessment Scale (BPFAS))
Study design	Parallel RCT, stratified by age and degree of undernutrition
Timeframe	Recruitment plus 2 year follow-up

3. What is the effectiveness of oro-motor interventions compared to usual care/ advice for children with faltering growth?

Why this is important

Difficulties in oro-motor skills can contribute to faltering growth, but not all children with faltering growth do have such difficulties. There is no evidence whether or not oro-motor interventions can help these children. If found to be effective oro-motor interventions could be used to a targeted group of children who would otherwise not necessarily benefit from other interventions for the overall population of children with faltering growth. Effective use of speech and language therapists' time for assessment and interventions related to oro-motor skills would contribute to an individualised approach to treatment and also a more targeted and therefore likely to be more cost effective use of their time.

Table 52: Research recommendation rationale

Research question	What is the effectiveness of oro-motor interventions compared to usual care/ advice for children with faltering growth?
Why this is needed	
Importance to 'patients' or the population	Not all children with faltering growth have oro-motor difficulties (e.g. difficulties with swallowing or oro-motor muscle tone). However, such difficulties can contribute to faltering growth in children and are commonly associated with medical conditions such as cleft lip and palate and neurodevelopmental disorders. When oro-motor difficulties are identified in children with Faltering Growth specialist assessment and support is required.
Relevance to NICE guidance	High priority due to lack of evidence regarding the efficacy of oro-motor interventions.

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Research question	What is the effectiveness of oro-motor interventions compared to usual care/ advice for children with faltering growth?
Relevance to the NHS	Currently the provision of oro-motor interventions is based on little evidence. Further evidence could have a significant impact on current NHS resources by focusing on those Speech and language therapy (SALT) interventions that have an evidence base.
National priorities	The National Service Framework for children, young people and maternity services aims for long-term and sustained improvement in children's health, and sets standards for health and social care services for children, young people and pregnant women. The Healthy Child Programme describes standards of care for screening and providing advice during pregnancy and the first 5 years of life. It includes broad recommendations on monitoring growth in infants and children.
Current evidence base	There is no evidence to support the view that oro-motor therapy significantly improves feeding skills in children with Faltering Growth. Similarly, there is no evidence supporting the effectiveness of oro-motor interventions in children with faltering growth.
Equality	Recognition assessment and management of faltering growth should take into consideration parents' and carers' socioeconomic, cultural, religious and ethnic environment, and potential language barriers. Access to appropriate nutrition may also differ across socioeconomic groups. Certain groups may be at greater risk of developing faltering growth, including preterm infants and children, children and infants born after intrauterine growth restriction. Those with learning-disabled parents or carers, asylum seekers, and looked-after children may find it more of a challenge to access services.
Feasibility	The techniques are non-invasive and therefore a study would be feasible.
Other comments	Potentially recruitment may be difficult because not all infants with faltering growth have oro-motor difficulties

Table 53: Research recommendation statements (PICO characteristics)

Criterion	Explanation
Population	Children with faltering growth and oro-motor difficulties: Subgroup: Infants and preschool children with Faltering Growth and developmental delay.
Intervention	A specified oro-motor intervention, focusing for example on improvements in: • facial or oral muscle tone • tongue movement • swallowing • jaw movement • oro-motor sensitivity
Comparator	• usual advice/treatment • or oro-motor interventions compared to each other
Outcome	• measurements of nutritional status (weight, length or height, head circumference, mid-arm circumference) • parental satisfaction • schedule for Oral-Motor Assessment (SOMA) (to assess oromotor functioning
Study design	Multicentre RCT study
Timeframe	5 years

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5.5 Monitoring

Growth monitoring

Review question: In children with suspected or confirmed faltering growth is an increased frequency of monitoring more effective compared to routine monitoring to improve outcome?

5.5.1 Introduction

It is presently recommended (NICE PH 11) that infants and children be measured at the same time as receiving standard immunisations. Suspicion of faltering growth, or confirmation of it, might be made as a consequence of those measurements, or as a result of measurements made at other times in response to concerns raised by parent /carer, or health care professional.

It is not presently known at what time interval subsequent measurements should be made to most effectively confirm or refute the presence of faltering growth, or to assess the benefit of any intervention offered to correct faltering growth. Early confirmation of the existence of faltering growth and the benefit of any intervention is likely to see the severity of the condition minimised and growth corrected as early as possible.

The aim of this review is to identify whether an increased frequency of monitoring is beneficial compared to routine monitoring when faltering growth is suspected or confirmed.

For full details see review protocol in Appendix D.

5.5.2 Description of clinical evidence

No relevant clinical study comparing increased frequency with routine monitoring was identified.

See Excluded studies list in Appendix H.

5.5.3 Summary of included studies

Not applicable.

5.5.4 Clinical evidence profile

Not applicable.

5.5.5 Economic evidence

No health economic evidence was identified for this topic from the overall health economic search.

A de novo health economic model was constructed to aid Committee decision making as a ‘what if’ analysis, but the data were too incomplete for the Committee to draw conclusions from it about the health economic consequences of increasing or decreasing the frequency of monitoring on the margin and consequently this model did not significantly influence Committee in making their recommendations. As it was not used as evidence to underpin recommendations, the details of the model are not provided here.

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5.5.6 Clinical evidence statements

Not applicable.

5.5.7 Evidence to recommendations

5.5.7.1 Relative value placed on the outcomes considered

The Committee agreed that the critical outcomes for decision making were: measurements of growth, health-related quality of life and parent or carer satisfaction. However, no study was identified and therefore recommendations were based on the experience and expertise of the Committee.

5.5.7.2 Considerations of clinical benefits and harms

The Committee considered the aim of growth monitoring in children with possible or definite faltering growth was to identify those who might require some form of intervention and to track their progress whether or not an intervention is employed. Recognition of worsening faltering growth, or of failure to improve, would potentially reduce the risk of worse outcomes for the child and family. The Committee recognised that if weight or length are measured too frequently, minor fluctuations in the values recorded are likely, which could lead to unwarranted anxiety for parents, carers and healthcare professionals and unnecessary investigations or interventions. Excessively frequent weighing may lead to longer term trends being missed. The Committee balanced the potential harms and benefits of growth monitoring by recommending different frequencies of measurement depending on the age of the child and the severity of faltering growth.

5.5.7.3 Consideration of economic benefits and harms

The economic benefit of growth monitoring is that it can function as an early detection and diagnosis of a problem, which may then be corrected more easily and using fewer NHS resources. The potential economic risk is twofold.

The first potential risk is that monitoring is carried out more frequently than is necessary. Since monitoring carries a direct cost to the NHS, any monitoring which is done for no substantial clinical reason, or for which the cost of the monitoring outweighs the potential benefits of new information will not be of net value to the NHS. This will happen most often if the monitoring is done very frequently, but may also happen if the metrics recorded are incomplete or of limited clinical value.

The second potential risk is more indirect – if monitoring is carried out some percentage of children will be found to have measurements/metrics which are a cause for concern, but who are otherwise entirely healthy. This could lead to unnecessary treatment being offered to these children, which carries a cost to the NHS, a potential harm to the child's quality of life and potentially risks of treatment such as hospital acquired infections depending on the kind of treatment suggested.

The Committee balanced these risks and benefits in making their recommendations, especially in making clinicians aware of the risks and allowing for considerable clinical judgement in the frequency of contact. It is the Committee's opinion that currently children may be over-monitored for no clear clinical benefit, so they expect their recommendations to reduce the amount of monitoring that takes place overall (although possibly increasing the monitoring of the very highest-risk children). Consequently the Committee made recommendations that will not lead to a substantial increase in spending of NHS resource, and should lead to a small decrease in overall resource spend.

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5.5.7.4 Quality of evidence

The literature searches identified no relevant studies comparing growth monitoring.

5.5.7.5 Other considerations

- The Committee acknowledged that it is important to record a baseline measurement of weight and length or height and head circumference for children with suspected faltering growth, to aid the interpretation of any subsequent measurements. It is important that measurements are recorded accurately and compared to appropriate reference values, so the Committee recommended that all measurements should be plotted on a current growth chart and documented in the parent held child health record.
- The period when an infant is establishing feeding is a critical time to ensure sufficient energy and fluid intake and the Committee considered monitoring at a maximum frequency of once daily may be necessary in those where there are severe concerns about weight loss in the neonatal period. Usually weighing would be carried out less frequently where the level of concern is lower.
- The Committee considered that the frequency of growth measurement should be linked to the typical rate of growth – for this reason more frequent measurements were recommended in younger children with a lower frequency after 6 and 12 months of age.
- The Committee agreed that it is not possible to measure height in non-ambulant children and that instead length should be measured and recorded.
- The Committee emphasised the importance of health care professional interpretation of all measurements and that measurement alone does not constitute an intervention.
- The Committee also recognised that exact monitoring frequencies are difficult to define and are dependent on many factors. Clinical judgment is needed to recognise when an infant or child may require a higher frequency of weighing than suggested. They therefore included the word ‘usually’ to highlight that there is some flexibility around these intervals.

In the absence of comparative studies, these recommendations were based on the clinical experience and opinion of the guideline committee.

5.5.7.6 Key conclusions

The Guideline Committee concluded that on-going measurement is essential for infants and preschool children with Faltering Growth to guide decision making and action. The Committee recognised wide variation in current practice and made recommendations based on a review of potential benefits and harms from excessive or insufficient measurement.

5.5.8 Recommendations

Weight loss in the early days of life

32. If an infant loses more than 10% of their birth weight in the early days of life, measure their weight again at appropriate intervals depending on the level of concern, but no more frequently than daily.

Faltering Growth after the early days of life

33. If there are concerns about faltering growth (see recommendation 4), measure the weight at appropriate intervals taking account of factors such as age and the level of concern, but usually no more often than:

- daily if less than 1 month old
- weekly between 1-6 months old

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- fortnightly between 6-12 months
- monthly from 1 year of age.

34. **Monitor weight if there are concerns about faltering growth (see recommendation 4), but be aware that weighing children more frequently than is needed (see recommendation 33) may add to parental anxiety (for example, minor short-term changes may cause unnecessary concern).**

35. **Be aware that weight loss is unusual except in the early days of life, and may be a reason for increased concern and more frequent weighing than is recommended (see recommendation 33).**

36. **If there are concerns about faltering growth monitor length or height at intervals, but no more often than every 3 months.**

5.5.9 Research recommendation

4. How frequently should children be measured to identify faltering growth?

Why this is important

It is important to know whether a particular frequency or schedule of measurement of infants and children would identify faltering growth at an earlier age and contribute to an earlier catch-up in weight. Present practice suggests routine measurements be taken at time of routine childhood immunisation. Is this schedule of measurement the most likely to confirm whether an infant or child has faltering growth as early as possible? It is unclear whether the present pattern of measurement is most effective for children for whom there are concerns about their growth. If an altered schedule of routine measurement was found to be identifying faltering growth at an earlier age and contribute to an early catch-up in weight, it would be necessary to consider how best to deliver such a schedule to the entire population of infants and children. Table 54: Research recommendation rationale

Research question	How frequently should children be measured to identify faltering growth?
Why this is needed	
Importance to 'patients' or the population	It is uncertain if a particular frequency of measurement of infants and children will result in earlier identification of faltering growth. Earlier identification would increase the chance of earlier assessment and intervention to rectify faltering growth. No evidence exists to indicate the optimum frequency of measurement.
Relevance to NICE guidance	Current practice as detailed in NICE PH11 which is based upon measures being made at the same time as administration of immunisation. However, it is unclear whether it is beneficial to weigh infants where concerns about faltering growth have been raised more frequently to monitor growth.
Relevance to the NHS	High. The result might indicate that measures be taken at time intervals that do not coincide with the current immunisation schedule and see considerable increase/alteration to the timing of sequential measurements of infants and children.
National priorities	The National Service Framework for children, young people and maternity services aims for long-term and sustained improvement in children's health, and sets standards for health and social care services for children, young people and pregnant women.

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Research question	How frequently should children be measured to identify faltering growth?
	The Healthy Child Programme describes standards of care for screening and providing advice during pregnancy and the first 5 years of life. It includes broad recommendations on monitoring growth in infants and children.
Current evidence base	The guideline identified that there is a gap in the evidence base. The systematic review of this topic did not find any comparative effectiveness studies addressing this topic.
Equality	Recognition assessment and management of faltering growth should take into consideration parents' and carers' socioeconomic, cultural, religious and ethnic environment, and potential language barriers. Access to appropriate nutrition may also differ across socioeconomic groups. Certain groups may be at greater risk of developing faltering growth, including preterm infants and children, children and infants born after intrauterine growth restriction. Those with learning-disabled parents or carers, asylum seekers, and looked-after children may find it more of a challenge to access services.
Feasibility	This is feasible because there already existing datasets that may allow secondary analysis
Other comments	This could be part of a secondary analysis of an existing long-term dataset such as the Avon Longitudinal Study of Parents and Children (ALSPAC)

Table 55: Research recommendation statements (PICO characteristics)

Criterion	Explanation
Population	New born infants and preschool children in high income countries with different screening regimes (followed until the age of 5 years)
Intervention	The standard regime of routine measurement of weight and length/height.
Comparator	More intensive regimes of routine measurement of weight and length/height.
Outcome	Faltering growth (including the age at which it is identified)
Study design	Prospective or retrospective cohort study
Timeframe	New born infants followed up until the age of 5 years

5.6 Referral

Review question: Does the use of specific criteria or protocols for the referral of infants and preschool children with suspected or confirmed faltering growth to secondary care improve outcome?

5.6.1 Introduction

The aim of this review is to provide guidance on criteria that may indicate that a child with faltering growth needs specialist services. Ideally, referral to secondary or tertiary care for infants and preschool children with suspected or confirmed faltering growth should avoid delays in commencing any necessary assessment, support or treatment not available in primary care. It should also prevent unnecessary interventions, costs to the NHS or distress to infant or preschool child and parents.

For full details see review protocol in Appendix D and excluded studies list in Appendix H.

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5.6.2 Description of clinical evidence

No relevant clinical study evaluating referral criteria to secondary care was identified.

5.6.3 Summary of included studies

Not applicable.

5.6.4 Clinical evidence profile

Not applicable.

5.6.5 Economic evidence

5.6.5.1 Introduction

Referral to hospital was thought to be of high economic importance. The Committee gave a variety of reasons for this, for example; the high cost of a hospital admission relative to treatment delivered in a community setting, the added burden of anxiety on parents and the risk of hospital acquired infection for the child. Because of the importance of this question and the limited evidence base, it was prioritised for de novo modelling.

The decision problem for the economic model is that – by definition – there is some trade-off clinicians must make between referring every case of faltering growth which requires hospitalisation to hospital and not referring cases which do not require hospitalisation. The schedule of these trade-offs forms an unknown ROC curve, which the model attempts to duplicate. By identifying where on this curve current practice lies, the Committee are able to estimate whether clinicians should behave in a way that is more sensitive (more referrals) or specific (fewer referrals) at the margin.

5.6.5.2 Economic literature

One paper was found of potential economic relevance; Thompson et al 'Increased length of stay and costs associated with weekend admissions for failure to thrive' (2013). This paper considered whether scheduled admissions to US hospitals during weekdays (Monday to Friday) cost more than scheduled admissions during weekends (Saturday and Sunday only). The paper found that weekend admission cost an average of $2195 (~£1907 2016 GBP) more per admission after correcting for age, gender and insurance status. Details of this study are included in Table 56

Table 56: Summary of economic characteristics of Thompson et al

Primary details	Design	Patient characteristics	Interventions	Outcome measures
Author: Thompson Year: 2013 Country: US	Type of analysis: Single-blind RCT Model structure: Retrospective observational Cycle length: N/A Time horizon:	23,332 children at 42 US hospitals from 2003-2011. Around 35% on Medicade. Subgroup analysis: None specified, but controlled for	N/A	Overall cost of admission. Average weekday admission cost around $12,000 (read of graph, no table) whereas weekend costs $14,000 for Saturday admission, $16,000 for Sunday admission.

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Primary details	Design	Patient characteristics	Interventions	Outcome measures
	Historic data relating to eight year period Perspective: US Public, Costs only Source of cost data: US hospital administrative data Currency unit: USD Cost year: 2013 Discounting: None performed – see below	demographic characteristics, number of diagnoses, number of interventions.		However many fewer weekend admissions – 978 on Saturday and 647 on Sunday compared to around 4500 every other day, suggesting possible confounder unaccounted for.

However the study could not demonstrate that the case-mix between the two groups was the same, nor that the effect would be persistent in a UK setting. Additionally the study assumed that marginal effects were static, which is to say that the – for example – the Monday and Sunday service both had spare capacity and could absorb more patients without increasing the marginal cost of treating those patients.

For these reasons the paper was thought to be useful for costing information but unlikely to be of high relevance to recommendations. Consequently a de novo cost-effectiveness model was requested by the Committee to their discussions.

5.6.5.3 Model design

Owing to very limited evidence on the long term economic impact of a referral for faltering growth, the model constructed is effectively a costing 'what if' analysis with some assumptions about quality of life included. Because of well-established weaknesses of models where significant parameters are based on assumptions, the output of the model was used by the Committee to guide their discussions rather than as a simple cost per QALY calculation as would be more typical of a health economic model.

The model is presented as a depth map, with specificity on the x-axis, sensitivity on the y-axis and total cost per true positive (i.e. correct diagnosis of faltering growth) on the z-axis. As the Committee were uncertain how sensitive and specific their referral criteria were, no more detailed analysis was planned or conducted.

5.6.5.3.1 Time horizon

The model has a one year time horizon. As assumptions around how long the quality of life burden of a false positive persist for are based on assumption rather than evidence, the time horizon of the model is altered slightly in sensitivity analysis.

