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[Intervention Review]

Enteral tube feeding for cystic fibrosis

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ABSTRACT

Background

Enteral tube feeding is routinely used in many cystic fibrosis centres when oral dietary and supplement intake has failed to achieve an adequate nutritional status. The use of this method of feeding is assessed on an individual basis taking into consideration the patients age and clinical status. This is a final update of a previously published review.

Objectives

To examine the evidence that in people with cystic fibrosis, supplemental enteral tube feeding improves nutritional status, respiratory function, and quality of life without significant adverse effects.

Search methods

We searched the Cochrane Cystic Fibrosis and Genetic Disorders Group Trials Register which comprises references identified from comprehensive electronic database searches and handsearches of relevant journals and abstract books of conference proceedings. We also contacted the companies that market enteral feeds and reviewed their databases.

Date of the most recent search of the Group's Cystic Fibrosis Trials Register: 10 July 2019.

Date of the most recent hand search of PubMed: 26 October 2018.

Selection criteria

All randomised controlled trials comparing supplemental enteral tube feeding for one month or longer with no specific intervention in people with cystic fibrosis.

Data collection and analysis

The searches identified 44 trials; however, none were eligible for inclusion in this review.

Main results

There are no trials included in this review.

Authors' conclusions

Supplemental enteral tube feeding is widely used throughout the world to improve nutritional status in people with cystic fibrosis. The methods mostly used, nasogastric or gastrostomy feeding, are expensive and may have a negative effect on self-esteem and body image. Reported use of enteral tube feeding suggests that it results in nutritional and respiratory improvement; but, efficacy has not been fully

assessed by randomised controlled trials. It is acknowledged, however, that performing a randomised controlled trial would be difficult due to the ethics of withholding an intervention in a group of people whose nutritional status necessitates it.

PLAIN LANGUAGE SUMMARY

Tube feeding (mainly via the nose into the stomach or directly into the stomach) in people with cystic fibrosis

Review question

We planned to review the evidence about the effects of tube feeding (via either the nose or the stomach) in people with cystic fibrosis.

Background

Cystic fibrosis is an inherited condition which causes damage to the lungs and pancreas (an organ needed to produce chemicals that help to digest food). People with cystic fibrosis often need more calories in order to achieve a good nutritional status because their condition means food is not absorbed well and they burn more energy at rest and when breathing than people who don't have cystic fibrosis. They also often have poor appetites. Supplements are often given via a tube which is either placed through the nose into the stomach (nasogastric feeding) or directly into the stomach (gastrostomy feeding)), often overnight but sometimes during the day too. This type of feeding helps to improve weight gain, nutritional status, lung function and may improve quality of life. This is important as it is known that in cystic fibrosis nutritional status is closely linked to lung function. However, tube feeding is expensive and may also impact on self-esteem and body image. Tubes through the nose may also become dislodged by coughing. Tube feeding may also cause nausea, vomiting and diarrhoea, but these issues are usually resolved by either changing the type of feed, the rate of feeding or the way pancreatic enzymes are given. This is a final update of a previously published review.

Search date

We last searched for evidence on: 22 October 2018.

Study characteristics

We found 44 trials in our searches, but none matched the design and duration of the trials we wanted to examine. We therefore did not include any trials in this review.

Key results

Ideally, more research is needed to compare tube feeding with oral supplements and with normal diet. New trials should also look at when tube feeding should be started for the best results. These trials may be difficult to run as it may be wrong not to provide people with the extra calories they need, and when they need them, in this way.

BACKGROUND

Description of the condition

The nutritional status of most people with cystic fibrosis (CF) may be compromised for several reasons. The majority of people with CF have a higher energy need, estimated to be up to 200% of normal requirements (Stallings 2008). This is thought to be partly due to an increased resting energy expenditure (Barclay 2007; Dorlochter 2002; Magoffin 2008; Moudiou 2007). Lung damage further increases calorie requirements as it increases the work of breathing (Zemel 2000). Oral calorie intake may be reduced by a poor appetite associated with respiratory infection, nausea from swallowed sputum or as a side effect of medications. Fat malabsorption leads to increased energy losses in the stools. However, even with the adequate control of fat malabsorption using pancreatic enzyme supplements people with CF may still be unable to meet their increased energy requirements (Gordon 2007; White 2004).

