Cochrane Library

Cochrane Database of Systematic Reviews

Enteral tube feeding for older people with advanced dementia (Review)

Sampson EL, Candy B, Jones L

Sampson EL, Candy B, Jones L.
Enteral tube feeding for older people with advanced dementia.
Cochrane Database of Systematic Reviews 2009, Issue 2. Art. No.: CD007209.
DOI: 10.1002/14651858.CD007209.pub2.

www.cochranelibrary.com

WILEY

TABLE OF CONTENTS

HEADER 1
ABSTRACT 1
PLAIN LANGUAGE SUMMARY 2
BACKGROUND 3
OBJECTIVES 4
METHODS 4
RESULTS 7
DISCUSSION 9
AUTHORS' CONCLUSIONS 10
ACKNOWLEDGEMENTS 10
REFERENCES 11
CHARACTERISTICS OF STUDIES 13
ADDITIONAL TABLES 16
CONTRIBUTIONS OF AUTHORS 23
DECLARATIONS OF INTEREST 23
SOURCES OF SUPPORT 23
DIFFERENCES BETWEEN PROTOCOL AND REVIEW 23
INDEX TERMS 23

[Intervention Review]

Enteral tube feeding for older people with advanced dementia

Elizabeth L Sampson[1], Bridget Candy[1], Louise Jones[1]

[1]Marie Curie Palliative Care Research Unit, Department of Mental Health Sciences, Royal Free & University College Medical School, London, UK

Contact address: Elizabeth L Sampson, Marie Curie Palliative Care Research Unit, Department of Mental Health Sciences, Royal Free & University College Medical School, Hampstead Campus, Rowland Hill Street, London, NW3 2PF, UK. e.sampson@medsch.ucl.ac.uk, e.sampson@medsch.ucl.ac.uk.

Editorial group: Cochrane Dementia and Cognitive Improvement Group.
Publication status and date: New, published in Issue 1, 2010.

Citation: Sampson EL, Candy B, Jones L. Enteral tube feeding for older people with advanced dementia. *Cochrane Database of Systematic Reviews* 2009, Issue 2. Art. No.: CD007209. DOI: 10.1002/14651858.CD007209.pub2.

ABSTRACT

Background

The use of enteral tube feeding for patients with advanced dementia who have poor nutritional intake is common. In one US survey 34% of 186,835 nursing home residents with advanced cognitive impairment were tube fed. Potential benefits or harms of this practice are unclear.

Objectives

To evaluate the outcome of enteral tube nutrition for older people with advanced dementia who develop problems with eating and swallowing and/or have poor nutritional intake.

Search methods

The Specialized Register of the Cochrane Dementia and Cognitive Improvement Group (CDCIG), *The Cochrane Library*, MEDLINE, EMBASE, PsycINFO, CINAHL and LILACS were searched in April 2008. Citation checking was undertaken. Where it was not possible to accept or reject, the full text of the citation was obtained for further evaluation.

Selection criteria

Randomized controlled trials (RCTs), controlled clinical trials, controlled before and after studies and interrupted time series studies that evaluated the effectiveness of enteral feeding via a nasogastric tube or via a tube passed by percutaneous endoscopic gastrostomy (PEG) were planned to be included. In addition, controlled observational studies were included. The study population comprised adults aged 50 and over (either sex), with a diagnosis of primary degenerative dementia made according to validated diagnostic criteria such as DSM-IV or ICD-10 (APA 1994; WHO 1993) and with advanced cognitive impairment defined by a recognised and validated tool or by clinical assessment and had poor nutrition intake and/or develop problems with eating and swallowing. Where data were limited we also considered studies in which the majority of participants had dementia.

Data collection and analysis

Data were independently extracted and assessed by one reviewer, checked by a second and if necessary, in the case of any disagreement or discrepancy it was planned that it would be reviewed by the third reviewer. Where information was lacking, we attempted contact with authors. It was planned that meta-analysis would be considered for RCTs with comparable key characteristics. The primary outcomes were survival and quality of life (QoL).

Main results

No RCTs were identified. Seven observational controlled studies were identified. Six assessed mortality. The other study assessed nutritional outcomes. There was no evidence of increased survival in patients receiving enteral tube feeding. None of the studies examined QoL and there was no evidence of benefit in terms of nutritional status or the prevalence of pressure ulcers.

Authors' conclusions

Despite the very large number of patients receiving this intervention, there is insufficient evidence to suggest that enteral tube feeding is beneficial in patients with advanced dementia. Data are lacking on the adverse effects of this intervention.