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5.6.5.3.2 Discount rate

Where appropriate, a discount rate of 3.5% is applied.

5.6.5.3.3 Comparisons

The clinical evidence review did not identify any 'benchmark' tests which could give sensitivity or specificity of signs of significant faltering growth such that referral would be necessary. Consequently the model assumes that clinicians face a trade-off between referring more children at the risk of referring healthy children versus referring fewer children at the risk of failing to refer children with very severe faltering growth. The model compares every possible point on this trade-off using a depth-map design.

This assumption has poor validity as in reality there is likely to be a spectrum of un-wellness due to faltering growth, with most mistaken referrals ('false positives') occurring around the margin between an obvious need for referral and an obvious need for no referral. This suggests a typical infant who is referred as a 'false positive' will derive some benefit from having their condition looked at by an expert, even if it could have been managed adequately in the community. Additionally, there may be some conditions which look like faltering growth and which require an admission to hospital but which nevertheless are not formally characterised as faltering growth. A 'misdiagnosis' of faltering growth in this situation is of no real economic importance as the child would go to hospital anyway, but is still counted as a 'false positive' in the model. These two factors will cause the model to over-estimate the importance of specificity (avoiding false positives), but since the conclusion on the importance of specificity is so clear even under strong sensitivity analysis it was thought appropriate to leave this assumption in the model.

5.6.5.3.4 Prevalence

The prevalence of faltering growth which might require treatment in a hospital was estimated by the Committee at 2%. Olsen 2007 was identified in the clinical literature review and suggested that anthropometric measurements under the 5th centile implied 'moderate' failure to thrive, which could be expected to correlate quite closely with faltering growth severe enough to require hospitalisation. The model uses Olsen's 5% figure, but this value is varied in sensitivity analysis.

5.6.5.3.5 Costs

There are two major costs associated with a referral to secondary or tertiary services. The first is the cost of whatever surveillance or diagnostic procedure is used in the first place in order to generate the referral. The second is the cost of the referral itself.

It is assumed in this model that the diagnostic costs are extremely low. This is confirmed by the Committee, who explain that the signs of a child who needs to be referred to hospital do not require expensive diagnostic techniques to identify. Even if this were not the case, the costs associated with identifying which children need to be referred to hospital are the same across infants with and without faltering growth, so this does not generate an opportunity cost.

The cost of hospital admission could be taken from Thompson 2013, but NHS costs are usually more accurately reflected in the NHS Reference Cost document, which gives the values for a faltering growth inpatient admission listed in Table 57. As the majority of infants have a complications and comorbidities (CC) score of more than zero, an average of all CC scores is taken for the model, giving the cost used in the model as £2783. It is assumed that both false and true positives incur this cost, while false negatives incur the same cost a year later when the mistake is realised by the clinician, at a discounted cost of £2689.

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Table 57: Cost of faltering growth inpatient admissions

Currency code	Average cost	Number of admissions
Paediatric Faltering Growth (Failure to Thrive) with CC Score 2+	£3,654.21	208
Paediatric Faltering Growth (Failure to Thrive) with CC Score 1	£2,604.67	88
Paediatric Faltering Growth (Failure to Thrive) with CC Score 0	£1,382.01	118

5.6.5.3.6 Health-related quality of life

The Committee described two major sources of quality of life detriment of admission to hospital. The first is hospital acquired illnesses for the child themselves (more specifically any lasting disabilities relating to these illnesses), and the second increased anxiety for the child's parents. The Committee also argued that parents of children with faltering growth who were misdiagnosed ('false negatives') would have a greater level of increased anxiety. There is no literature on either of these sources of quality of life decrement for children with faltering growth or their parents specifically, and it was therefore thought appropriate to adopt conservative assumptions on both issues.

In keeping with other NICE Guidelines, it is assumed the utility decrement for increased anxiety is 0.07, representing a transition from 'mild' to 'moderate' anxiety on the standard EQ-5D form. This may be an overestimate of the effect as parents of children who are diagnosed with faltering growth may be very anxious to begin with. This utility decrement is multiplied by 1.85, as it is assumed that in a two-parent household both the mother and the father are equally anxious about the well-being of their child, and ONS figures indicate that around 15% of families are lone parent (https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/families/bulletins/familiesandhouseholds/2016 - note that if 15% of families are lone parent this means that only 8% of parents are in lone parent families). However the Committee noted that some parents would not be made anxious by their child going to hospital – some parents would be reassured by the healthcare system taking an interest in their children. They estimated the proportion of these parents at around 50%, but cautioned that this was an educated guess, and probably only right to the approximate order of magnitude. Consequently the average QALY decrement for a false admission to hospital was 0.065 and the average decrement for a false negative (a non-admission to hospital where one should have taken place) is 0.13.

The model assumes that there is no quality of life decrement associated with hospital acquired infections, as no value could be assigned to these by either the literature or the Committee. The model further assumes that parents of correctly diagnosed children do not become anxious. This assumption is justified because it is assumed their child will begin to get better after treatment, and so while there may be a spike in anxiety for the few days or weeks the child is at the hospital, there is no effect of the misdiagnosis 'hanging over' the family resulting in hypersensitivity to normal variation in infant behaviour (for example, a phase of picky eating).

The model uses the lower-bound of the standard NICE cost-effectiveness threshold of £20,000 as the assumed willingness to pay for an additional QALY.

5.6.5.3.7 Summary of model outcomes

To summarise the outcomes of the model, a true negative is the best outcome since it costs the NHS nothing and does not expose the child to the risks of hospital. A true positive is the

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next best outcome as it costs a significant amount of money but incurs no QALY decrement (as it is assumed that the treatment is clinically worthwhile). A false positive incurs both costs and a QALY burden, whereas a false negative incurs slightly fewer costs as the treatment is discounted into the future, but greater QALY burden. These are tabulated in Table 58. It is possible to express these QALY decrements in monetary terms by assuming that society is willing to pay £20,000 per QALY. In the table below this conversion is not performed, but elsewhere this calculation is done without any intermediate step.

Table 58: Summary of model inputs as they relate to model endpoints

	Costs	QALYs
True Positive	£2783	No change
True Negative	No change	No change
False Positive	£2783	-0.065
False Negative	£2689	-0.130

5.6.5.4 Sensitivity analysis

A number of planned sensitivity analyses were undertaken. The rationale behind the choice of these is given in Table 59. As the results are presented as a range of cost-per-diagnosis costs depending on assumptions about the sensitivity and specificity of clinicians' ability to refer accurately, one way deterministic sensitivity analysis would have been inappropriate; instead scenario analysis was undertaken to better test extreme values of the model or plausible alternate values of the key parameters.

Table 59: Planned sensitivity analyses and their justification

Analysis	Description	Justification
Base case	No variation from base case described above	For comparison
2% FG prevalence	Committee estimate of prevalence of genuinely concerning FG	Committee estimate probably more accurate than Olsen, who considered 'moderate' FG
9% FG prevalence	Committee estimate of prevalence of any FG whatsoever	As extreme value to test results
Single parent only	Assuming only one parent bares burden of hospitalisation-associated anxiety	This sensitivity analysis is in line with similar analysis is other NICE Guidelines
£30,000 / QALY threshold	Upper limit of conventional cost per QALY threshold considered by NICE	This sensitivity analysis is in line with similar analysis is other NICE Guidelines
False positive 0%	No QALY burden to parents for a false positive result	Pre-planned sensitivity analysis with Committee
False positive 25%	QALY burden to parents half as severe (25% of burden of false negative)	Pre-planned sensitivity analysis with Committee
False positive 100%	QALY burden to parents twice as severe (full burden of false negative)	Pre-planned sensitivity analysis with Committee
True positive carries anxiety cost	All true positives carry an anxiety cost equal to a false positive	Test assumption that parents of children who are faltering are already anxious and therefore anxiety not an opportunity cost in this group

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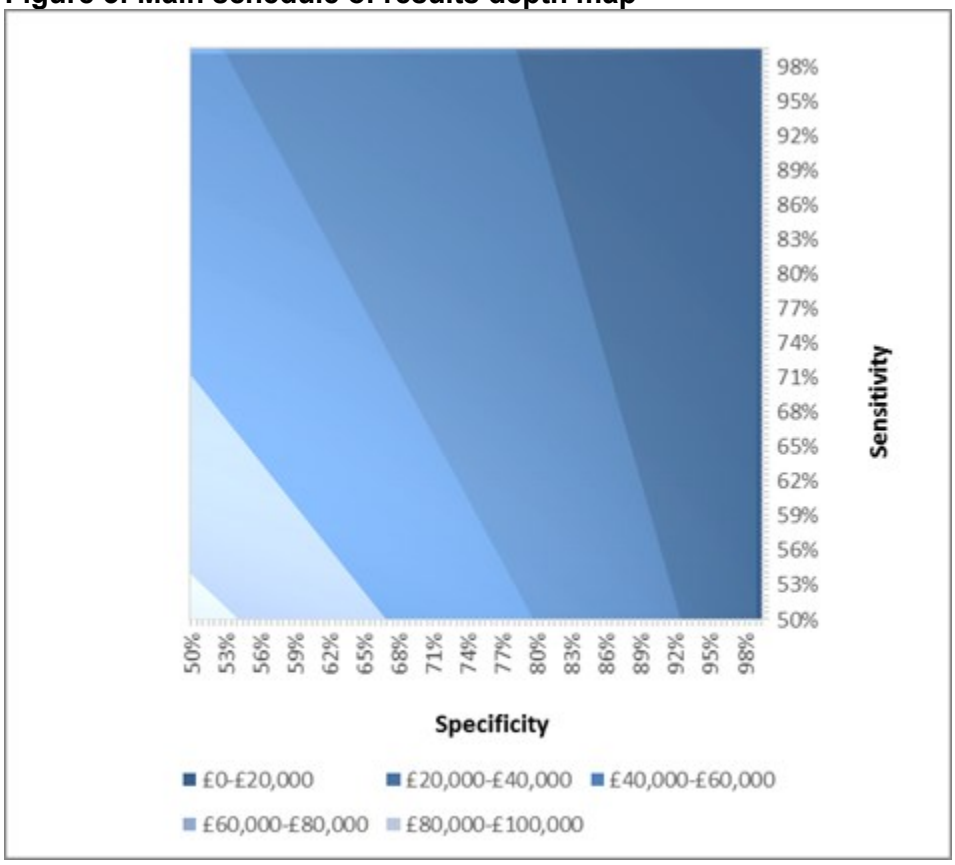
Analysis	Description	Justification
False negative carries small cost	All false negative have additional cost of £100 added to represent future GP appointments	Unlikely that FN is 'free' from the point of view of later health costs, but difficult to assign a cost in the base case as it depends on highly specific factors about the case
False negative carries moderate cost	All false negative have additional cost of £1000 added to represent future emergency admission	Unlikely that FN is 'free' from the point of view of later health costs, but difficult to assign a cost in the base case as it depends on highly specific factors about the case
False negative carries large cost	All false negative have additional cost of £5000 added to represent future long-term disability	Unlikely that FN is 'free' from the point of view of later health costs, but difficult to assign a cost in the base case as it depends on highly specific factors about the case

5.6.5.5 Results

The results of the model are shown in Figure 3 (please note that the x-axis is truncated). This shows that costs decrease as both sensitivity and specificity improve, which is to be expected as true positives and negatives are preferable to errors.

Figure 3: Main schedule of results depth map



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The key result which the Committee commented on was the relationship between specificity and sensitivity. In the base case at higher values of specificity the NHS would prefer clinicians to be one percentage point more specific even if this came at the cost of being nearly two and a half percentage points less sensitive. The Committee noted that this result had strong face validity, as they believed the importance of keeping healthy infants away from hospital was a significant issue in the management of faltering growth; they added that there was a strong case that over-referral was common.

The cost per true positive varies depending on the specificity and sensitivity of the measure used. Some example points are highlighted in Table 60. The Committee believed that the costs for the more accurate combinations were not excessive given the lifelong and important health gain associated with the proper treatment of faltering growth, and that therefore their recommendations were likely to be cost-effective

Table 60: Cost per child with faltering growth in the population - at various possible sensitivity / specificity combinations

Sensitivity	Specificity	Cost per child with faltering growth in the population
50%	50%	£86,486
50%	75%	£48,059
75%	50%	£57,223
50%	90%	£24,532
90%	50%	£47,214
75%	90%	£15,644
90%	75%	£14,450

As the Committee was unable to estimate a QALY gain from having treatment, the implicit assumption of the model is that early treatment does not affect later health outcomes. The Committee disagreed with this assumption, but understood that there was no consistent modelling approach that could overcome the problem. Consequently they used the values presented above as part of an assessment of the value of accurate diagnosis.

5.6.5.6 Sensitivity analysis

As described in Section 5.6.5.5, the important outcome to the Committee was whether any planned sensitivity analysis altered the conclusion that specificity was to be preferred to sensitivity at the margin. Consequently the metric reported for sensitivity analysis is the ratio at which sensitivity would be traded away for specificity at a point where the test was 75% sensitive and specific – that is to say the ratio at which the NHS is indifferent between more sensitivity or more specificity. Values above 2.3 indicate that specificity has become more than the base case, values below 2.3 indicate it has become less important. The critical point for the Committee was whether the ratio ever fell below one, which would indicate that sensitivity had become more important than specificity at the margin. The use of the point 75% sensitivity / 75% specificity is arbitrary, but the direction of the conclusion would not change if a different point was chosen as the relationship between the components of the model is linear. These results are displayed in Table 61.

Table 61: Results of sensitivity analysis, expressed as indifference ratio between more sensitivity and specificity

Analysis	Indifference ratio
Base case	2.33

ISBN 978-1-4731-2693-0

Analysis	Indifference ratio
2% FG prevalence	2.67
9% FG prevalence	1.97
Single parent only	2.37
£30,000 / QALY threshold	2.30
False positive 0%	2.12
False positive 25%	2.24
False positive 100%	2.45
True positive carries anxiety cost	2.33
False negative carries small cost	2.32
False negative carries moderate cost	2.24
False negative carries large cost	1.95

Having considered the sensitivity analysis, the Committee agreed it did not change the overall conclusion, and that the results of the sensitivity analysis were in line with what they would have expected.

5.6.6 Clinical evidence statements

Not applicable.

5.6.7 Evidence to recommendations

5.6.7.1 Relative value placed on the outcomes considered

The Committee considered health-related quality of life, parent or carer satisfaction, adverse effects of not being referred and hospital admission or readmission rates as the critical outcomes for these recommendation. They considered that secondary care referral may be based on measurements of growth or other primary healthcare professional concerns. However, no study was identified and recommendations were drafted based on the experience and expertise of the Committee.

5.6.7.2 Consideration of clinical benefits and harms

The Committee recognised that infants and children with signs or symptoms of an underlying condition would benefit from further investigations, diagnosis and treatment of that condition in secondary care. Children with an underlying condition may be subject to adverse effects due to not being referred, including delayed diagnosis and treatment. The Committee could not provide a comprehensive list of what possible symptoms to look for because many conditions could lead to weight loss as a by-product and it would be difficult to name them all. However, in infants and children without symptoms or signs of an underlying condition referral to secondary care may lead to unnecessary investigations (for example blood tests) or interventions that are not needed.

The Committee was also particularly concerned that infants and children who lose weight very quickly or who are severely undernourished should be referred promptly. How fast this weight loss should be and how severe this undernutrition would depend on many different factors such as age, initial weight, length and other possible contributing factors. The Committee therefore agreed that this could not be clearly defined and should be left to clinical judgement on a case by case basis.

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The Committee recognised that admission to hospital is rarely necessary and that it carries risks for both the infant or child and the parents or carers. Such risks may include infections, disruption of feeding or eating routines and raised parental anxiety.

The Committee balanced these potential harms and benefits by recommending targeted referral to secondary care for those most likely to benefit.

5.6.7.3 Consideration of economic benefits and harms

Referral to secondary care carries and increased cost, especially for conditions or investigations that require admission for prolonged periods. Thompson (2013) described above finds an average cost of around £10,000 per admission (depending on whether it was a weekday or weekend admission) although the cost in an NHS setting is likely to be closer to £2000-£3000. Consequently the healthcare system has a strong incentive to use accurate criteria to prioritise referral, if they are available.

The economic model suggests that ensuring that healthy children are not referred to secondary or tertiary care is extremely important. The Committee commented that this was their experience of managing the condition, as referrals to hospital can have a number of negative consequences that clinicians would rather avoid. The Committee also discussed how failing to refer children who needed it was an undesirable outcome, as delaying referral could lead to serious permanent disability or death. The economic model did not incorporate these outcomes as there was no robust evidence pointing to their likelihood given a missed referral. The Committee used their clinical judgement to balance the two competing rationales for more specificity and more sensitivity respectively. The Committee concluded that even despite the risks associated with a missed diagnosis the model was correct when it identified specificity as being the more important factor to consider because the number of children with faltering growth was small relative to the general population, so the harms of a false positive were multiplied across a much larger group of people.

The Committee considered the situation of a child with something sufficiently concerning that clinicians would want to admit them to hospital for treatment, but which is misdiagnosed as faltering growth by the clinician. While this might occur from time to time in clinical practice, the results of the modelling were sufficiently strong that edge cases such as this were unlikely to impact the Committee's conclusion.

Although each referral for faltering growth is potentially expensive and the absolute number of referrals per year may be relatively high, the Committee are clear that their recommendations should reduce the number of hospital referrals for faltering growth. Therefore these recommendations are likely to have a low resource impact, in the direction of saving the NHS money.

5.6.7.4 Quality of evidence

The literature searches did not identify any relevant evidence.