Description of the intervention

Enteral tube feeding is usually performed via the nasogastric or gastrostomy route. Nasogastric feeding involves passing a fine bore nasogastric tube through the nose into the stomach. This is usually done by the people with CF themselves or their carers on a daily, weekly or monthly basis. In children, gastrostomy tubes are usually sited under general anaesthetic. The tube is placed directly into the stomach. Subsequent changes may require general anaesthesia depending on the type of tube used. In adults, gastrostomy tubes are usually placed under endoscopic guidance (PEG) as this does not require a general anaesthetic.

Whatever the type of tube, feeds can be administered as a continuous infusion (usually overnight) or as bolus feeding during the day. The person with CF or their carer is required to set up the equipment for feeding. Although this constitutes additional work, for many it is often a relief when tube feeding is commenced. Before the introduction of tube feeding, meal times may have become a battleground, because the child with CF is unable to consume sufficient energy to promote growth.

There are very few complications associated with enteral tube feeding. Those that do occur are usually minor and very easily treated. The main complications of nasogastric feeding are that the tube may become displaced by coughing; also, it may block and may therefore need changing frequently. Nasogastric tubes may also cause nasal irritation (Pencharz 1984). Gastrostomy insertion can be associated with post-insertional pain, but this is usually short-lived and can usually be managed with adequate pain relief. Leakage and infection around the gastrostomy site occasionally occurs, this usually responds to application of a steroid and antibiotic cream. In a minority of people, overnight feeding may result in an increased tendency to gastro-oesophageal reflux and easy vomiting (Truby 2009). In severe cases this may necessitate a Nissen fundoplication (Truby 2009); less severe cases can be treated medically. Problems such as nausea, vomiting and diarrhoea are usually resolved by either changing the type of feed, rate of infusion, method of pancreatic enzyme replacement therapy or addition of adjunctive therapies.

How the intervention might work

A major objective in CF care is to achieve normal growth in childhood and to maintain this in adult life. In a minority of people with CF, routine treatments and oral supplements fail to realise normal nutritional status. Some of these people have been given high-calorie liquid enteral tube feeds, usually overnight, delivered by a pump via nasogastric or gastrostomy tubes.

Why it is important to do this review

It is well established that nutritional and respiratory status are closely linked in CF (Corey 1998; Pedreira 2005; Zemel 2000). In recent trials, poor weight (Sharma 2000), height (Beker 2001) and body mass index (BMI) (Stern 2006) have been shown to be independent predictors of mortality in CF. Enteral tube feeding can be a highly effective way of improving the well-being of a person with CF. Although it can give rise to issues regarding body image as tubes can be unsightly. Poor weight and undernutrition have also been associated with poor body image. Consideration should be given to all aspects of body image.

This is an updated version of previously published reviews (Conway 1999; Conway 2008; Conway 2012; Morton 2015). Due to a lack of research in this area we do not envisage undertaking any future updates of this review.

OBJECTIVES

We planned to test the hypotheses that enteral tube feeding is:

1. associated with better nutritional status;
2. associated with better respiratory function;
3. associated with improved quality of life;
4. not associated with significant adverse effects.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials (RCTs), published and unpublished.

Types of participants

People with CF (both males and females) of any age, diagnosed clinically and by sweat testing or genetic profiling, for whom supplemental enteral tube feeds would be considered. People at all stages of CF disease would be included.

Types of interventions

Trials of one month duration or longer, whatever the supplement brand or dosage regimen used, and whatever the pancreatic enzyme dosage schedule used. Trials comparing a period of enteral tube feeding in people with CF with a group of pair-matched participants not receiving enteral tube feeding. Trials comparing different types of enteral tube feeding and different types of enteral feed formulae with each other were excluded.