5.6.7.5 Other considerations

The Committee considered that although most infants and children with faltering growth could be managed in primary care it was important to set goals to monitor the success of any primary care interventions. If these goals were not met (or in the presence of sustained faltering growth) the Committee agreed that referral to secondary care was appropriate. These referral would only very rarely result in hospital admissions. Although unlikely, some children with faltering growth could have an underlying causative condition without other signs and symptoms. Not referring these children to secondary care could result in a potential harmful delay in their diagnosis and treatment. To mitigate this harm the Committee

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recommended that clinicians should think about undertaking further investigations for a child with sustained faltering growth, or if symptoms or signs emerge during follow-up.

These recommendations were based on the clinical experience and opinion of the Committee.

5.6.7.6 Key conclusions

The Committee concluded that it was important to identify those children who had the highest need or are most likely to benefit from referral. They also agreed that there should be processes in place that allows for monitoring of goals in primary care and if these are not achieved this would also be another reason for a referral to secondary care.

5.6.8 Recommendations

37. **Together with parents and carers, establish a management plan with specific goals for every infant or child where there are concerns about faltering growth. This plan could include:**
    - assessments or investigations
    - interventions
    - clinical and growth monitoring
    - when reassessment to review progress and achievement of growth goals should happen.

38. **If an infant or child with faltering growth has any of the following discuss with, or refer to, an appropriate paediatric specialist care service:**
    - symptoms or signs that may indicate an underlying disorder
    - a failure to respond to interventions delivered in a primary care setting
    - slow linear growth or unexplained short stature (see recommendation 7)
    - rapid weight loss or severe undernutrition
    - features that cause safeguarding concerns (see the NICE guideline on child maltreatment).

39. **Do not admit infants or children with faltering growth to hospital unless they are acutely unwell or there is a specific indication requiring inpatient care, such as a plan to begin tube feeding (see recommendation 29).**

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6 Organisation of care

Review question: In the management of infants and preschool children what is the most effective service delivery with regard to the configuration and working arrangements of multidisciplinary teams?

6.1 Introduction

The aim of this review is to identify the most effective service design with regards to:

- How multidisciplinary teams are organised (including the role of midwifes and health visitors)
- The level of intensity and workload of the team with regards to the management and assessment of faltering growth (e.g. how many hours per week individual healthcare professionals dedicate to this task).
- Care provided in varied settings (including primary, secondary and tertiary but excluding neonatal intensive care units).

For full details see review protocol in Appendix D. See also the study selection flow chart in Appendix F, full GRADE profiles in Appendix J, forest plots in Appendix I and exclusion list in Appendix H.

6.2 Description of clinical evidence

Three randomised controlled studies have been included in this systematic review for service configuration for children with faltering growth (Black 1995; Black 2007; Hutchenson 1997; Raynor 1999; Wright 1998). Two of these studies (Black 2007; Hutchenson 1997) are follow-up papers of the study conducted by Black 1995.

Two studies were conducted in the UK (Raynor 1999; Wright 1998), whereas the other studies have been conducted in the US.

The sample size ranged between 83 and 229 children with faltering growth; however, the definition of faltering growth varied as follows:

- Wright 1998 identified children as failing to thrive if the second weight standard deviation score showed a fall from the baseline weight at 6 weeks, after adjustment for regression to the mean using the thrive index method.
- Black 1995 (and consequently also Black 2007 and Hutchenson 1997) included children with weight for age below the fifth percentile.
- Raynor 1999 included all children with weight below the third percentile and referred to a failure to thrive clinic.

Three main comparisons of interventions were reported by the studies:

1. Structured health visitor management versus weight monitoring only (Wright 1998), where the intervention consisted of a structured health visitor management, with dietetic, paediatric, and social work input as required (a multidisciplinary group initially comprising a liaison health visitor and a research paediatrician, and a paediatric dietitian. The staff provided introductory training for health visitors in the intervention practices as well as twice yearly sessions thereafter).
2. Home intervention versus growth and nutrition clinic (Black 1995; Black 2007; Hutchenson 1997), where all children received nutrition intervention at the growth and nutrition clinic. The home intervention (HI) was based on an ecologic model with The Hawaii Early Learning Program as a curriculum. HI was scheduled weekly during 1 year and was conducted by lay-home visitors and supervised by a community health nurse. Home

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visitors asked families about their strengths, needs and priorities, and developed an individualized family service plan with specific goals and objectives. The home visitors did not weigh the children or limit their attention to dietary intake or feeding. They addressed the parent-child relationship in multiple contexts, including feeding.

3. Specialised home visit versus outpatient clinic only (Raynor 1999), where children in both groups attended the consultant led outpatient clinic. In addition, the intervention group received intensive home visiting from a specialist health visitor for a period of 1 year. During the health visiting intervention, an initial assessment was carried out by weekly visits, lasting 60-90 minutes, over a 4 to 5 week period within the home. The assessment included a semi-structured interview, observation of a mealtime, and assessment of parent-child interactions.

Given the heterogeneity of the studies in population and interventions used, it was not possible to pool the data.

The three studies covered a number of outcomes, such as growth (weight and height), cognitive development, hospital admission rate, and parents´ satisfaction with the intervention.

However, the following outcomes from the review protocol were not reported in the available evidence:

- health-related quality of life

6.3 Summary of included studies

A summary of the studies that were included in this review are presented in Table 62.

Table 62: Summary of included studies

Study	Intervention	Comparison	Population	Outcomes
Black 1995	The home intervention was scheduled weekly during 1 year and was conducted by lay-home visitors and supervised by a community health nurse. Home visitors asked families about their strengths, needs, priorities and they developed an individualized family service plan with specific goals and objectives.	Growth and nutrition clinic	Children with weight for age below the fifth percentile.	• anthropometric measurements (weight for age, weight for height, height for age) • cognitive development
Black 2007	Same as Black 1995	Same as Black 1995	Same as Black 1995	• anthropometric measurements when the child was 8 years old (weight for age, weight for

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Study	Intervention	Comparison	Population	Outcomes
				height, height for age) • cognitive development when the child was 8 years old
Hutchenson 1997	Same as Black 1995	Same as Black 1995	Children with weight for age below the fifth percentile.	• anthropometric measurements when the child was 4 years old (weight for age, weight for height, height for age) • cognitive development when the child was 4 years old
Raynor 1999	Children in both groups attended the consultant led outpatient clinic. In addition, the intervention group received intensive home visiting from a specialist health visitor for a period of 1 year. During the health visiting intervention, an initial assessment was carried out by weekly visits, lasting 60-90 minutes, over a 4 to 5 week period within the home.	Children attended the consultant led outpatient clinic.	Children with weight below the third percentile and referred to a failure to thrive clinic.	• weight • height • mental and psychomotor development • referrals to a community dietitian • admission rates • adherence
Wright 1998	The intervention consisted of a structured health visitor management, with dietetic, paediatric, and social work input as required (a multidisciplinary group initially comprising a liaison health visitor and a research paediatrician, and a paediatric dietitian. The staff	Weight monitoring.	Failing to thrive children, defined as the second weight standard deviation score showed a fall from the baseline weight at 6 weeks, after adjustment for regression to the mean using the thrive index method.	• weight • parent/carer satisfaction

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Study	Intervention	Comparison	Population	Outcomes
	provided introductory training for health visitors in the intervention practices as well as twice yearly sessions thereafter).			

6.4 Clinical evidence profile

The clinical evidence profiles for this review question are presented in Table 63, Table 64, and Table 65.

Table 63: Clinical summary for structured health visitor management compared to routine weighing only for faltering growth

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk routine weighting only	Corresponding risk Structured health visitor management			
Anthropometric measurements at home visit - Weight SD score Follow-up: 3 years	The mean anthropometric measurements at home visit - weight in the control group was -1.26 (±0.94)	The mean anthropometric measurements at home visit - weight in the intervention groups was 0.33 higher (0.01 to 0.65 higher)	-	133 (1 study)	Low[1,2]
Anthropometric measurements at home visit - Weight deficit Follow-up: 3 years	The mean anthropometric measurements at home visit - weight deficit in the control group was -0.9 (±0.85)	The mean anthropometric measurements at home visit - weight deficit in the intervention groups was 0.36 higher (0.07 to 0.65 higher)	-	133 (1 study)	Low[1,3]
Anthropometric measurements at home visit - Height SD score Follow-up: 3 years	The mean anthropometric measurements at home visit - height in the control group was	The mean anthropometric measurements at home visit - height in the intervention groups was 0.34 higher (0.03 to 0.65 higher)	-	133 (1 study)	Low[1,4]

ISBN 978-1-4731-2693-0

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk routine weighting only	Corresponding risk Structured health visitor management			
	-1.13 (±0.92)				
Anthropometric measurements at home visit - Height deficit Follow-up: 3 years	The mean anthropometric measurements at home visit - height deficit in the intervention groups was -0.58 (±0.92)	The mean anthropometric measurements at home visit - height deficit in the intervention groups was 0.3 higher (0.01 lower to 0.61 higher)	-	133 (1 study)	Low[1,5]
Weight (SD score) at last follow up SD score Follow-up: 3 years	The mean weight (SD score) at last follow up in the control group was -1.49 (±1.06)	The mean weight (SD score) at last follow up in the intervention groups was 0.33 higher (0.06 to 0.6 higher)	-	229 (1 study)	Low[1,6]
Weight deficit at last follow up Follow-up: 3 years	The mean weight deficit at last follow up in the control group was -1.17 (±0.93)	The mean weight deficit at last follow up in the intervention groups was 0.35 higher (0.11 to 0.59 higher)	-	229 (1 study)	Low[1,7]
Parents' ratings satisfaction at home interview of service received, and perceptions of child's early problems using Likert scales. Values are means (SD) - service received from the health visitor structured interviews Follow-up: 3 years	The mean parent or carer satisfaction - service received from the health visitor in the control group was 3.8 (±1.1)	The mean parent or carer satisfaction - service received from the health visitor in the intervention groups was 0.3 higher (0.05 lower to 0.65 higher)	-	134 (1 study)	Low[1,8]
Parents' ratings satisfaction at home interview of service received, and perceptions of child's early problems using Likert scales. Values	The mean parent or carer satisfaction - how often saw the heath	The mean parent or carer satisfaction - how often saw the heath visitor in the intervention groups was 0.2 higher	-	134 (1 study)	Low[1,9]

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Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk routine weighting only	Corresponding risk Structured health visitor management			
are means (SD)- how often saw the heath visitor structured interviews Follow-up: 3 years	visitor in the control group was 3.2 (±0.98)	(0.13 lower to 0.53 higher)			
Parents' ratings satisfaction at home interview of service received, and perceptions of child's early problems using Likert scales. Values are means (SD) - how did you feel about getting your child weighted? structured interviews Follow-up: 3 years	The mean parent or carer satisfaction - how did you feel about getting your child weighed? in the control group was 2.9 (±1.2)	The mean parent or carer satisfaction - how did you feel about getting your child weighed? in the intervention groups was 0.2 lower (0.68 lower to 0.28 higher)	-	134 (1 study)	Low[1,10]
Parents' ratings satisfaction at home interview of service received, and perceptions of child's early problems using Likert scales. Values are means (SD) - how would you describe your child's appetite - at 1 year? structured interviews Follow-up: 1 years	The mean parent or carer satisfaction - how would you describe your child's appetite - at 1 year? in the control groups was 2.9 (±1.9)	The mean parent or carer satisfaction - how would you describe your child's appetite - at 1 year? in the intervention groups was 0.4 lower (1.01 lower to 0.21 higher)	-	134 (1 study)	Low[1,11]
Parents' ratings satisfaction at home interview of service received, and perceptions of child's early problems using Likert scales. Values are means (SD) - how would you describe your child's appetite - at time of interview? structured interviews Follow-up: 3 years	The mean parent or carer satisfaction - how would you describe your child's appetite - at time of interview? in the control group was 2.9 (±2)	The mean parent or carer satisfaction - how would you describe your child's appetite - at time of interview? in the intervention groups was 0.5 higher (0.11 lower to 1.11 higher)	-	134 (1 study)	Low[1,12]

CI confidence interval; SD standard deviation; MID minimally important difference.
1 Evidence was downgraded by 1 due to unclear/unreported allocation concealment, unclear/unreported blinding, and unclear/unreported incomplete outcome data.

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2 Evidence was downgraded by 1 due to serious imprecision as 95%CI crossed one default MID (±0.50 x 0.94 = ±0.47)
3 Evidence was downgraded by 1 due to serious imprecision as 95%CI crossed one default MID (±0.50 x 0.85 = ± 0.425)
4 Evidence was downgraded by 1 due to serious imprecision as 95%CI crossed one default MID (±0.50 x 0.92 = ±0.46)
5 Evidence was downgraded by 1 due to serious imprecision as 95%CI crossed one default MID (±0.50 x 0.92 = ±0.47)
6 Evidence was downgraded by 1 due to serious imprecision as 95%CI crossed one default MID (±0.50 x 1.06= ±0.53)
7 Evidence was downgraded by 1 due to serious imprecision as 95%CI crossed one default MID (±0.50 x 0.93 = ±0.46)
8 Evidence was downgraded by 1 due to serious imprecision as 95%CI crossed one default MID (±0.50 x 1.1 = ±0.55)
9 Evidence was downgraded by 1 due to serious imprecision as 95%CI crossed one default MID (±0.50 x 0.98 = ± 0.49)
10 Evidence was downgraded by 1 due to serious imprecision as 95%CI crossed one default MID (±0.50 x 1.12 = ± 0.6)
11 Evidence was downgraded by 1 due to serious imprecision as 95%CI crossed one default MID (±0.50 x 1.9 = ±0.95)
12 Evidence was downgraded by 1 due to serious imprecision as 95%CI crossed one default MID (±0.50 x 2 = ±1)

Table 64: Clinical summary for specialised home visit + outpatient clinic compared to clinic only for faltering growth

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk clinic only	Corresponding risk Specialised home visit + outpatient clinic			
Weight SD score Follow-up: 1 year	The mean weight in the control group was 0.42 (±0.63)	The mean weight in the intervention groups was 0.17 higher weight SD score (0.1 lower to 0.44 higher)	-	83 (1 study)	Moderate[1]
Height (SD score) Follow-up: 1 year	The mean height in the control group was -0.2 (±0.85)	The mean height in the intervention groups was 0.13 height SD score higher (0.2 lower to 0.46 higher)	-	83 (1 study)	Moderate[2]
Mental developmental index Bayley Scales of Infant Development Follow-up: 1 year	The mean mental developmental index in the control group was 3.8 (±11.88)	The mean mental developmental index in the intervention groups was 1.6 lower (7.16 lower to 3.96 higher)	-	65 (1 study)	Moderate[3]
Psychomotor developmental index Bayley Scales of Infant Development	The mean psychomotor developmental index in the control group	The mean psychomotor developmental index in the intervention groups was	-	65 (1 study)	Moderate[4]

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Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk clinic only	Corresponding risk Specialised home visit + outpatient clinic			
Follow-up: 1 year	was 5.6 (±13.3)	2.6 higher (4.6 lower to 9.8 higher)			
Referrals to a community dietitian Follow-up: 1 year	293 per 1000	12 per 1000 (0 to 170)	RR 0.04 (0 to 0.58)	83 (1 study)	High
Admissions to hospital Follow-up: 1 year	378 per 1000	163 per 1000 (64 to 367)	RR 0.43 (0.17 to 0.97)	74 (1 study)	Moderate[5]
Adherence missed more than 3 outpatient appointment Follow-up: 1 year	378 per 1000	136 per 1000 (45 to 329)	RR 0.36 (0.12 to 0.87)	74 (1 study)	Moderate[6]

CI confidence interval, RR risk ratio, MID minimally important difference.
1 Evidence was downgraded by 1 due to serious imprecision as 95%CI crossed one default MID (±0.5 x 0.63 = ±0.315)
2 Evidence was downgraded by 1 due to serious imprecision as 95%CI crossed one default MID (±0.5 x 0.85 = ±0.425)
3 Evidence was downgraded by 1 due to serious imprecision as 95%CI crossed one default MID (±0.5 x 11.8 = ±5.94)
4 Evidence was downgraded by 1 due to serious imprecision as 95%CI crossed one default MID (±0.5 x 13.39 = ±6.69)
5 Evidence was downgraded by 1 due to serious imprecision as 95%CI crossed one default MID (0.8)
6 Evidence was downgraded by 1 due to serious imprecision as 95%CI crossed one default MID (0.8)

Table 65: Clinical summary for lay home visit + growth and nutrition clinic compared to clinic only for faltering growth

Outcomes	Illustrative comparative risks* (95% CI)		No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk clinic only	Corresponding risk Lay home visit + growth and nutrition clinic		
Weight for age - younger (< 12 months at recruitment) Follow-up: 1 year	The mean weight for age - younger (< 12 months at recruitmen	The mean weight for age - younger (< 12 months at recruitment) in the intervention groups was 0.2 weight z score lower (0.76 lower to 0.36 higher)	54 (1 study)	Low[1,2]