Types of outcome measures

Primary outcomes

1. Growth and nutritional status
 - a. weight of participant (kg)
 - b. percentage weight for height
 - c. percentage weight for age
 - d. percentage ideal body weight (IBW)
 - e. weight standard deviation score (z score)
 - f. BMI (as defined as weight divided by height squared)
 - i. standard deviation score (z score)
 - ii. percentile position (*post hoc* change)
 - g. other indices of nutritional status
2. Respiratory function
 - a. vital capacity (VC)
 - b. forced vital capacity (FVC)
 - c. forced expiratory volume in the first second of the forced vital capacity (FEV₁)
 - d. average forced expiratory flow rate over the middle 50% of the FVC (FEF₂₅₋₇₅)
3. Mortality

Secondary outcomes

1. Cost of treatment
2. Adherence to therapy
3. Quality of life
4. Adverse events such as vomiting, sensation of bloatedness, nocturia, loss of daytime appetite, tube blockage, tube infection, skin excoriation, and any other adverse event noted

We planned to group the outcome data into those measured at one, three, six and 12 months, then annually thereafter. If outcome data were recorded at other time periods then consideration would have been given to examining these as well.

Search methods for identification of studies

Trials were eligible for consideration regardless of language or publication status (published, unpublished, in press, and in progress).

Electronic searches

We identified relevant trials from the Group's Cystic Fibrosis Trials Register using the terms: nutrition AND enteral.

The Cystic Fibrosis Trials Register is compiled from electronic searches of the Cochrane Central Register of Controlled Trials (CENTRAL) (updated each new issue of the Cochrane Library), weekly searches of MEDLINE, a search of Embase to 1995 and the prospective handsearching of two journals - *Pediatric Pulmonology* and the *Journal of Cystic Fibrosis*. Unpublished work is identified by searching through the abstract books of three major cystic fibrosis conferences: the European Cystic Fibrosis Conference, the International Cystic Fibrosis Conference and the North American Cystic Fibrosis Conference. For full details of all searching activities for the register, please see the relevant sections of the [website](#).

Date of the most recent search of the Group's Cystic Fibrosis Trials Register: 22 October 2018.

PubMed was searched using the terms: Cystic fibrosis AND (enteral tube feeding OR nasogastric feeding OR gastrostomy feeding OR jejunostomy feeding OR nutrition).

Date of the most recent search of PubMed: 26 October 2018.

Searching other resources

We looked for additional RCTs in reference lists of identified papers.

We have contacted the companies that manufacture enteral feeds for data on RCTs of enteral tube feeding in CF on their files.

Data collection and analysis

We have outlined the methods originally planned for this review below.

Selection of studies

Up until the 2012 update, all three authors independently considered trials for inclusion in the review; for the 2015 update and thereafter two authors performed this task. The authors did not find any trials which met the inclusion criteria.

Data extraction and management

If trials are included in future updates of the review, then two authors will independently extract data using a standard data extraction form. If any disagreements occur, we plan to resolve these by discussion with a third person from the Cochrane Cystic Fibrosis and Genetic Disorders Review Group.

If trials report quality of life changes, we will summarise these in the review. If adverse events are mentioned, we will report these in the review.

Assessment of risk of bias in included studies

The review authors will assess any trials that meet the inclusion criteria for methodological quality and risk of bias using the risk of bias tool as described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We will examine suitable trials in particular for details of concealment of treatment allocation, generation of a randomisation sequence, the degree of blinding in the trial, and whether all randomised participants were included in the analysis.

Measures of treatment effect

For future updates of this review, if we find and include any trials, we will apply the following methods. For binary outcome measures, we aim to calculate a pooled estimate of the treatment effect for each outcome across trials, (the odds of an outcome among treatment allocated participants to the corresponding odds among controls). For continuous outcomes, we plan to record either mean change from baseline for each group or mean post-treatment or intervention values and standard deviation or standard error for each group. For continuous outcomes we also plan to calculate a pooled estimate of treatment effect by calculating the mean difference.