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	t) in the control groups was -1.1 (±1)			
Weight for age - older (> 12 months at recruitment) Follow-up: 1 year	The mean weight for age - older (> 12 months at recruitment) in the control group was -1.7 (±0.7)	The mean weight for age - older (> 12 months at recruitment) in the intervention groups was 0.1 weight z score lower (0.42 lower to 0.22 higher)	62 (1 study)	Moderate[5]
Weight for height Follow-up: 1 year	The mean weight for height in the control group was -1.5 (±1)	The mean weight for height in the intervention groups was 0.2 weight z score lower (0.51 lower to 0.11 higher)	111 (1 study)	Moderate[6]
Weight for height - younger (< 12 months at recruitment) Follow-up: 1 year	The mean weight for height - younger (< 12 months at recruitment) in the control group was -0.8 (±1.1)	The mean weight for height - younger (< 12 months at recruitment) in the intervention groups was 0.2 weight z score lower (0.87 lower to 0.47 higher)	54 (1 study)	Moderate[7]
Weight for height - older (> 12 months at recruitment) Follow-up: 1 year	The mean weight for height - older (> 12 months at recruitment) in the control group was -1.3 (±0.6)	The mean weight for height - older (> 12 months at recruitment) in the intervention groups was 0.2 weight z score lower (0.47 lower to 0.07 higher)	62 (1 study)	Moderate[8]
Weight for height Follow-up: 4 years	The mean weight for height in the control group was -1.5 (±0.8)	The mean weight for height in the intervention groups was 0.2 weight z score lower (0.52 lower to 0.12 higher)	74 (1 study)	Moderate[9]
Weight for height BMI Follow-up: 8 years	The mean weight for height in the control	The mean weight for height in the intervention groups was 1.28 higher	96 (1 study)	Moderate[10]

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	group was 15.7 (±2.28)	(0.12 lower to 2.68 higher)		
Height for age Follow-up: 1 year	The mean height for age in the control group was -1.2 (±1.1)	The mean height for age in the intervention groups was 0.4 height z score higher (0.01 lower to 0.81 higher)	111 (1 study)	Moderate[11]
Height for age - younger (< 12 months at recruitment) Follow-up: 1 year	The mean height for age - younger (< 12 months at recruitment) in the control group was -1 (±1)	The mean height for age - younger (< 12 months at recruitment) in the intervention groups was 0.2 height z score higher (0.36 lower to 0.76 higher)	54 (1 study)	Moderate[12]
Height for age - older (> 12 months at recruitment) Follow-up: 1 year	The mean height for age - older (> 12 months at recruitment) in the control group was -0.9 (±1)	The mean height for age - older (> 12 months at recruitment) in the intervention groups was 0.2 height z score higher (0.33 lower to 0.73 higher)	62 (1 study)	Moderate[13]
Height for age Follow-up: 4 years[3]	The mean height for age in the control group was -1 (±1)	The mean height for age in the intervention groups was 0.2 height z score higher (0.28 lower to 0.68 higher)	74 (1 study)	Moderate[14]
Height for age (z score) Follow-up: 8 years[4]	The mean height for age in the control group was -0.62 (±0.93)	The mean height for age in the intervention groups was 0.4 height z score higher (0 to 0.8 higher)	96 (1 study)	Moderate[15]
Cognitive development Bailey Scales of Infant Development Follow-up: 1 year	The mean cognitive development in the control group was 83.22 (±16.22)	The mean cognitive development in the intervention groups was 2.93 height z score higher (3.12 lower to 8.98 higher)	111 (1 study)	Moderate[16]

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Cognitive development - younger (< 12 months at recruitment) Bailey Scales of Infant Development Follow-up: 1 year	The mean cognitive development - younger (< 12 months at recruitment) in the control group was 86.1 (±18.7)	The mean cognitive development - younger (< 12 months at recruitment) in the intervention groups was 3.2 higher (6.45 lower to 12.85 higher)	54 (1 study)	Moderate[17]
Cognitive development - older (> 12 months at recruitment) Bailey Scales of Infant Development Follow-up: 1 year	The mean cognitive development - older (> 12 months at recruitment) in the control group was 80.8 (±15.2)	The mean cognitive development - older (> 12 months at recruitment) in the intervention groups was 1.1 higher (5.79 lower to 7.99 higher)	62 (1 study)	Moderate[18]
Cognitive development Bailey Scales of Infant Development Follow-up: 4 years[3]	The mean cognitive development in the control group was 74.81 (±14.9)	The mean cognitive development in the intervention groups was 6.39 higher (0.69 to 12.09 higher)	111 (1 study)	Moderate[19]
Cognitive development IQ Follow-up: 8 years[4]	The mean cognitive development in the control group was 78.66 (±14.8)	The mean cognitive development in the intervention groups was 2.35 lower (7.75 lower to 3.05 higher)	96 (1 study)	Moderate[20]

IQ intelligence quotient, MID minimally important difference.
1 Evidence was downgraded by 1 due to unclear incomplete outcome data.
2 Evidence was downgraded by 1 due to serious imprecision as 95% CI crossed one default MID (±0.5 x 1=± 0.5)
3 At child's age 4
4 At child's age 8
5 Evidence was downgraded by 1 due to serious imprecision as 95% CI crossed one default MID (±0.5 x 0.7 =± 0.35)
6 Evidence was downgraded by 1 due to serious imprecision as 95% CI crossed one default MID (±0.5 x 1 =± 0.5)
7 Evidence was downgraded by 1 due to serious imprecision as 95% CI crossed one default MID (±0.5 x 1.1 =± 0.55)
8 Evidence was downgraded by 1 due to serious imprecision as 95% CI crossed one default MID (±0.5 x 0.6 =± 0.3)
9 Evidence was downgraded by 1 due to serious imprecision as 95% CI crossed one default MID (±0.5 x 0.8 =± 0.4)
10 Evidence was downgraded by 1 due to serious imprecision as 95% CI crossed one default MID (±0.5 x 2.28 =± 1.14)
11 Evidence was downgraded by 1 due to serious imprecision as 95% CI crossed one default MID (±0.5 x 1.1 =± 0.55)
12 Evidence was downgraded by 1 due to serious imprecision as 95% CI crossed one default MID (±0.5 x 1 =± 0.5)

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13 Evidence was downgraded by 1 due to serious imprecision as 95% CI crossed one default MID (±0.5 x 1 =± 0.5)
14 Evidence was downgraded by 1 due to serious imprecision as 95% CI crossed one default MID (±0.5 x 1.1 =± 0.55)
15 Evidence was downgraded by 1 due to serious imprecision as 95% CI crossed one default MID (±0.5 x 0.93 =± 0.465)
16 Evidence was downgraded by 1 due to serious imprecision as 95% CI crossed one default MID (±0.5 x 16.22 =± 8.11)
17 Evidence was downgraded by 1 due to serious imprecision as 95% CI crossed one default MID (±0.5 x 18.7 =±9.35)
18 Evidence was downgraded by 1 due to serious imprecision as 95% CI crossed one default MID (±0.5 x 15.2 =± 7.6)
19 Evidence was downgraded by 1 due to serious imprecision as 95% CI crossed one default MID (±0.5 x 14.9 =± 7.45)
20 Evidence was downgraded by 1 due to serious imprecision as 95% CI crossed one default MID (±0.5 x 14.8 =± 7.4)

6.5 Economic evidence

6.5.1 Introduction

The management of faltering growth is complex, and can range from informal advice given to a parent to requiring the skilled cooperation of multiple highly experienced practitioners.

The general health economic consideration is that the more specialists a child has access to, the better their life outcomes are likely to be. This will pay off in terms of both QALYs (for example, better educational outcomes) but also in direct economic savings by preventing admissions to hospital. In principle there is value in creating a health economic model looking at every speciality mentioned in the recommendations (for example, whether a child should have access to a GP or not). In practice, such a model would not significantly help inform Committee opinion as a GP is important for the healthcare of faltering growth infants and therefore it is not necessary to review the evidence on this uncontroversial point.

However, the use of health visitors is an area of genuine clinical uncertainty and potentially high economic impact, so a model based on the provision of additional health visitors on the margin was created to help guide Committee recommendations.

6.5.2 Review of the literature

No economic evidence was found looking at the cost and effectiveness of different service delivery models.

As this question was of high importance to the Committee and could potentially carry a high resource impact, it was prioritised for de novo modelling.

6.5.3 Methods

6.5.3.1 Basic model structure

The model is a basic decision tree structure, where infants can be provided with health visitors or not and this health visitor will cause a difference in various outcomes of importance to the healthcare system, for example improving growth or maternal mental health measures. Figure 4 summarises the structure of this model. The economic question is whether the cost of a health visitor programme is outweighed by the benefits of such an intervention, which can be taken to mean whether the ICER of the two branches of the

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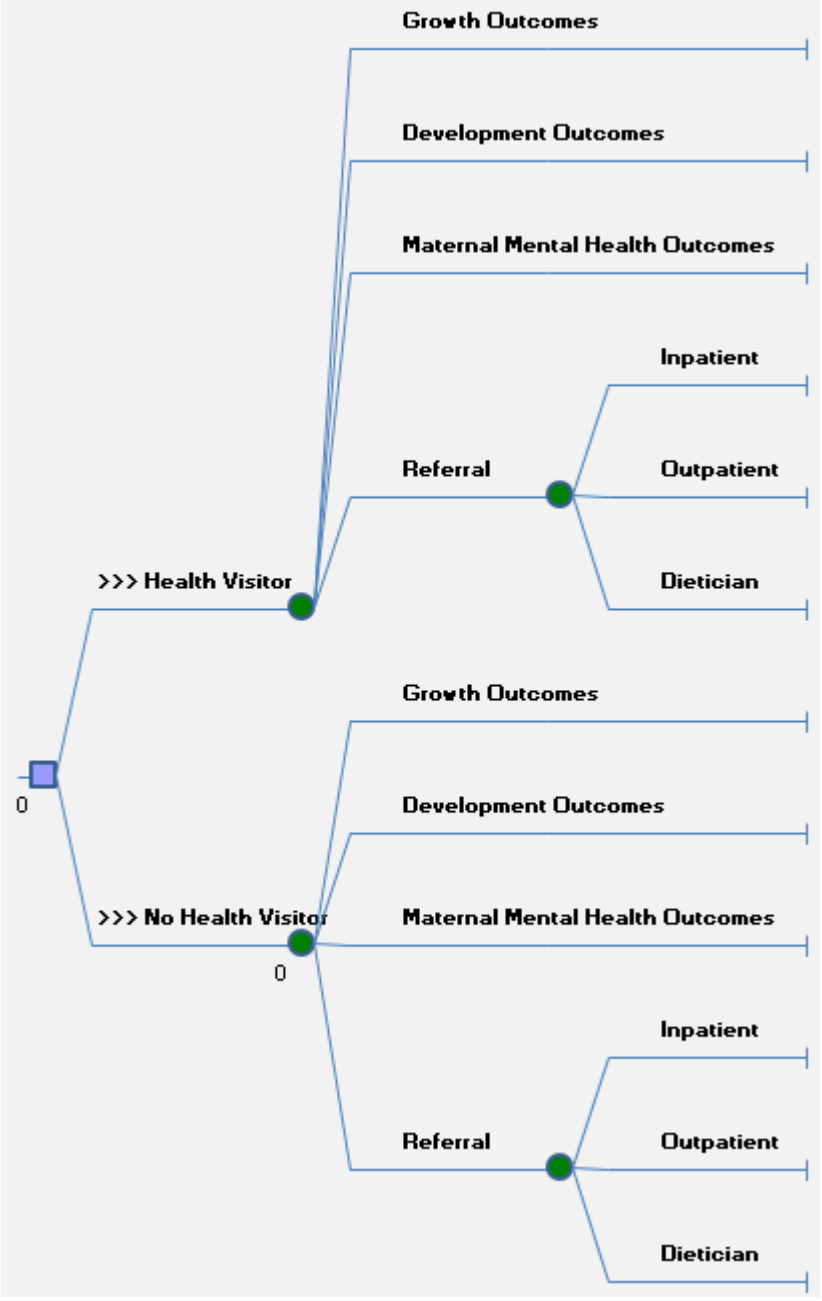
decision tree is below the NICE cost-effectiveness threshold (currently around £20,000 / QALY).

Figure 4: Schematic diagram of decision tree structure



6.5.3.2 Time horizon

The time horizon is one year, which is a limitation of the design of the model imposed by the availability of evidence. It is therefore assumed any positive benefit of the intervention ceases after one year.

6.5.3.3 Discount rate

As the time horizon is one year or less, no discount rate was specified in keeping with the NICE reference case.

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6.5.3.4 Intervention and comparison

The intervention is described in three papers identified in the evidence review, Black 2007, Raynor 1999, and Wright 1998. In addition two papers were included because they had more information about the intervention, but no new results (for example they were interim reporting of outcomes). These were Black 1995 and Hutcheson 1997 where there is disagreement about the exact method followed (and for the purposes of costing analysis), Wright 1998 is taken as the primary source, owing to having the clearest description of the methodology and sources of costs. Information about these studies is recorded in Table 66. As these papers were not health economics studies, the relevant outcome information has already been recorded in Table 62 and Table 63 and so is not duplicated here.

Table 66: Details of clinical studies with outcomes of relevant to the health economic model

Primary details	Design	Patient characteristics	Interventions	Outcome measures (of possible relevance to HE only)
Author: Black Year: 2007 Country: US	Type of analysis: Single-blind RCT Model structure: N/A Cycle length: N/A Time horizon: 8 years Perspective: US Public Source of cost data: N/A Currency unit: N/A Cost year: N/A Discounting: N/A	Children with weight for age below the fifth percentile. Primarily low income and urban setting. Recruited 1989-1992 Subgroup analysis: None specified	Intervention: Support for caregiver based on ecological theory. Support delivered by three part-time lay home visitors supervised by community nurse. One hour weekly visits scheduled but not all carried out – average of 19.2 (11.5) Control: Not specified – implied to be standard care with no health visitors	Infant growth Infant mental and motor performance Infant home and school behaviour Maternal mental health measured at baseline but not followed up
Author: Raynor Year: 1999 Country: UK	Type of analysis: Single-blind RCT Model structure: N/A Cycle length: N/A	Children with weight below the third percentile and referred to a failure to thrive clinic. Approximately representative	Interventions: Standard care plus consultant-led outpatient clinic plus 'intensive' home visitor contact with access to specialists (e.g. dietician). Unclear how	Infant growth Infant mental and motor performance Dietary analysis Infant behaviour Maternal mental health Referral to support services

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Primary details	Design	Patient characteristics	Interventions	Outcome measures (of possible relevance to HE only)
	Time horizon: 1 year Perspective: UK NHS Source of cost data: N/A Currency unit: N/A Cost year: N/A Discounting: N/A	of general UK population based on reported demographic characteristics Recruited 1994-1996 Subgroup analysis: None specified	much contact time in intervention group. Control: As standard care, but with addition of consultant-led outpatient clinic	
Author: Wright Year: 1998 Country: UK	Type of analysis: Single-blind RCT Model structure: N/A Cycle length: N/A Time horizon: 1 year Perspective: UK NHS Source of cost data: N/A Currency unit: N/A Cost year: N/A Discounting: N/A	Failing to thrive children, defined as the second weight standard deviation score showed a fall from the baseline weight at 6 weeks, after adjustment for regression to the mean using the thrive index method. Slightly poorer than UK average	Interventions: 'Parkin project' – liaison health visitor and paediatrician at 0.5 WTE and paediatric dietician at 0.05 WTE. Contact time unclear. Control: As standard care, with outcome measures recorded without knowledge of control health visitors.	Infant growth Parental assessment of performance
Author: Black Year:	As Black 2007	As Black 2007	As Black 2007	As Black 2007

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Primary details	Design	Patient characteristics	Interventions	Outcome measures (of possible relevance to HE only)
1995 Country: UK				
Author: Hutcheson Year: 1997 Country: UK	As Black 2007	As Black 2007	As Black 2007	As Black 2007

In Wright 1998, the intervention is described as being 2.5 days of health visitor and research paediatrician and 0.25 days of paediatric dietitian per week. Every family in the intervention group received a standardised health visitor assessment. Thereafter the intervention was intended to reflect real-world practice as much as possible, so input from the multidisciplinary team was only offered if deemed appropriate by the health visitor after assessment. Control families were offered frequent weighing of their child from an independent research assistant, but otherwise the study did not change the standard of care they received.

In both arms if there were concerns about the baby raised then these concerns were dealt with in a conventional manner – it is implied that this did not alter subsequent management on the trial.

6.5.3.5 Outcome modelling assumptions

6.5.3.5.1 'Incalculable' costs

The principles of health economic evaluation are to include all relevant sources of costs and benefits. Usually benefits are captured with a global quality of life (QoL) instrument such as an EQ-5D, which allows for the aggregate benefit of an intervention to be parameterised. However in paediatric interventions this is not possible – children cannot fill out an EQ-5D and therefore we cannot capture all relevant benefits in a single QoL instrument. A solution to this issue is to list all outcomes reported in the academic literature and estimate the QoL for each outcome. However, this is not possible for all outcomes; the QoL impact of some is too complex to measure in infancy and the QoL impact of others has simply not yet been measured. Consequently there are some outcomes for which we have very strong anecdotal evidence of being important to high quality of life but which it is not possible to assign a particular QALY value. These parameters are referred to throughout as being 'incalculable', and synthesis of these values was performed by the Committee in discussion rather than by the health economist through a modelling approach.

It might be possible to argue that the benefits of a paediatric intervention could be captured by offering a global quality of life instrument to children in the experiment when the reach adulthood, on the argument that we are only interested in paediatric QALYs insofar as they lead to a lasting improvement in adult QALYs. This is a hypothetical question which nonetheless would be outside the method most commonly adopted by NICE, which is to assume that we are interested in children's QALYs for their own sake (while not discounting the fact that we are also interested in those children's adulthood QALYs too). The point is

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academic, however, as the closest we have to these data is Hutchenson 1997 which follows up until early school age and not close enough to adulthood to consider taking this approach.

6.5.3.5.2 Parental Mental Health

An important outcome in the model is that of maternal mental health, accounting for a significant amount of the justification for providing the service. In many guidelines mental health is included as an assumption, for example by assuming some fraction of parents will become distressed or anxious at the news their child is ill. Generally, such an assumption would be gender-independent; that mothers and fathers would react similarly to the news and therefore the only relevant figure to consider is how many one- and two-parent families exist in the UK. However as there is a direct source for maternal mental health and no corresponding source for paternal mental health it was thought inappropriate to include an assumption that paternal mental health would be similarly affected. Nonetheless, for obvious reasons it should not be concluded from this that in a single-parent family where the father is the primary caregiver that the intervention should not be provided on the basis that there is no maternal mental health factor.