Unit of analysis issues

We will consider cross-over trials for inclusion if data can be obtained for the first period and the intervention and comparison groups are similar at baseline.

Dealing with missing data

In order to allow an intention-to-treat analysis, we will seek data on the number of participants with each outcome event, by allocated treatment group, irrespective of adherence and whether or not the participant was later thought to be ineligible or otherwise excluded from treatment or follow-up.

Assessment of heterogeneity

We propose to examine heterogeneity between study results using the I^2 test recommended by Higgins (Higgins 2003).

Assessment of reporting biases

We will compare the protocols of included studies with the final published papers to identify any outcomes which have been measured, but not reported. If the study protocols are not available, we will compare the 'Methods' section with the 'Results' section of the published paper.

Sensitivity analysis

We plan to perform a sensitivity analysis based on the risk of bias of the trials.

RESULTS

Description of studies

Results of the search

The searches identified 44 trials; however, none were eligible for inclusion in this review. The reasons are summarised in the 'Characteristics of excluded studies' section of the review.

Included studies

No studies were eligible for inclusion in this review.

Excluded studies

The 44 trials were excluded from the review for a variety of reasons. A total of 11 trials were longitudinal, open trials with single group pre- and post-intervention outcomes (Bacon 2009; Beadle 2011; Best 2011; Boland 1986; Caraher 2012; Efrati 2006; Moore 1986; O'Loughlin 1986; Pencharz 1984; Rosenfeld 1999; White 2013); two were case-controlled studies (Shepherd 1988; Van Biervliet 2018); nine were retrospective case series (Bradley 2012; Jerkins 2012; Martinez-Zaro 2011; Nagakumar 2012; Steinkamp 1994; Truby 2009; Van Biervliet 2004; Vandeleur 2013; White 2014); four were retrospective observational longitudinal studies (Declercq 2018; Fisher 2015; Hollander 2017; Van Biervliet 2017); two were retrospective registry-based reviews (Libeert 2018; Van Dyke 2011); and four further trials were not RCTs (Bertrand 1984; Chinuck 2011; Levy 1985; Steinkamp 1990). Four trials compared different feed formulations (Erskin 1998; Gottrand 1999; Kane 1990; Pelekanos 1990); three trials looked at enteral calorie supplements rather than enteral tube feeds (Armand 2004; Kane 1991; Steinkamp 2000); and a further trial compared formulae with and without added dietary fibre (Evans 2009). Three trials were of insufficient duration (Gavin 1999; Geukers 2005; Shepherd 1983) and one was a cross-over trial with no first-arm data available (Daniels 1989).

Risk of bias in included studies

No trials were included.

Effects of interventions

No trials were included.

DISCUSSION

Summary of main results

We have found no RCTs which fulfil the inclusion criteria for this review. The excluded trials are of varying duration and most include relatively small numbers of participants. Most trials ($n = 32$) did not use a randomised design (Bacon 2009; Beadle 2011; Bertrand 1984; Best 2011; Boland 1986; Bradley 2012; Caraher 2012; Chinuck 2011; Declercq 2018; Efrati 2006; Fisher 2015; Hollander 2017; Jerkins 2012; Levy 1985; Libeert 2018; Martinez-Zaro 2011; Moore 1986; Nagakumar 2012; O'Loughlin 1986; Pencharz 1984; Rosenfeld 1999; Shepherd 1988; Steinkamp 1990; Steinkamp 1994; Truby 2009; Van Biervliet 2004; Van Biervliet 2017; Van Biervliet 2018; Vandeleur 2013; Van Dyke 2011; White 2013; White 2014). Three trials were of insufficient duration (Gavin 1999; Geukers 2005; Shepherd 1983). In eight trials the intervention did not meet the review's inclusion criteria: four trials compared different feed formulations (Erskin 1998; Gottrand 1999; Kane 1990; Pelekanos 1990); three trials looked at enteral calorie supplements (Armand 2004; Kane 1991; Steinkamp 2000); and a further trial compared formulae with and without added dietary fibre (Evans 2009). The remaining trial was a cross-over trial with no first-arm data available (Daniels 1989).

Overall completeness and applicability of evidence

No studies were eligible for inclusion in the review.

Potential biases in the review process

We have comprehensively searched the literature independently in order to potentially avoid bias. Additional searching including searching conference abstracts and contacting nutritional companies in order to avoid missing any evidence.

Agreements and disagreements with other studies or reviews

Enteral tube feeding is widely accepted as a treatment or intervention in CF centres, but the evidence-base for this does not include RCTs.

The identified and subsequently excluded trials report beneficial effects of enteral tube feeding and have shown that enteral tube feeding is associated with an increase in total energy intake resulting in significant improvements in body weight (Beadle 2011; Hollander 2017), height (Beadle 2011; Declercq 2018) and height velocity (O'Loughlin 1986). Improvements in BMI are reported by several trials (Declercq 2018; Hollander 2017; Libeert 2018). Improvements in nutritional status are also reported, including significant increases in body fat (Pencharz 1984; White 2014), lean tissue and other biochemical markers of nutritional status (Moore 1986; Van Biervliet 2018). In addition, a slower rate of decline in respiratory function (Libeert 2018; White 2013) or an improvement in lung function (Declercq 2018; Steinkamp 1994), reductions in the number of infections leading to fewer hospital admissions (Libeert 2018) and an improvement in physical activity (O'Loughlin 1986) have all been reported. In general, the papers report that both nasogastric and gastrostomy tube feeding are well-tolerated by people with CF.

There were few adverse effects associated with enteral tube feeding reported in the excluded studies. These were generally mild and included transient nausea (Boland 1986), vomiting (Fisher 2015), gastro-oesophageal reflux (Van Dyke 2011), abdominal pain and loose stools (Truby 2009), naso-pharyngeal irritation with nasogastric feeding (Pencharz 1984) and overgranulation and infection of the gastrostomy site (Vandeleur 2013).

Two excluded studies reported that participants were self-conscious and had a poor body image post-gastrostomy or jejunostomy placement (Caraher 2012; Chinuck 2011). Awareness of these issues together with careful preparation and counselling of individuals allowing for a period of adjustment, adaptation and acceptance is important.

AUTHORS' CONCLUSIONS

Implications for practice

No firm conclusions can be drawn about supplemental enteral tube feeding from the information currently available. Clinicians must balance possible potential benefit against the invasive nature and cost of procedures and products involved for each individual. There are no eligible trials of supplemental enteral feeding for one month or more. Data from other studies, either of shorter duration or not controlled, do indicate that nutritional status can be improved; but it is not clear if this is translated into improved health.

There are no trials included in the review and we have not identified any relevant trials up to July 2019. We therefore do not plan to update this review until new trials are published.

Implications for research

This systematic review has identified that there are no well-designed, adequately-powered, multicentre randomised

controlled trials to assess the efficacy and possible adverse effects of supplemental enteral tube feeding compared to normal oral feeding and oral supplement feeding in cystic fibrosis. However, such trials would be very difficult to undertake in these individuals as ethical approval is unlikely to be granted for a trial withholding an intervention which will probably be of benefit.

Any future randomised controlled trials could address issues such as the most appropriate timing of the introduction of enteral tube feeding (Oliver 2004; Walker 1998), different effects of tube feeding at different stages of disease severity, appropriate methods of administration, enzyme therapy and appropriate feed composition. Consideration should also be given to the impact of enteral feeding alone versus enteral feeding combined with a prescribed exercise programme on other nutritional outcomes such as fat-free mass (kg) and fat-free mass index (defined as fat-free body mass divided by height squared). These trials should be of sufficient length to fully assess the impact of any improvement on nutritional status, respiratory illness, the frequency of respiratory exacerbations, respiratory function tests, morbidity and mortality and quality of life.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Armand 2004	Trial of enteral supplements, i.e. oral calorie supplements rather than enteral tube feeds.
Bacon 2009	Not a RCT, retrospective database review comparing pre- and post-intervention.
Beadle 2011	Not a RCT, retrospective database review comparing pre- and post-intervention.