This assumption can be tested in sensitivity analysis by varying the scaling of various parameters connected to maternal mental health. For example if paternal mental health where the father is not the primary caregiver is assumed to be equally important as maternal mental health then this could be modelled as an improvement in mental health of twice the magnitude the model initially assumes (alternatively a doubling of societal willingness to pay for a maternal mental health QALY). As the sensitivity analysis shows that even a small improvement in these parameters make the intervention cost-effective paternal mental health is not modelled separately.

6.5.3.5.3 Costs

The most significant costs associated with the intervention are the salaries of the clinicians delivering the intervention and excess hospital contact days which are prevented.

Salaries are taken from the standard source of the PSSRU Unit Cost of Health and Social Care document, while the time each provider spends with a child is described in the Wright 1998 paper, based on 7.5 working hours / day, 5 working days / week and 48 working weeks / year. The values in Wright 1998 are based on a year-long intervention in a population of 95 children, and are 2.5 days / week for the health visitor and paediatrician and 0.25 days / week for the paediatric dietician. Additionally, faltering growth could lead to a referral to a community dietician and it is estimated each referral takes around 1.5 hours.

Costs of referrals are taken from the standard source of the NHS Reference Costs, with some calculations made as indicated in Table 68. The impact of the intervention on the number of such referrals is taken from Raynor 1999.

Table 67: Cost of salaries

Parameter	WTE Salary (including oncosts)	Source	Cost per child on intervention
Health visitor	£46,994	PSSRU Unit Costs 2015, 'Health Visitor'	£454.15
Research Paediatrician	£163,650	PSSRU Unit Costs 2015, 'Consultant: Medical'	£1229.85
Paediatric Dietitian	£163,650	PSSRU Unit Costs 2015, 'Consultant: Medical'	£122.99

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Parameter	WTE Salary (including oncosts)	Source	Cost per child on intervention
Community Dietitian	£37,439	PSSRU Unit Costs 2015, 'Hospital Dietitian'	N/A – Cost depends on referrals, not a fixed amount, but in base case is likely to be around £179.35

Table 68: Cost of referrals

Parameter	Cost	Source
Cost per day of admission to hospital	£634.23	NHS Reference Costs, 2015, Elective Inpatient Excess Bed Days, Paediatric Faltering Growth (Failure to Thrive) with CC Score X[a]
Cost of outpatient attendance	£223.37	NHS Reference Costs, 2015, Paediatric Outpatient[b]

(a) CC = Complications and Comorbidities. It would be usual to assume a CC score of 0, but in the case of Paediatric Faltering Growth 72% of admissions have 2+ CCs noted. Consequently the average of all CC scores was taken for this costing
(b) No specific tariff for Faltering Growth, so weighted average of every paediatric outpatient attendance

6.5.3.6 Health-related quality of life

The studies record several outcomes we can be fairly certain impact on a child's quality of life. For example, height and weight might impact on Quality of Life indirectly (through acting as a proxy for physical development) and directly (through causing depression or anxiety if the child is short for age). A large population-based study (Coste, 2012) found a negligible effect on height on QoL but this was in a population with no pre-existing reason to worry about their height and might not be representative of children with Faltering Growth. It can be inferred that height and weight are of critical importance to those in the field of faltering growth, as all included studies (Raynor 1999, Wright 1998 and Black 2007) describe these parameters, although Black 2007 could not be included as the data were presented in the wrong format.

We might expect something similar for cognitive and motor development, although it is better demonstrated that cognitive underdevelopment has a direct impact on life expectancy and so lifetime QALYs. However, the measure used (Bayley) is not cross-checked against a standard QoL instrument such as the EQ5D so it is difficult to assign a QALY value to these improvements. Black 2007 uses the standard Bayley while Raynor 1999 uses a combined mental development index and a separate physical development index. Wright 1998 uses a survey of parental experience as a proxy which could not be included in the model.

The QoL improvement which can be costed is improvements to maternal mental health. The measure in Raynor 1999 is the fraction of mothers reporting a Hospital Anxiety and Depression Scale (HADS) score <8. This is the cut-off (on the HADS) of moving from 'mild' to 'no' anxiety which – assuming the language is the same on the two instruments – would correspond to a QoL decrement of 0.07. Although this would be a standard method of assessing maternal mental health, it comes with a number of caveats; on a technical level we might be concerned that the EQ-5D tariff carries an additional QALY decrement if the move from 'no' to 'mild' anxiety represents the only less-than-perfect health state the woman experiences and on a more conceptual level we might be concerned that a move from HADS 21 to HADS 0 would be treated the same as a move from HADS 9 to HADS 7, despite the former representing an almost unbelievable transformation in the outlook of the mother (demonstrated in Figure 5).

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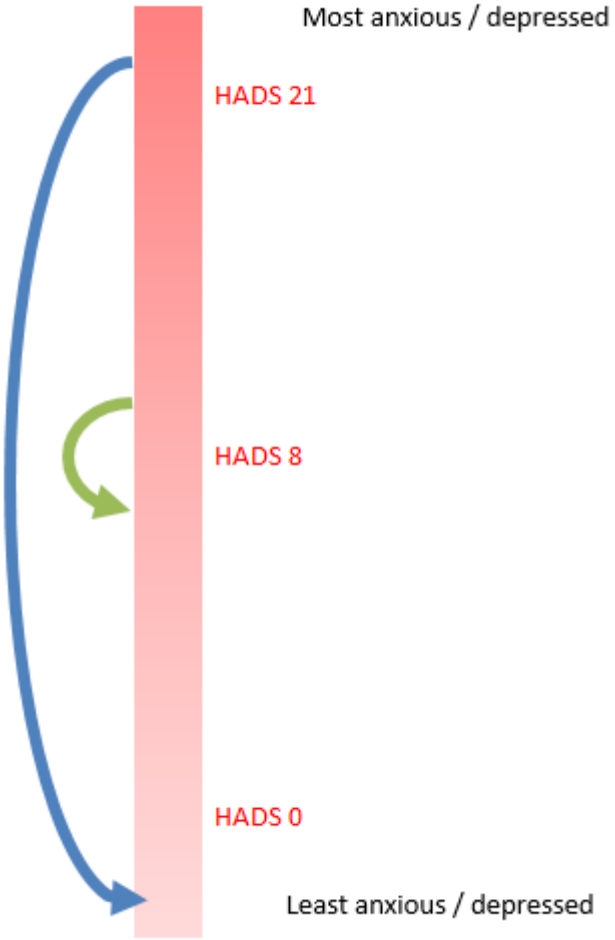
Figure 5: Diagrammatic representation of weakness of HADS <8 approach



At NICE's standard lower-bound threshold of £20,000 / QALY, this 0.07 improvement would be worth £1400.

6.5.4 Results

6.5.4.1 Main schedule of results

As described in section 6.5.3.6, these results are split into those effects which are 'calculable' and those effects which are not. By 'calculable' it is meant that it was possible to assign a specific cost or monetary benefit to the parameter, whereas by 'incalculable' it is meant that the parameter is clearly of importance to society but it was not possible to assign a specific number to use in later equations. This might be because of lack of evidence or might be because the parameter is resistant in principle to being handled in this manner; for example cognitive development might have extremely complex and nonlinear interactions in adult life with healthcare outcomes such as self-care, and therefore even in principle it is not possible to assign a particular number to this parameter. The 'incalculable' effects were considered by the Committee as part of their recommendations, but are not considered anywhere else in the health economic analysis.

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Table 69: Main Schedule of Results – 'Incalculable' Effects

Outcome	Expected Effect	Unit
Weight	0.27	Average weight for height z score (higher better)
Height	0.13	Average height for age z score (higher better)
Cognitive Development	-1.60	Average mental development index (from Bayley, higher better)
Motor Development	2.70	Average psychomotor development index (from Bayley, higher better)
Behavioural Questionnaire	-9.00	Raynor et al (1999) developed specifically for trial (lower better)
Diet	-0.02	>85% expected energy intake (lower better)

Table 70: Main schedule of results – 'Calculable' effects

Unit	Expected Effect	Unit (per 100 children / mothers)	Value at £20,000 / QALY (per 100 children / mothers)
Maternal Mental Health	40.90	Mothers scoring 8 or less on HAD scale (higher better)	£58,078
Outpatient Appointments	-5.40	Outpatient appointments (not days, lower better)	£1,207
Hospital Admissions	-94.56	Inpatient admissions (not days, lower better)	£59,973
Referred to Community Dietitian	23.10	Referrals to community dietitians (lower better)	£1,346

The net cost of the intervention is £117,815 per 100 children, or around £1200 per child. This cost is comprised of £180,698 of direct costs of the intervention (mostly staff costs) subtract £62,884 of various direct cost savings, such as fewer hospital days. Additionally, society has an interest in paying to promote god health for children and mothers. As there is an estimate of the QALY gain of improving maternal mental health we can use the formula for net monetary benefit to calculate the net effect of the intervention:

$$NMB = \Delta QALYs * £20{,}000 - \Delta Costs$$

An estimated 40.9 mothers will receive a benefit on the HAD scale worth 0.07 QALY, which is a total QALY gain of 2.9. At £20,000 / QALY society would value this QALY gain at £58,079. This indicates that the intervention costs society £597 per child and that therefore the value of the 'incalculable' effects must be worth at least this to justify recommending the intervention.

6.5.4.2 Sensitivity analysis

Figure 6 shows a 'tornado' diagram of the change to the net cost of the intervention vs a 10% change in various named parameters. A 'tornado' diagram is intended to show for which parameters uncertainty would have the biggest likelihood of altering a recommendation, with larger bars (approximately) representing more important outcomes to the cost-effectiveness of the intervention.

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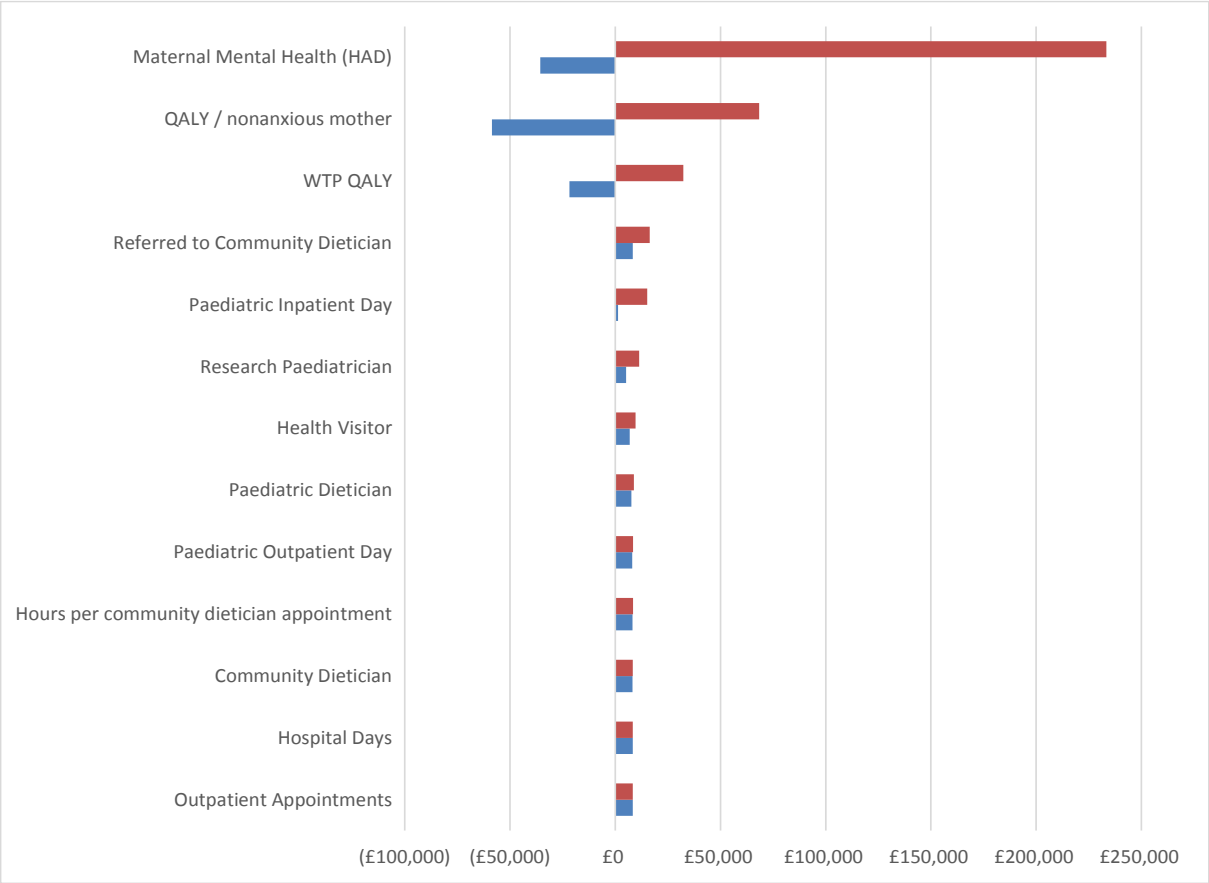
Figure 6: Tornado diagram of 10% change in named parameter vs net total cost of intervention



The interpretation of Figure 6 is that the red bar indicates the net total cost of the intervention if the parameter moves in the direction of the intervention becoming more expensive / less effective and the blue bar if the parameter moves in the direction of the intervention becoming less expensive / more effective. The x-axis is the net total cost of the intervention, such that a value of £0 indicates that society would be indifferent between the intervention and no intervention based on the effects to which it is possible to assign a cost alone. Therefore if two values lie very close together on the right-hand side of the £0 line, the interpretation is that the intervention has a net cost to society based on the calculable effects, and that even quite significant changes to this parameter are unlikely to affect this conclusion.

It is clear that even quite large changes in some parameters are unlikely to change our judgement about the cost-effectiveness of the intervention; the change in overall cost brought about by a 10% change in the cost of employing a dietitian and cost of an outpatient or hospital day are almost invisible to the naked eye.

While changes to the rate of referral to a community dietitian, the cost of a paediatric inpatient day and salary of the research paediatricians and health visitor also do not change our overall judgement as the direction of the net cost-effect of the intervention, changes to these parameters do produce swings in the results that do not quite cross the line of no effect.

Three parameters might change our view on the effectiveness of the intervention significantly. These are; the proportion of mothers scoring under 8 on the HADS index, the QALY gain per non-anxious mother and the social willingness to pay per QALY. These

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parameters are all thematically linked, in the sense of dealing with 'the effect on mothers' mental health' (WTP QALY is linked by the fact that only maternal mental health has a direct QALY impact). This is especially important as the effect of the intervention on maternal mental health is somewhat uncertain, as explained in Figure 5 in section 6.5.3.6. Note specifically that the extreme results still do not indicate that the intervention has a negative effect on mother's mental health, only that the effect it does have is so small that society is unwilling to use the money that it could save by not offering the intervention to purchase the improvement in maternal mental health.

Excluding maternal mental health entirely would indicate that the cost of the intervention per child was £1178. This would translate to requiring 0.06 QALY additionally from the 'incalculable' costs over the course of the child's lifetime. Committee opinion is that such an improvement is plausible, and so the lack of specific sensitivity around maternal mental health outcomes appears justifiable.

6.5.4.3 Conclusions

Results indicate that if the small benefits to weight, height, cognitive and motor development are worth at least £597.36, then the intervention is cost-effective at NICE's standard threshold of £20,000 / QALY. This is - based on the effects to which it is possible to assign a direct cost alone. Alternatively, if these benefits are worth 0.03 QALY over the lifetime of the child then the NHS would consider the intervention cost-effective. Judgement on whether this is likely to be the case is a matter of detailed clinical opinion, as the studies upon which this model was based did not find a statistically significant effect for any of these parameters.

The total cost of the intervention per child is £1807, though with cost savings from various sources such as reduced hospital attendance this would bring the net cost to £1178. This indicates that the change is highly likely to be considered 'high cost impact' by NICE standards if the intervention is applied in a community with no pre-existing follow-up care. However the expectation of the Committee is that most children should already be receiving a service somewhat like they describe, and the principal change in the recommendations will be standardisation. Consequently the Committee think it is unlikely that the recommendations – taken together or individually – will have a high resource impact, although they are likely to affect different healthcare geographies differently depending on local provision. As the underpinning evidence for the model is three RCTs, it is thought the justification for the recommendation is sufficient to support the recommendation even in areas where resource impact will be greater.

6.6 Clinical evidence statements

6.6.1 Structured health visitor management compared to routing monitoring only

Weight

Low quality evidence from one study with 229 participants found that there is no clinically significant difference between the two interventions for improving weight (when measured as SD score or weight deficit) in children with faltering growth.

Height

Low quality evidence from one study with 229 participants found that there is no clinically significant difference between the two interventions for improving height (when measured as SD score or weight deficit) in children with faltering growth.

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Parent or carer satisfaction

Low quality evidence from one study with 229 participants found that there is no clinically significant difference between the two groups for parent satisfaction with the intervention.

6.6.2 Specialised home visit + outpatient clinic compared to outpatient clinic only

Weight

Moderate quality evidence from one study with 83 participants found that there is no clinically significant difference between the two interventions when measuring weight at 1 year follow up.

Height

Moderate quality evidence from one study with 83 participants found that there is no clinically significant difference between the two interventions when measuring height at 1 year follow up.

Mental development

Moderate quality evidence from one study with 83 participants found that there is no clinically significant difference between the two interventions when measuring mental development at 1 year follow up.

Psychomotor development

Moderate quality evidence from one study with 83 participants found that there is no clinically significant difference between the two interventions when measuring psychomotor development at 1 year follow up.

Admissions and referrals

Moderate quality evidence from one study with 83 participants found that there is no clinically significant difference between the two interventions in both referral rates to a community dietitian and admission rates to hospital.

Adherence

Moderate quality evidence from one study with 83 participants found that there is no clinically significant difference between the two interventions when measuring adherence to intervention (measured as missing ≥ 3 outpatient appointments).

6.6.3 Lay home visit + growth and nutrition clinic compared to clinic only

Anthropometric measurements

Low to moderate quality evidence from three studies with 130 participants found that there is no clinically significant difference between the two interventions when measuring weight for age, weight for height, and height for age at 1 year follow up and when the child is 4 and 8 years old.

However, moderate evidence from one study found that there may be a clinically beneficial effect of the intervention for BMI measured when the child is 8 years old, but there is uncertainty around the estimate.

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Cognitive development

Moderate quality evidence from three studies with 130 participants found that there is no clinically significant difference between the two interventions when measuring cognitive development at 1 year follow up and when the child is 4 and 8 years old.

6.7 Evidence to recommendations

6.7.1 Relative value placed on the outcomes considered

The aim of this review is to identify the most effective service with regards to:

- How multidisciplinary teams are organised (including the role of midwives and health visitors)
- The level of intensity and workload of the team with regards to the management and assessment of faltering growth
- Care in varied settings (including primary, secondary and tertiary but excluding neonatal intensive care units)

The presented evidence covered most of the critical and important outcomes identified by the Committee, such as health related quality of life, parent or carer satisfaction, adherence to interventions, as well as growth, cognition and neurodevelopment, and admission and re-admission to hospital. The only outcome that was not reported in the evidence was adverse effects of interventions.

The Committee focused on measurement of growth, health related quality of life and parent/carer satisfaction should be the critical outcomes for decision-making since the child´s growth and parental satisfaction with treatment were crucial for a successful organisation of care.

6.7.2 Consideration of clinical benefits and harms

The Committee reviewed the evidence presented and used it together with their clinical experience and the health economic evidence to make recommendations on service configuration and service delivery for infants and children with faltering growth or where there are concerns about weight loss in the early days of life and their families.

The Committee decided that there should be a pathway that sets out the roles of healthcare professionals in primary as well as secondary care. They agreed that this pathway should be clear about routes of referral and co-ordination of specialists. Such a pathway would ensure that there is a consistent approach and that infants or children are not subjected to unnecessary tests or investigations. Good co-ordination would also ensure the smooth transition from primary to secondary care if necessary. For this to happen the Committee also felt that a lead healthcare professional should be identified who to co-ordinate care and act as the first point of contact. This was seen as an important aspect of care to promote positive relationship building between the family and healthcare staff. It was discussed that this may not be the same person when referral from primary to secondary care has taken place.

The Committee firstly agreed that assessment, support and intervention should be delivered at the community level. The potential positive effects of having a health visitor visit the home were discussed and taken into consideration. Some of the benefits that were discussed by the Committee were: visits can provide detailed observation and assessment, visits can inform tailored advice / information, visits may reduce anxiety for the parent or carer through monitoring of growth over time, and also may reduce stress and save time for the child and family. The Committee recognised the key role of anxiety reduction in the family, as this is likely to have an effect on the child’s health and emotional well-being in the long term. They

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agreed that community interventions may prevent admissions to hospital and may therefore reduce the emotional impact. The relevance of health visitors has been highlighted in a Policy Report, developed by the Royal College of Nursing (https://www.rcn.org.uk/professional-development/publications/pub-006200).

In addition, the Committee discussed the importance of multidisciplinary team working (MDT). A recommendation was made on which key professionals or skills/expertise would usually be involved. The key coordinators of this MDT would usually include someone from the midwifery team or a health visitor or the GP mainly depending on the age of the infant or child. This MDT should be able to access advice from a district level team that will include: an infant feeding specialist (who could be a health visitor or a trained person – usually with Baby Friendly Initiative accreditation), a paediatric dietitian, and a paediatrician. Although the Committee decided not to be over-prescriptive, they aimed to provide guidance on minimum expertise, and highlighted the need for training in some cases where this minimum expertise was not yet met. They agreed that the pathway of care should be specific, and the role of each of the healthcare professionals should be clear. This should take into account the needs of the individual infant or preschool child with faltering growth and the parents or carers and their circumstances.

When discussing health services at secondary care level, the Committee agreed that access to additional expertise may be needed, for example occupational therapy and psychological services and speech and language therapist (with expertise in paediatric eating and drinking). Based on the health economic model (see below), the Committee discussed that it would be cost effective to have the psychologist and occupational therapist expertise linked to secondary care. The importance of effective communication with primary care was highlighted, and the Committee agreed that routes of access to specialist services should be clear.

6.7.3 Economic considerations

There was robust evidence linking enhanced community based care to positive health outcomes in a number of areas. Some of these outcomes, such as hospital admissions and outpatient appointments, are assigned a definitive cost in conventional sources of health economic information, such as the NHS Reference Costs. Others, such as weight gain or cognitive function, are not possible to assign a cost to as evidence linking these outcomes to a specific cost base does not exist.

Of particular economic interest is the strong evidence linking enhanced care to positive maternal mental health outcomes. While the quality of life value for reducing anxiety in mothers was costed using standard quality of life measurement tools, Committee opinion is that this may be an underestimate of societal willingness to pay for this outcome, as it did not take into account paternal anxiety and did not take into account mothers who were already highly anxious being prevented from becoming more so. As maternal mental health outcomes were the key drivers of the cost effectiveness of the model the fact that these benefits are likely to be underestimated by the evidence reinforces the strength of the Committee's recommendation.

The intervention is cost-effective at £20,000 per QALY with high certainty, as economic modelling suggests that when considering the calculable effects alone the intervention is almost cost neutral, meaning that if there is a positive clinical value to the outcomes which were not costed in the model the entire intervention is likely to be cost-effective.

Different models of service delivery – especially considering factors such as frequency of service, linkages with other services and training / seniority of staff would likely have an effect on the cost of delivering the service in practice. Nevertheless, the Committee argued that – although there was high variation in current clinical practice – the models of service

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delivery implied by the recommendations were unlikely to represent so significant a departure from current practice as to imply a high resource impact.

6.7.4 Quality of evidence

Three randomised controlled trials were included in this evidence review. The quality of the evidence for this review ranged from low to high. Main risks of bias were: lack of information on the randomisation method used; concealment of allocation unreported or unclear, and lack of blinding of investigators.

The Committee also agreed that results from the Black 1995 study should be interpreted with attention to the length of the intervention that was provided. They acknowledged, based on their expertise and experience that very lengthy interventions were not effective, and that prolonged intervention has the potential to increase anxiety rather than be reassuring.

6.7.5 Other considerations

The Committee agreed that communication with parents should be optimised at all levels, and recommended having a key person as point of contact for the family. Often this key contact would be the health visitor. Furthermore the Committee observed that the family should know how to get in touch with this key person to coordinate the care that is provided for them.

Finally the Committee also discussed whether this topic should be prioritised for further research. They agreed that the evidence did not provide sufficient detail on the emotional cost of looking after a child with faltering growth and the impact that good services could have on the costs of service provisions for the NHS. Based on this uncertainty they thought that future guidance would benefit from further research in this area.

6.7.6 Key conclusions

Based on the clinical and health economic evidence, the Committee concluded that health visitors and other services in the Community should be the first line approach for the care of infants and preschool children with faltering growth. The involvement of these healthcare professionals would not only benefit the child, but would also have a positive impact on the parents or carers, for example by helping to reduce levels of anxiety. The Committee also agreed that a multidisciplinary approach, in which the health visitor in the point of contact between parents or carers and other services, should be used in the community as well as in secondary care settings. They therefore drafted guidance on the professionals and skill sets that should be represented in such teams.

6.8 Recommendations

40. **Ensure there is a pathway of care for infants and children where there are concerns about faltering growth or weight loss in the early days of life that:**
    - clearly sets out the roles of healthcare professionals in primary and secondary care settings
    - establishes and makes clear the process for referral to and co-ordination of specialist care in the pathway

41. **Provide community-based care for infants and children where there are faltering growth concerns or weight loss in the early days of life with a team (the 'primary care team') that includes, for example:**
    - a midwife

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- a health visitor
- a GP.

42. Ensure that the primary care team has access to the following healthcare professionals with expertise relevant to faltering growth:

- infant feeding specialist
- consultant paediatrician
- paediatric dietitian
- speech and language therapist with expertise in feeding and eating difficulties
- clinical psychologist
- occupational therapist.

43. Consider identifying a lead healthcare professional to coordinate care and to act as the first point of contact for parents of children with faltering growth, for example if several professionals are involved.

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7 Information and support

Review question: What is the effectiveness of information and support intervention for faltering growth?

What are the barriers and facilitators in the provision of information and support to successfully address the needs of families with an infant or preschool child in whom concerns about growth have been raised?

7.1 Introduction

Within this chapter, the Committee sought to define the effectiveness and value of providing support and information to families when their child is diagnosed with faltering growth. The committee acknowledged that provision of relevant and useful information is an important part of any clinical practice and is valued by parents and carers. It is essential that the information is clear, and given in simple, non-medical language and should be provided both verbally and in writing.

The Committee also discussed the possible areas of support that parents would value when caring for a child with faltering growth. The committee agreed that possible areas requiring support may include the difficulties of recognising faltering growth, the care plans available for management, the potential stigma of having a child with faltering growth, and the expected longer term outcomes.

7.2 Description of clinical evidence

The objective of this review was to discover what information and support interventions were effective or perceived as making a positive difference to families with infants or preschool children in whom concerns about growth had been raised. For full details see review protocol in Appendix D.

No relevant evidence was identified. For details see excluded clinical studies in Appendix H.

7.3 Summary of included studies

No study was identified for this systematic review.

7.4 Clinical evidence profile

No evidence was identified.

7.5 Economic evidence

Owing to the expected low resource impact, this question was not prioritised for health economic analysis. No economic evidence was found in the global review of the economic literature.

7.6 Clinical evidence statements

No relevant study addressing the question of this systematic review was identified.

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7.7 Evidence to recommendations

7.7.1 Relative value placed on the outcomes considered

The objective of this review was to discover what information and support interventions were effective or perceived as making a positive difference to families with infants or preschool children in whom concerns about growth had been raised. We looked for quantitative or qualitative evidence that addressed this topic. For the quantitative part of the review the Committee considered measurements of growth and health related quality of life to be critical outcomes for this review topic. Other outcomes, such as parent or carer satisfaction, adherence to information or support intervention; cognition or hospital admissions were also considered to be important.

In the qualitative review the Committee anticipated a number of themes, such as potential stigma attached to having a child with faltering growth, difficulties in the recognition of faltering growth, experience with healthcare professionals or perceptions about peer group support (direct or online). However, the Committee also acknowledged that there may be other themes that would come from the literature which would also be considered.

However, neither quantitative nor qualitative evidence was identified and the Committee based their recommendations on consensus informed by the experience and expertise of its members.

7.7.2 Consideration of clinical benefits and harms

The NICE patient experience guideline was considered as a starting point when drafting the recommendations. However, it was acknowledged that these should be extrapolated with caution, as the Patient Experience Guideline is directed to the patient experience of adults only.

There was an overall agreement that both content and method of information delivery should be predominantly reflected in the recommendations. It was acknowledged that good information provision was an important part of clinical practice and that is a particular part of care that parents value. The Committee also agreed that information is most helpful if individualised and tailored to the particular circumstances and cultural background of the parents and child (for instance taking account of the particular food choices that are made by the family). When sharing information, any potential difficulties in understanding or communication should be anticipated and taken into account. This may include, for example, cognitive or hearing impairment, or learning difficulties. Information shared in both written and verbal forms may be helpful.

It was recognised that excessively technical information or jargon can be a barrier to effective information provision.

The Committee agreed that the parents' understanding about their child's growth should be explored by health care professionals, to promote parent involvement in assessment and management. Additionally, health care professionals should ensure that families and carers are aware of where relevant, reliable information is available and how to access it.

The Committee acknowledged that parents or carers of a child with faltering growth are concerned about the child´s wellbeing and that there is an emotional impact that this has on them. Because of this, getting varying perspectives and explanations from different health care professionals can be distressing. Possible parental anxieties can also have an impact on healthcare professionals and possible training needs and support for them was also discussed. However, the Committee agreed that making specific recommendations addressing those needs of healthcare professionals was outside the remit of this guideline.

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There may be occasions through the assessment and management pathway when parents and carers need to deal with uncertainty. For this reason, making sure that parents have the correct information and feel fully supported is vital to maintaining engagement.

7.7.3 Consideration of economic benefits and harms

Information provision rarely carries a large direct economic cost, especially in conditions like faltering growth where some information is already provided and the Committee are required only to improve the accuracy and quality of that information. The principal cost of information provision is the clinical time to explain the information (and possibly the printing costs of booklets / leaflets etc.). This clinical time will be the same whether the information is of a high or low quality, so there is no economic reason to ever prefer lower-quality information to higher-quality information.

Supporting interventions can be more expensive depending on what form the support takes, especially if it involves committing clinical time to children who are faltering but otherwise healthy (i.e. on the basis of parental desire for support alone). Owing to a lack of evidence about the benefits of such interventions and in recognition of the high opportunity cost of these supportive interventions the Committee could not make strong recommendations in this area.

Good information may have indirect economic benefits. If patients feel under-informed they may use healthcare services more often as they are unsure what is 'normal' in their condition and what they should worry about. The reverse of this is also true; if patients are not well informed about what is a potentially worrying development in their condition they may neglect to see a clinician until the condition has progressed. This is especially true in the case of faltering growth where the primary patient (the child) is usually unable to articulate the state of their own condition and parents and carers must make the decision for them on the basis of the information they have been provided. In cases where the information provided encourages seeking more treatment, it is understood that if this information is of a high quality then the treatment sought should be cost-effective, and so of a net benefit to the NHS.

As information provision carries a low or zero cost to the NHS, the Committee's recommendations will not carry a high resource impact.

7.7.4 Quality of evidence

No study was identified to address the review question.

7.7.5 Other considerations

The Committee recognised the following areas as important for health professionals to discuss with parents and carers of children with faltering growth:

- Information on growth (and how to interpret a growth chart). The Committee agreed that health care professionals should inform parents and carers that monitoring growth may take time and that further tests may be required.
- Information on potential implications for future health, such as prognosis and timescale of faltering growth. Health care professionals should not be afraid of sharing this information; the Committee recognised that this topic may cause concern and anxiety in parents and carers, but should be tackled as soon as possible.
- Information on possible underlying causes of faltering growth.
- Information on available peer support, and where to access it.
- Information about how to tackle difficulties and concerns that parents and carers may be having.

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- The Committee discussed that advice on mealtime management could be part of the information provided, based on assessment of current family practices.
- The Committee also talked about some available NHS online resources that could be useful to parents, for instance: *The Eatwell Guide*: http://www.nhs.uk/Livewell/Goodfood/Pages/the-eatwell-guide.aspx; *Baby and toddler meal ideas*: http://www.nhs.uk/Conditions/pregnancy-and-baby/Pages/childrens-meal-ideas.aspx; and *Starting your baby on their first solid foods*: https://www.nhs.uk/start4life/first-foods.

Equally, exploring the concerns and the parents' understanding of the condition should be done prior to information sharing.

7.7.6 Key conclusions

Due to the lack of evidence, the recommendations are based on the experience and expertise of the Committee.

The Committee discussed that information and support provided to parents and carers and the preschool child (where possible) is central to good clinical practice. Information should be individualised to each person, taking into account their circumstances. This includes consideration of whether there are any issues that may hinder an individual understanding of information or where special support needs have to be addressed (such as learning disabilities, mental health needs or physical disabilities). The focus of the information should be on the current condition of the child, but also on prognosis and future health.

7.8 Recommendations

1. **Recognise the emotional impact that concerns about faltering growth or weight loss in the early days of life can have on parents and carers and offer them information about available:**
    - professional support
    - peer support.

2. **Follow the principles in the NICE guideline on patient experience in NHS services in relation to communication (including different formats and languages), information and shared decision-making.**

3. **Provide information on faltering growth or weight loss in the first days of life, to parents or carers that is:**
    - specific to them and their child
    - clearly explained and understandable to them
    - spoken and in writing.

4. **If there is concern about faltering growth in an infant or child or weight loss in the early days of life, discuss with the parents or carers:**
    - the reasons for the concern, and how the growth measurements are interpreted
    - any worries or issues they may have
    - any possible or likely causes or factors that may be contributing to the problem
    - the management plan (see recommendation 37).

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7.9 Research recommendation

5. What are the experiences and concerns of parents of children with faltering growth?

Why this is important

Having a child with faltering growth can be a distressing experience. Parents can feel blamed or unheard. Faltering growth happens when children are young so can have a long-term impact on the child-parent relationship. There are no studies that describe parental experiences or concerns and therefore there is a gap in the evidence. Research on this topic would help to improve understanding of the needs and concerns of parents who have children with faltering growth which will then enable healthcare professionals to better address them. Understanding the experiences, expectations and needs of parents should inform the design of effective intervention strategies that are tailored to the family.