Enteral tube feeding for cystic fibrosis (Review)

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Study	Reason for exclusion
Bertrand 1984	Not a RCT.
Best 2011	Not a RCT, pre-post retrospective study.
Boland 1986	Not a RCT.
Bradley 2012	Not a RCT, retrospective case-control study.
Caraher 2012	Not a RCT. Pre-post intervention study.
Chinuck 2011	Not a RCT.
Daniels 1989	Cross-over RCT, no data available for the first arm of the trial.
Declercq 2018	Not a RCT. Retrospective observational longitudinal study.
Efrati 2006	Not a RCT. Pre-post intervention study.
Erskine 1998	Comparison of two types of formulae; study period inadequate.
Evans 2009	Comparison of formulae with and without added dietary fibre.
Fisher 2015	Not a RCT, retrospective data collection.
Gavin 1999	Not a RCT and insufficient duration.
Geukers 2005	Study period inadequate (given for 4 days only, not "at least 1 month").
Gottrand 1999	Comparison of two types of formula (high versus normal fat content).
Hollander 2017	Not a RCT, retrospective case series.
Jenkins 2012	Not a RCT, retrospective case series.
Kane 1990	Comparison of formulae (varying concentrations of carbohydrate).
Kane 1991	Trial of enteral supplements, i.e. oral calorie supplements rather than enteral tube feeds.
Levy 1985	Not a RCT, participants retrospectively pair-matched.
Libeert 2018	Not a RCT. Retrospective registry- based review.
Martinez-Zaro 2011	Not a RCT. Retrospective database review of national online home enteral feeding register.
Moore 1986	Not a RCT.
Nagakumar 2012	Not a RCT. Case series.
O'Loughlin 1986	Not a RCT.
Pelekanos 1990	Comparison of 3 different types of formulae, insufficient study period.
Pencharz 1984	Not a RCT; study period of enteral tube feeding insufficient - only 12 days.
Rosenfeld 1999	Not a RCT. Pre-post intervention study.

Study	Reason for exclusion
Shepherd 1983	Study period insufficient - 4 days only.
Shepherd 1988	Inadequate study period confined to respiratory exacerbation time only.
Steinkamp 1990	Not a RCT, participants with CF age- and weight-matched to participants without CF.
Steinkamp 1994	Not a RCT, retrospective case series.
Steinkamp 2000	Trial of enteral supplements i.e. oral calorie supplements rather than enteral tube feeds.
Truby 2009	Not a RCT. It is a case series and a retrospective review.
Van Biervliet 2004	Not a RCT, retrospective case series.
Van Biervliet 2017	Not a RCT, retrospective observational longitudinal study.
Van Biervliet 2018	Not a RCT, a case-controlled study with low participant numbers (n = 9).
Vandeleur 2013	Not a RCT, retrospective case series.
Van Dyke 2011	Not a RCT. Retrospective review of CF Foundation Registry Data comparing early and late intervention.
White 2013	Not a RCT. Longitudinal, open study with single pre- and post-intervention outcomes.
White 2014	Not a RCT. Retrospective case series.

CF: cystic fibrosis

RCT: randomised controlled trial

WHAT'S NEW

Date	Event	Description
8 April 2021	Review declared as stable	Due to a lack of research in this area the Editorial Board of the Cystic Fibrosis and Genetic Disorders Review Group have decided to no longer update this review.

HISTORY

Protocol first published: Issue 3, 1998

Review first published: Issue 3, 1999

Date	Event	Description
10 July 2019	New citation required but conclusions have not changed	A new author team have taken on this review. The conclusions of the review have not changed. Due to a lack of research in this area we do not envisage undertaking any future updates of this review.