Table 71: Research recommendation rationale

Research question	What are the experiences and concerns of parents of children with faltering growth?
Why this is needed	
Importance to 'patients' or the population	The identification of Faltering Growth in children can cause anxiety in parents. There is a limited time-frame in which this issue can be managed (childhood, before puberty and growth ends) and concerns over a child's nutrition, general health and final stature are far-reaching and can affect many other aspects of parenting. Many parents want to know possible outcomes of FG and what it will mean in the long-term, as well as what they need to do in the present with managing/monitoring their child's health.
Relevance to NICE guidance	High: There is very little evidence for how best to inform and support parents of children with Faltering Growth.
Relevance to the NHS	The relevance to the NHS is high, because improving the parental experience has the potential to improve the quality of life of the child and parents.
National priorities	The National Service Framework for children, young people and maternity services aims for long-term and sustained improvement in children's health, and sets standards for health and social care services for children, young people and pregnant women. The Healthy Child Programme describes standards of care for screening and providing advice during pregnancy and the first 5 years of life. It includes broad recommendations on monitoring growth in infants and children.
Current evidence base	The guideline identified that there is a gap in the evidence base. The systematic review of this topic did not find any comparative effectiveness or qualitative evidence addressing this topic. Currently information on this is anecdotal.
Equality	Recognition assessment and management of faltering growth should take into consideration parents' and carers' socioeconomic, cultural, religious and ethnic environment, and potential language barriers. Access to appropriate nutrition may also differ across socioeconomic groups. Certain groups may be at greater risk of developing faltering growth, including preterm infants and children, children and infants born after intrauterine growth restriction. Those with learning-disabled parents or carers, asylum seekers, and looked-after children may find it more of a challenge to access services.
Feasibility	Access to children and their families would be needed at a sensitive time. This could be managed by using practitioners known to the families, or through a network of support groups.
Other comments	Parental support was recognised as extremely important in the

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Table 72: Research recommendation statements (characteristics of this qualitative study)

Criterion	Explanation
Population	Parents of children who are identified as having faltering growth. The population of children with FG considered should be from 0-5, include both sexes and be as ethnically diverse as possible (so as to capture issues in the wider family context). Recruitment strategy should include patients in acute and community settings, and ideally be comprised of multiple centres within different regions nationally.
Phenomena of interest	Concerns, experiences and treatment expectations (both in terms of outcomes and service delivery) of parents of children with faltering growth in order to derive variables most important to this population.
Context	Support for parents whose child is identified with faltering growth.
Study design	Utilizing person centred methodology, this information can be used to construct a standardized checklist with high face validity that could be used by clinicians to optimize tailored support and intervention. The study aims to explore the factors that facilitate the management and parenting of a child with faltering growth and how best to support the parents. The semi-structure interview may have some descriptive (closed-ended) and some open-ended questions. Descriptive questions: • Who did you best want to support you in the management of your child (heath visitor, GP, peer support etc.)? • Did you feel satisfied with the monitoring? Qualitative topics (open ended questions) – these will be piloted to be developmental age appropriate and will vary according to child or parent/carer. Examples of these may be: • Describe how healthcare professional advised you on the management of the FG? • What options were you provided with? How did you feel when your child was identified with FG? A multi-phase study using person centred methodology, commencing in Phase 1 with an open survey of views and experiences of parents in four areas related to FG: 1. Parental concerns related to the FG 2. Impact of the FG on all family members 3. Desired outcomes of intervention 4. Desired aspects of service delivery Themes to be grouped and investigated in depth via focus groups and individual interview. Preliminary questionnaire based on the themes to be used in Phase 2 survey with emphasis on assessing salience across different age ranges and types of population (e.g. in terms of severity) as well as ensuring saturation of themes. Phase 3 Finalization and testing of measure in terms of acceptability and feasibility; if possible to be linked to specified preferred outcomes. Measure can be used as baseline and follow up measure at different time points as required.
Timeframe	3 years

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9 Glossary and abbreviations

9.1 Glossary of terms

Table 73: Glossary

Term	Definition
Abstract	Summary of a study, which may be published alone or as an introduction to a full scientific paper.
Arm (of a clinical study)	Subsection of individuals within a study who receive one particular intervention, for example placebo arm.
Association	Statistical relationship between 2 or more events, characteristics or other variables. The relationship may or may not be causal.
Attrition bias	Systematic differences between comparison groups for withdrawal or exclusion of participants from a study.
Available case analysis (ACA)	Analysis of data that is available for participants at the end of follow-up.
Baseline	The initial set of measurements at the beginning of a study (after run-in period where applicable) with which subsequent results are compared.
Before-and-after study	A study that investigates the effects of an intervention by measuring particular characteristics of a population both before and after taking the intervention, and assessing any change that occurs.
Bias	Influences on a study that can make the results look better or worse than they really are. Bias can occur by chance, deliberately or as a result of systematic errors in the design and execution of a study. It can also occur at different stages in the research process, for example during the collection, analysis, interpretation, publication or review of research data. For examples see Confounding factor, Performance bias, Publication bias Selection bias.
Carer (caregiver)	Someone who looks after family, partners or friends in need of help because they are ill, frail or have a disability.
Case-control study	A study to find out the cause(s) of a disease or condition. This is done by comparing a group of patients who have the disease or condition (cases) with a group of people who do not have it (controls) but who are otherwise as similar as possible (in characteristics thought to be unrelated to the causes of the disease or condition). This means the researcher can look for aspects of their lives that differ to see if they may cause the condition. Such studies are retrospective because they look back in time from the outcome to the possible causes of a disease or condition.
Case series	Report of a number of cases of a given disease, usually covering the course of the disease and the response to treatment. There is no comparison (control) group of patients.
Child	Pre-school children from 1 year of age.
Clinical audit	A systematic process for setting and monitoring standards of clinical care. Whereas ‘guidelines’ define what the best clinical practice should be, ‘audit’ investigates whether best practice is being carried out. Clinical audit can be described as a cycle or spiral. Within the cycle there are stages that follow a systematic process of establishing best practice, measuring care against specific criteria, taking action to improve care and monitoring to sustain improvement. The spiral suggests that as the process continues, each cycle aspires to a higher level of quality.
Clinical effectiveness	How well a specific test or treatment works when used in the 'real world' (for example when used by a doctor with a patient at home), rather than in a carefully controlled clinical trial. Trials that assess clinical

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Term	Definition
	effectiveness are sometimes called management trials. Clinical effectiveness is not the same as efficacy.
Clinical efficacy	The extent to which an intervention is active when studied under controlled research conditions.
Clinician	A healthcare professional who provides patient care. For example a doctor, nurse or physiotherapist.
Cochrane Review	The Cochrane Library consists of a regularly updated collection of evidence-based medicine databases including the Cochrane Database of Systematic Reviews (reviews of RCTs prepared by the Cochrane Collaboration).
Cohort study	A study with 2 or more groups of people – cohorts – with similar characteristics. One group receives a treatment, is exposed to a risk factor or has a particular symptom and the other group does not. The study follows their progress over time and records what happens.
Comorbidity	A disease or condition that someone has in addition to the health problem being studied or treated.
Concealment of allocation	The process used to ensure that the person deciding to enter a participant into an RCT does not know the comparison group into which that individual will be allocated. This is distinct from blinding and is aimed at preventing selection bias. Some attempts at concealing allocation are more prone to manipulation than others and the method of allocation concealment is used as an assessment of the quality of a trial.
Confidence interval (CI)	There is always some uncertainty in research. This is because a small group of patients is studied to predict the effects of a treatment on the wider population. The confidence interval is a way of expressing how certain we are about the findings from a study, using statistics. It gives a range of results that is likely to include the 'true' value for the population. The CI is usually stated as '95% CI', which means that the range of values has a 95 in 100 chance of including the 'true' value. For example, a study may state that “based on our sample findings, we are 95% certain that the 'true' population blood pressure is not higher than 150 and not lower than 110”. In such a case the 95% CI would be 110 to 150. A wide confidence interval indicates a lack of certainty about the true effect of the test or treatment – often because a small group of patients has been studied. A narrow confidence interval indicates a more precise estimate (for example if a large number of patients have been studied).
Confounding factor	Something that influences a study and can result in misleading findings if it is not understood or appropriately dealt with. For example, a study of heart disease may look at a group of people who exercise regularly and a group who do not exercise. If the ages of the people in the 2 groups are different, then any difference in heart disease rates between the 2 groups could be because of age rather than exercise. Therefore age is a confounding factor.
Continuous outcome	Data with a potentially infinite number of possible values within a given range. Height, weight and blood pressure are examples of continuous variables.
Control group	A group of people in a study who do not receive the treatment or test being studied. Instead, they may receive the standard treatment (sometimes called 'usual care') or a dummy treatment (placebo). The results for the control group are compared with those for a group receiving the treatment being tested. The aim is to check for any differences. Ideally, the people in the control group should be as similar as possible to those in the treatment group, to make it as easy as possible to detect any effects due to the treatment.

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Term	Definition
Cost–benefit analysis (CBA)	Cost-benefit analysis is one of the tools used to carry out an economic evaluation. The costs and benefits are measured using the same monetary units (for example UK pounds) to see whether the benefits exceed the costs.
Cost–consequence analysis (CCA)	Cost-consequence analysis is one of the tools used to carry out an economic evaluation. This compares the costs (such as treatment and hospital care) with the consequences (such as health outcomes) of a test or treatment with a suitable alternative. Unlike cost–benefit analysis or cost-effectiveness analysis, it does not attempt to summarise outcomes in a single measure (such as the quality adjusted life year) or in financial terms. Instead, outcomes are shown in their natural units (some of which may be monetary) and it is left to decision-makers to determine whether, overall, the treatment is worth carrying out.
Cost-effectiveness analysis (CEA)	Cost-effectiveness analysis is one of the tools used to carry out an economic evaluation. The benefits are expressed in non-monetary terms related to health, such as symptom-free days, heart attacks avoided, deaths avoided or life years gained (that is, the number of years by which life is extended as a result of the intervention).
Cost-effectiveness model	An explicit mathematical framework which is used to represent clinical decision problems and incorporate evidence from a variety of sources in order to estimate the costs and health outcomes.
Cost–utility analysis (CUA)	Cost–utility analysis is one of the tools used to carry out an economic evaluation. The benefits are assessed in terms of both quality and duration of life, and expressed as quality adjusted life years (QALYs). See also Utility.
COX proportional hazard model	In survival analysis, a statistical model that asserts that the effect of the study factors (for example the intervention of interest) on the hazard rate (the risk of occurrence of an event) in the study population is multiplicative and does not change over time.
Credible interval (CrI)	The Bayesian equivalent of a confidence interval.
Decision analysis	An explicit quantitative approach to decision-making under uncertainty, based on evidence from research. This evidence is translated into probabilities, and then into diagrams or decision trees which direct the clinician through a succession of possible scenarios, actions and outcomes.
Dichotomous outcomes	Outcome that can take one of 2 possible values, such as dead/alive, smoker/non-smoker, present/not present (also called binary data).
Discounting	Costs and perhaps benefits incurred today have a higher value than costs and benefits occurring in the future. Discounting health benefits reflects individual preference for benefits to be experienced in the present rather than the future. Discounting costs reflects individual preference for costs to be experienced in the future rather than the present.
Dominance	A health economics term. When comparing tests or treatments, an option that is both less effective and costs more is said to be 'dominated' by the alternative.
Drop-out	A participant who withdraws from a trial before the end.
Economic evaluation	An economic evaluation is used to assess the cost effectiveness of healthcare interventions (that is, to compare the costs and benefits of a healthcare intervention to assess whether it is worth doing). The aim of an economic evaluation is to maximise the level of benefits – health effects – relative to the resources available. It should be used to inform and support the decision-making process; it is not supposed to replace the judgement of healthcare professionals. There are several types of economic evaluation: cost–benefit analysis, cost–consequence analysis, cost-effectiveness analysis, cost-

ISBN 978-1-4731-2693-0

Term	Definition
	minimisation analysis and cost–utility analysis. They use similar methods to define and evaluate costs, but differ in the way they estimate the benefits of a particular drug, programme or intervention.
Effect (as in effect measure, treatment effect, estimate of effect, effect size)	A measure that shows the magnitude of the outcome in 1 group compared with that in a control group. For example, if the absolute risk reduction is shown to be 5% and it is the outcome of interest, the effect size is 5%. The effect size is usually tested, using statistics, to find out how likely it is that the effect is a result of the treatment and has not just happened by chance.
Effectiveness	How beneficial a test or treatment is under usual or everyday conditions.
Efficacy	How beneficial a test, treatment or public health intervention is under ideal conditions (for example in a laboratory).
Epidemiological study	The study of a disease within a population, defining its incidence and prevalence and examining the roles of external influences (for example infection, diet) and interventions.
EQ-5D (EuroQol 5 dimensions)	A standardised instrument used to measure health-related quality of life. It provides a single index value for health status.
Equivalence study	A trial designed to determine whether the response to 2 or more treatments differs by an amount that is clinically unimportant. This is usually demonstrated by showing that the true treatment difference is likely to lie between a lower and an upper equivalence level of clinically acceptable differences.
Evidence	Information on which a decision or guidance is based. Evidence is obtained from a range of sources including RCTs, observational studies, expert opinion (of clinical professionals or patients).
Exclusion criteria (clinical study)	Criteria that define who is not eligible to participate in a clinical study.
Exclusion criteria (literature review)	Explicit standards used to decide which studies should be excluded from consideration as potential sources of evidence.
Extended dominance	If Option A is both more clinically effective than Option B and has a lower cost per unit of effect when both are compared with a do-nothing alternative, then Option A is said to have extended dominance over Option B. Option A is therefore more cost effective and should be preferred, other things remaining equal.
Extrapolation	An assumption that the results of studies of a specific population will also hold true for another population with similar characteristics.
False negative	A diagnostic test result that incorrectly indicates that an individual does not have the disease of interest, when they do actually have it.
False positive	A diagnostic test result that incorrectly indicates that an individual has the disease of interest, when they actually do not have it.
Fixed-effect model	In meta-analysis, a model that calculates a pooled effect estimate using the assumption that all observed variation between studies is caused by random sample variability. Studies are assumed to estimating the same overall effect.
Follow-up	Observation over a period of time of an individual, group or initially defined population whose appropriate characteristics have been assessed in order to observe changes in health status or health-related variables.
Food or feeding aversion	Behaviours sometime observed in infants or children indicating a persistent unwillingness to eat. Such behaviours, depending on age, might including signs of distress when presented with food, spitting of food or avoiding behaviour.
Forest plot	A graphical representation of the individual results of each study included in a meta-analysis together with the combined meta-analysis result. The plot also allows readers to see the heterogeneity among the

ISBN 978-1-4731-2693-0

Term	Definition
	results of the studies. The results of individual studies are shown as squares centred on each study's point estimate. A horizontal line runs through each square to show each study's confidence interval. The overall estimate from the meta-analysis and its confidence interval are shown at the bottom, represented as a diamond. The centre of the diamond represents the pooled point estimate, and its horizontal tips represent the confidence interval.
Generalisability	The extent to which the results of a study hold true for groups that did not participate in the research.
Gold standard	A method, procedure or measurement that is widely accepted as being the best available to test for or treat a disease.
GRADE, GRADE profile	A system developed by the GRADE Working Group to address the short-comings of present grading systems in healthcare. The GRADE system uses a common, sensible and transparent approach to grading the quality of evidence. The results of applying the GRADE system to clinical trial data are displayed in a table known as a GRADE profile.
Harms	Adverse effects of an intervention.
Hazard ratio	A hazard is the rate at which events happen, so that the probability of an event happening in a short time interval is the length of time multiplied by the hazard. Although the hazard may vary with time, the assumption in proportional hazard models for survival analysis is that the hazard in one group is a constant proportion of the hazard in the other group. This proportion is the hazard ratio.
Health economics	Study or analysis of the cost of using and distributing healthcare resources.
Health-related quality of life (HRQoL)	A measure of the effects of an illness to see how it affects someone's day-to-day life.
Heterogeneity	The term is used in meta-analyses and systematic reviews to describe when the results of a test or treatment (or estimates of its effect) differ
Imprecision	Results are imprecise when studies include relatively few patients and few events and thus have wide confidence intervals around the estimate of effect.
Incidence	The incidence of a disease is the rate at which new cases occur in a population during a specified period.
Inclusion criteria (clinical study)	Specific criteria that define who is eligible to participate in a clinical study.
Inclusion criteria (literature review)	Explicit criteria used to decide which studies should be considered as potential sources of evidence.
Incremental cost	The extra cost linked to using one test or treatment rather than another. Or the additional cost of doing a test or providing a treatment more frequently.
Incremental cost effectiveness ratio (ICER)	The difference in the mean costs in the population of interest divided by the differences in the mean outcomes in the population of interest for one treatment compared with another.
Incremental net benefit (INB)	The value (usually in monetary terms) of an intervention net of its cost compared with a comparator intervention. The INB can be calculated for a given cost-effectiveness (willingness to pay) threshold. If the threshold is £20,000 per QALY gained then the INB is calculated as: (£20,000×QALYs gained) minus incremental cost.
Indirectness	The available evidence is different to the review question being addressed, in terms of population, intervention, comparison and outcome (PICO).
Infant	A baby up to 1 year of age