Date	Event	Description
10 July 2019	New search has been performed	<p>A new search of the Cochrane Cystic Fibrosis and Genetic Disorders Review Group's Cystic Fibrosis Trials Register did not identify any new references potentially eligible for inclusion in the review.</p> <p>Additional searches identified nine references to six trials; all of these six new trials were excluded (Declercq 2018; Fisher 2015; Hollander 2017; Libeert 2018; Van Biervliet 2017; Van Biervliet 2018).</p>
13 April 2015	Amended	Contact details updated.
8 April 2015	New citation required but conclusions have not changed	<p>The previous lead author on this review, Dr Steve Conway, has now stepped down from the team.</p> <p>As we have not been able to include any new information in this systematic review, our conclusions have remained the same.</p>
8 April 2015	New search has been performed	A search of the Cystic Fibrosis and Genetic Disorders Group's Cystic Fibrosis Trials Register identified two references potentially eligible for inclusion in this review (Gavin 1999 ; Kane 1990). Additional searching of PubMed and conference abstract books identified a further five references (Chinuck 2011 ; Jerkins 2012 ; Van Dyke 2011 ; White 2013 ; White 2014). All seven references have been excluded.
18 October 2012	New citation required but conclusions have not changed	As no new trials could be included in the review at this update, the conclusions of the review have not changed.
18 October 2012	New search has been performed	<p>A search of the Group's Cystic Fibrosis Trials Register and hand-searching of conference proceedings identified 17 references to 15 additional trials; none of these were eligible for inclusion in the review and have been listed as excluded studies.</p> <p>The Background section has been updated.</p>
13 April 2010	Amended	It was previously decided not to update this review until new trials were identified. However, this decision has been revised and we will continue to update this review every two years from now on.
13 April 2010	New search has been performed	A search of the Group's Cystic Fibrosis Trials Register identified two new trials potentially eligible for this review (Geukers 2005 ; Kane 1991). The authors identified one paper independently (Truby 2009). All three of these have been excluded.
1 April 2008	Review declared as stable	There are no trials included in the review up to April 2008. We therefore do not plan to update this review until new trials are published, although we will search the Group's Cystic Fibrosis Trials Register on a two-yearly cycle.
1 April 2008	New search has been performed	A search of the Group's Cystic Fibrosis Trials Register did not identify any references eligible for inclusion in this review.
1 April 2008	Amended	Converted to new review format.
14 February 2008	New search has been performed	The plain language summary has been updated in light of current guidance from The Cochrane Collaboration.

Date	Event	Description
		The Group's Cystic Fibrosis Trials Register was searched in November 2007. No new references were found.
14 February 2008	New citation required and conclusions have changed	Substantive amendment.
20 February 2007	New search has been performed	The Group's Cystic Fibrosis Trials Register was searched in November 2006. No new references were found.
16 February 2006	New search has been performed	The Group's Cystic Fibrosis Trials Register was searched in August 2005. No new references were found.
15 November 2004	New search has been performed	The Group's Cystic Fibrosis Trials Register was searched in August 2004. No new references were found.
27 October 2003	New search has been performed	The Group's Cystic Fibrosis Trials Register was searched in October 2003. One new study was found which has been excluded (Pelekanos 1990).
2 April 2002	New search has been performed	The Group's specialised register was searched in February 2002. Additional reports of the Excluded Study - Daniels 1984 (now amended to Daniels 1989 as full data published) have been added to the review.
23 September 1999	Amended	Review reformatted.

CONTRIBUTIONS OF AUTHORS

Each author independently evaluated each paper and contributed equally to the final review paper.

DECLARATIONS OF INTEREST

Dee Shimmin has no declarations of interest to make.

Jacqueline Lowdon has received payment from Nutricia as co-editor of a quarterly paediatric newsletter and sponsorship from Gilead to attend a CF conference.

Tracey Remington has no declarations of interest to make.

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Internal sources

- No sources of support supplied

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

At the update in 2012, we added the outcome BMI percentile position as we feel this is a clinically relevant outcome.

INDEX TERMS**Medical Subject Headings (MeSH)**

Cystic Fibrosis [*therapy]; Dietary Supplements; Enteral Nutrition [*methods]; Nutritional Status; Quality of Life; Randomized Controlled Trials as Topic

MeSH check words

Humans