ISBN 978-1-4731-2693-0

Term	Definition
Intention-to-treat analysis (ITT)	An assessment of the people taking part in a clinical trial, based on the group they were initially (and randomly) allocated to. This is regardless of whether or not they dropped out, fully complied with the treatment or switched to an alternative treatment. Intention-to-treat analyses are often used to assess clinical effectiveness because they mirror actual practice: that is, not everyone complies with treatment and the treatment people receive may be changed according to how they respond to it.
Intervention	In medical terms this could be a drug treatment, surgical procedure, diagnostic or psychological therapy. Examples of public health interventions could include action to help someone to be physically active or to eat a more healthy diet.
Kappa statistic	A statistical measure of inter-rater agreement that takes into account the agreement occurring by chance
Length of stay	The total number of days a patient stays in hospital.
Licence	See Product licence.
Life years gained	Mean average years of life gained per person as a result of the intervention compared with an alternative intervention.
Likelihood ratio	The likelihood ratio combines information about the sensitivity and specificity. It tells you how much a positive or negative result changes the likelihood that a patient would have the disease. The likelihood ratio of a positive test result (LR+) is sensitivity divided by (1 minus specificity).
Linear Growth	This is the increase in length (under 2 years of age) or height (2 years or older) over time in infants and children
Loss to follow-up	Patients who have withdrawn from the clinical trial at the point of follow-up.
Markov model	A method for estimating long-term costs and effects for recurrent or chronic conditions, based on health states and the probability of transition between them within a given time period (cycle).
Mean	An average value, calculated by adding all the observations and dividing by the number of observations.
Mean difference	In meta-analysis, a method used to combine measures on continuous scales (such as weight), where the mean, standard deviation and sample size in each group are known. The weight given to the difference in means from each study (for example how much influence each study has on the overall results of the meta-analysis) is determined by the precision of its estimate of effect.
Median	The value of the observation that comes half-way when the observations are ranked in order.
Meta-analysis	A method often used in systematic reviews. Results from several studies of the same test or treatment are combined to estimate the overall effect of the treatment.
Minimal important difference (MID)	Threshold for clinical importance which represents the minimal important difference for benefit or for harm; for example the threshold at which drug A is less effective than drug B by an amount that is clinically important to patients.
Monte Carlo	A technique used to approximate the probability of certain outcomes by running multiple simulations using random variables.
Multivariate model	A statistical model for analysis of the relationship between 2 or more predictors, (independent) variables and the outcome (dependent) variable.
Net monetary benefit (NMB)	The value (usually in monetary terms) of an intervention net of its cost. The NMB can be calculated for a given cost-effectiveness (willingness to

ISBN 978-1-4731-2693-0

Term	Definition
	pay) threshold. If the threshold is £20,000 per QALY gained then the NMB is calculated as: (£20,000×QALYs gained) minus cost.
Non-inferiority trial	A trial designed to determine whether the effect of a new treatment is not worse than a standard treatment by more than a pre-specified amount. A one-sided version of an equivalence trial.
Number needed to treat (NNT)	The average number of patients who need to be treated to get a positive outcome. For example, if the NNT is 4, then 4 patients would have to be treated to ensure 1 of them gets better. The closer the NNT is to 1, the better the treatment. For example, if you give a stroke prevention drug to 20 people before 1 stroke is prevented, the number needed to treat is 20.
Observational study	Individuals or groups are observed or certain factors are measured. No attempt is made to affect the outcome. For example, an observational study of a disease or treatment would allow 'nature' or usual medical care to take its course. Changes or differences in one characteristic (for example whether or not people received a specific treatment or intervention) are studied without intervening. There is a greater risk of selection bias than in experimental studies.
Odds ratio (OR)	Odds are a way to represent how likely it is that something will happen (the probability). An odds ratio compares the probability of something in one group with the probability of the same thing in another. An odds ratio of 1 between 2 groups would show that the probability of the event (for example a person developing a disease, or a treatment working) is the same for both. An odds ratio greater than 1 means the event is more likely in the first group. An odds ratio less than 1 means that the event is less likely in the first group. Sometimes probability can be compared across more than 2 groups – in this case, one of the groups is chosen as the 'reference category' and the odds ratio is calculated for each group compared with the reference category. For example, to compare the risk of dying from lung cancer for non-smokers, occasional smokers and regular smokers, non-smokers could be used as the reference category. Odds ratios would be worked out for occasional smokers compared with non-smokers and for regular smokers compared with non-smokers. See also Confidence interval, Relative risk.
Opportunity cost	The loss of other healthcare programmes displaced by investment in or introduction of another intervention. This may be best measured by the health benefits that could have been achieved had the money been spent on the next best alternative healthcare intervention.
Oral liquid nutritional supplement	A high energy liquid feed designed for enteral use, usually selected and prescribed after specialist advice from a paediatric dietitian.
Outcome	The impact that a test, treatment, policy, programme or other intervention has on a person, group or population. Outcomes from interventions to improve the public's health could include changes in knowledge and behaviour related to health, societal changes (for example a reduction in crime rates) and a change in people's health and wellbeing or health status. In clinical terms, outcomes could include the number of patients who fully recover from an illness or the number of hospital admissions, and an improvement or deterioration in someone's health, functional ability, symptoms or situation. Researchers should decide what outcomes to measure before a study begins.
p value	The p value is a statistical measure that indicates whether or not an effect is statistically significant. For example, if a study comparing 2 treatments found that one seems more effective than the other, the p value is the probability of obtaining these results by chance. By convention, if the p value is below 0.05 (that is, there is less than a 5% probability that the results occurred by chance) it is considered that there

ISBN 978-1-4731-2693-0

Term	Definition
	probably is a real difference between treatments. If the p value is 0.001 or less (less than a 1% probability that the results occurred by chance), the result is seen as highly significant. If the p value shows that there is likely to be a difference between treatments, the confidence interval describes how big the difference in effect might be.
Performance bias	Systematic differences between intervention groups in care provided apart from the intervention being evaluated. Blinding of study participants (both the recipients and providers of care) is used to protect against performance bias.
Placebo	A fake (or dummy) treatment given to participants in the control group of a clinical trial. It is indistinguishable from the actual treatment (which is given to participants in the experimental group). The aim is to determine what effect the experimental treatment has had over and above any placebo effect caused because someone has received (or thinks they have received) care or attention.
Placebo effect	A beneficial (or adverse) effect produced by a placebo and not due to any property of the placebo itself.
Post-hoc analysis	Statistical analyses that are not specified in the trial protocol and are generally suggested by the data.
Power (statistical)	The ability to demonstrate an association when one exists. Power is related to sample size; the larger the sample size, the greater the power and the lower the risk that a possible association could be missed.
Prevalence	The prevalence of a disease is the proportion of a population that are cases at a point in time.
Primary care	Healthcare delivered outside hospitals. It includes a range of services provided by GPs, nurses, health visitors, midwives and other healthcare professionals and allied health professionals such as dentists, pharmacists and opticians.
Primary outcome	The outcome of greatest importance, usually the one in a study that the power calculation is based on.
Product licence	An authorisation from the Medicines and Healthcare Products Regulatory Agency (MHRA) to market a medicinal product.
Prognosis	A probable course or outcome of a disease. Prognostic factors are patient or disease characteristics that influence the course. Good prognosis is associated with low rate of undesirable outcomes; poor prognosis is associated with a high rate of undesirable outcomes.
Prospective study	A research study in which the health or other characteristic of participants is monitored (or 'followed up') for a period of time, with events recorded as they happen. This contrasts with retrospective studies.
Protocol (review)	A document written prior to commencing a review that details exactly how evidence to answer a review question will be obtained and synthesised. It defines in detail the population of interest, the interventions, the comparators/controls and the outcomes of interest (PICO).
Publication bias	Publication bias occurs when researchers publish the results of studies showing that a treatment works well and don't publish those showing it did not have any effect. If this happens, analysis of the published results will not give an accurate idea of how well the treatment works. This type of bias can be assessed by a funnel plot.
Quality of life	See Health-related quality of life.
Quality adjusted life year (QALY)	A measure of the state of health of a person or group in which the benefits, in terms of length of life, are adjusted to reflect the quality-of-life. One QALY is equal to 1 year of life in perfect health. QALYS are calculated by estimating the years of life remaining for a patient following

ISBN 978-1-4731-2693-0

Term	Definition
	a particular treatment or intervention and weighting each year with a quality-of-life score (on a scale of 0 to 1). It is often measured in terms of the person's ability to perform the activities of daily life, and freedom from pain and mental disturbance.
Random effect model	In meta-analysis, a model that calculates a pooled effect estimate using the assumption that each study is estimating a different true treatment effect due to real differences between studies. Observed variation in effects are therefore caused by a combination of random sample variability (within-study variation) and heterogeneity between studies (between-study variation). The overall effects is an average of the estimated true study effects.
Randomisation	Assigning participants in a research study to different groups without taking any similarities or differences between them into account. For example, it could involve using a random numbers table or a computer-generated random sequence. It means that each individual (or each group in the case of cluster randomisation) has the same chance of receiving each intervention.
Randomised controlled trial (RCT)	A study in which a number of similar people are randomly assigned to 2 (or more) groups to test a specific drug or treatment. One group (the experimental group) receives the treatment being tested, the other (the comparison or control group) receives an alternative treatment, a dummy treatment (placebo) or no treatment at all. The groups are followed up to see how effective the experimental treatment was. Outcomes are measured at specific times and any difference in response between the groups is assessed statistically. This method is also used to reduce bias.
Reference standard	The test that is considered to be the best available method to establish the presence or absence of the outcome – this may not be the one that is routinely used in practice.
Relative risk (RR)	The ratio of the risk of disease or death among those exposed to certain conditions compared with the risk for those who are not exposed to the same conditions (for example the risk of people who smoke getting lung cancer compared with the risk for people who do not smoke). If both groups face the same level of risk, the relative risk is 1. If the first group had a relative risk of 2, subjects in that group would be twice as likely to have the event happen. A relative risk of less than 1 means the outcome is less likely in the first group. Relative risk is sometimes referred to as risk ratio.
Reporting bias	See Publication bias.
Resource implication	The likely impact in terms of finance, workforce or other NHS resources.
Retrospective study	A research study that focuses on the past and present. The study examines past exposure to suspected risk factors for the disease or condition. Unlike prospective studies, it does not cover events that occur after the study group is selected.
Review question	The plan or set of steps to be followed in a study. A protocol for a systematic review describes the rationale for the review, the objectives and the methods that will be used to locate, select and critically appraise studies, and to collect and analyse data from the included studies.
Secondary care	Care provided in hospitals.
Secondary outcome	An outcome used to evaluate additional effects of the intervention deemed a priori as being less important than the primary outcomes.
Selection bias	Selection bias occurs if: • The characteristics of the people selected for a study differ from the wider population from which they have been drawn; or • There are differences between groups of participants in a study in terms of how likely they are to get better.

ISBN 978-1-4731-2693-0

Term	Definition
Sensitivity	How well a test detects the thing it is testing for. If a diagnostic test for a disease has high sensitivity, it is likely to pick up all cases of the disease in people who have it (that is, give a 'true positive' result). But if a test is too sensitive it will sometimes also give a positive result in people who don't have the disease (that is, give a 'false positive').
Sensitivity analysis	A means of representing uncertainty in the results of an analysis. Uncertainty may arise from missing data, imprecise estimates or methodological controversy. Sensitivity analysis also allows for exploring the generalisability of results to other settings. The analysis is repeated using different assumptions to examine the effect on the results. • One-way simple sensitivity analysis (univariate analysis) – each parameter is varied individually in order to isolate the consequences of each parameter on the results of the study. • Multi-way simple sensitivity analysis (scenario analysis) – 2 or more parameters are varied at the same time and the overall effect on the results is evaluated. • Threshold sensitivity analysis – the critical value of parameters above or below which the conclusions of the study will change are identified. • Probabilistic sensitivity analysis – probability distributions are assigned to the uncertain parameters and are incorporated into evaluation models based on decision analytical techniques (for example Monte Carlo simulation).
Significance (statistical)	A result is deemed statistically significant if the probability of the result occurring by chance is less than 1 in 20 ($p<0.05$).
Specificity	The proportion of true negatives that are correctly identified as such. For example, in diagnostic testing the specificity is the proportion of non-cases correctly diagnosed as non-cases. In terms of literature searching a highly specific search is generally narrow and aimed at picking up the key papers in a field and avoiding a wide range of papers. See also Sensitivity.
Spontaneous pregnancy	Pregnancy that was not assisted by reproductive treatment.
Stakeholder	An organisation with an interest in a topic on which NICE is developing a clinical guideline or piece of public health guidance. Organisations that register as stakeholders can comment on the draft scope and the draft guidance. Stakeholders may be: • manufacturers of drugs or equipment • national patient and carer organisations • NHS organisations • organisations representing healthcare professionals.
Standard deviation (SD)	A measure of the spread or dispersion of a set of observations, calculated as the average difference from the mean value in the sample.
Subgroup analysis	An analysis in which the intervention effect is evaluated in a defined subset of the participants in a trial, or in complementary subsets.
Systematic review	A review in which evidence from scientific studies has been identified, appraised and synthesised in a methodical way according to predetermined criteria. It may include a meta-analysis.
Thrive index	Measure of change in weight standard deviation over time, conditional on initial weight, to allow for regression to the mean. The thrive index compares a child's actual weight SD to their expected weight SD
Time horizon	The time span over which costs and health outcomes are considered in a decision analysis or economic evaluation.
Townsend Score	The Townsend index is a measure of material deprivation within a population. The measure incorporates four variables: employment, car ownership, home ownership and household overcrowding.

ISBN 978-1-4731-2693-0

Term	Definition
Treatment allocation	Assigning a participant to a particular arm of a trial.
True negative	A diagnostic test result that correctly indicates that an individual does not have the disease of interest when they actually do not have it.
True positive	A diagnostic test result that correctly indicates that an individual has the disease of interest when they do actually have it.
Undernutrition	This is what happens when nutrition is not sufficient. An infant or child with undernutrition may be abnormally thin, may weigh less than expected for their length or height, and if prolonged undernutrition can lead to stunting (length or height less than expected for age).
Univariate	Analysis which separately explores each variable in a data set.
Utility	In health economics, a utility is the measure of the preference or value that an individual or society places upon a particular health state. It is generally a number between 0 (representing death) and 1 (perfect health). The most widely used measure of benefit in cost-utility analysis is the quality-adjusted life year, but other measures include disability-adjusted life years (DALYs) and healthy year equivalents (HYEs).
Weight nadir	This is the lowest weight point.

9.2 Acronyms and abbreviations

Table 74: Acronyms and abbreviations

Abbreviation	Definition
ACA	Available case analysis
aHR	Adjusted hazard ratio
ALSPAC	Avon Longitudinal Study of Parents and Children
AMED	Allied and complementary medicine
aORs	Adjusted odds ratios
ARD	Absolute risk difference
aRRs	Adjusted risk ratios
BMI	Body mass index
BPFAS	Behavioral Pediatric Feeding Assessment Scale
BPT	Behavioural Parent Training
BW	Birthweight
BWL	Birthweight loss
CASP	Critical Appraisal Skills Programme
CBA	Cost- benefit analysis
CCA	Cost-consequence analysis
CCTR	Cochrane Controlled Trials Register
CDSR	Cochrane Database of Systematic reviews
CEBP	Child Eating Behaviour Questionnaire
CHQ	Child Health Questionnaire
CI	Confidence interval
CINAHL	Cumulative index of nursing and allied health literature
CrI	Credible interval
CUA	Cost utility analysis
DALYs	Disability adjusted life years
DARE	Database of Abstracts and reviews
DH	Department of Health

ISBN 978-1-4731-2693-0

Abbreviation	Definition
EF	Enriched Formula
EPDS	Edinburgh Postnatal Depression Scale
EPHPP	Effective public Health Practice Project
FG	Faltering growth
FTT	Failure to thrive
g	Gram
GCA	Gestational corrected age
GI	Gastrointestinal
GMS	Gateshead Millennium Study
GP	General practitioner
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HADS	Hospital Anxiety and Depression Scale
HCP	Healthcare professional
HI	Home intervention
HR	Hazard ratio
HRG	Healthcare resource group
HRQoL	Health-related quality of life
HTA	Health technology assessment
HYEs	Healthy year equivalents
ICER	Incremental cost-effectiveness ratios
IQ	Intellectual quotient
IQR	Interquartile range
ITT	Intention to treat
IUGR	Intrauterine growth restriction
KG	Kilogram
kJ	Kilocalorie
LETR	Linking evidence to recommendations
mEq/L	Milliequivalent per litre
MID	Minimally important difference
ml	Millimetre
MR	Means ratio
MUAC	Mid upper arm circumference
N/A	Not applicable
N/R	Non reported
NC	Not calculable
NG	Normal growth
NGA	National Guideline Alliance
NHS	National Health Service
NHS EED	NHS Economic Evaluation Database
NICE	National Institute for Health and Care Excellence
NICU	Neonatal intensive care unit
NIHR	National Institute for Health Research
NMB	Net Monetary Benefit
NMB	Net monetary benefit
NNT	Number needed to treat

ISBN 978-1-4731-2693-0

Abbreviation	Definition
NOFFT	Non organic failure to thrive
NPV	Negative predictive value
OFC	Occipital-frontal circumference
ORs	Odds ratios
OT	Occupational therapist
P	P-value
PICO	Population, intervention, comparison, outcome
PPV	Positive predictive value
PRISMA	Preferred reporting items for systematic reviews and metal-analyses
PsycINFO	Psychological information database
QALY	Quality adjusted life year
QOL	Quality of life
RCOG	Royal College of Obstetricians and Gynaecologists
RCT	Randomised controlled trial
RDI	Reference Daily intake
RR	Risk ratio/relative risk
RRs	Risk Ratios
RTFR	Response to food refusal
SD	Standard deviation
SDE	Standard Dietary Education
SE	Standard error
SGA	Small for gestational age
SMD	Standardised mean differences
SOMA	Schedule of oral-motor assessment
SOS	Sensory intervention
SRs	Systematic reviews
TF	Term (standards) Formula
UK	United Kingdom
USA	United States of America
UTI	Urinary tract infection
VAS	Visual Analogue Scale
VLBW	Very low birthweight
WHO	World Health Organization
Wk	Weeks
WTP	Willingness to pay

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