PLAIN LANGUAGE SUMMARY

There is insufficient evidence to suggest that enteral tube feeding is beneficial in patients with advanced dementia. Data are lacking on the adverse effects of this intervention

Patients with advanced dementia often develop dysphagia (difficulties swallowing). They also experience changes in appetite and apraxia (difficulty co-coordinating movements) and may have difficulties feeding themselves. Two methods of enteral tube feeding are commonly used: the administration of food and fluids via a nasogastric tube (a tube that is passed through the nose and into the stomach) or via a percutaneous endoscopic gastrostomy (PEG) where a feeding tube is inserted into the stomach and is accessed through a permanent incision in the abdominal wall. The decision to use artificial hydration and nutrition in someone with dementia is often emotive and complex. Relatives and carers may request the intervention because they are concerned that the patient may starve; clinicians may be aware of the risks but feel pressurised by institutional, societal or even legal directives to intervene. We found no conclusive evidence that enteral tube nutrition is effective in terms of prolonging survival, improving quality of life, or leading to better nourishment or decreasing the risk of pressure sores. It may actually increase the risk of developing pneumonia due to inhaling small quantities of the feed and even death. This area is difficult to research but better designed studies are required to provide more robust evidence.

BACKGROUND

Description of the condition

Dementia is a progressive neurodegenerative syndrome. According to United Nations population estimates, in 2001 there were 24.3 million people in the world with dementia; in 2040 the number will have increased to 81.1 million (Ferri 2005). This increase is not uniform across regions, with numbers forecast to increase by more than 300% by 2040 in developing countries, such as India and China (Ferri 2005). In the US, the number of people with dementia is projected to increase by 2050 to 13.2 million (Hebert 2003). Dementia has a number of underlying aetiologies. In community samples the commonest cause is Alzheimer's disease, followed by vascular dementia, Lewy Body dementia and rarer syndromes such as frontotemporal lobar degeneration (FTLD) (Stevens 2002). The prevalence of dementia increases with age. It is estimated that the prevalence doubles every five years beyond the age of 65 years (NIH 1999). At age 85 and older, in the case of Alzheimer's disease, the prevalence is nearly 50% (Hendrie 1998; Kawas 1998; Small 1999). The disease course of dementia is highly heterogeneous. In one analysis from a UK population based cohort study with 14 year follow-up the median survival times in the 438 people who developed dementia was 4.5 years (Xie 2008). In a Canadian cohort study with a five year follow-up the median survival was 3.3 years (Wolfson 2001).

Most forms of dementia are characterised by early changes in memory or higher cognitive functions accompanied by decline in ability to carry out activities of daily living, psychiatric symptoms and behavioural problems. Decline in functional ability passes through a number of stages, from early difficulties with complex tasks, such as managing financial affairs, to the terminal phases where patients become increasingly immobile and bed bound (Njegovan 2001). Advanced dementia is usually defined by use of a recognised and validated tool, such as the Functional Assessment stage (FAST) tool (Reisberg 1994) by use of any other validated measure or by clinical assessment. A FAST score of stage 7A or above indicates that a patient has incontinence of both urine and faeces, very limited speech and needs assistance with all activities of daily living. The Clinical Dementia Rating: CDR (Morris 1993) is another example of such a rating scale.

Description of the intervention

Poor food intake is common in people with dementia and may occur in the early stages of disease, even before a diagnosis has been made. Poor food intake may have a variety of causes in people with dementia. They may fail to recognise food, they may lose the normal physiological drivers of appetite and satiety due to changes in limbic or hypothalamic function, or may, in advanced dementia, develop physical difficulties with the act of swallowing, for example failing to manage the food bolus properly once it is in the mouth (oral phase dysphagia), or aspirate when swallowing (pharyngeal phase dysphagia) (Finucane 1999). It is in advanced dementia that the decision to intervene by feeding artificially via an enteral tube more commonly occurs.

How the intervention might work

For the purpose of this review we defined "enteral tube feeding" as the administration of food and fluids via a nasogastric tube or via a percutaneous endoscopic gastrostomy (PEG) tube. In PEG, which is more commonly used in this condition, the feeding tube is passed through the endoscope into the stomach and guided out through an incision in the abdominal wall. The aim of this practice is to prevent aspiration pneumonia and malnutrition, and the consequences of malnutrition including pressure ulcers, infection, infection, starvation and death. We did not consider the intravenous administration of fluids as this tends to occur more commonly as a short-term intervention during episodes of acute physical illness and is rarely used for long-term nutritional support in patients with dementia.

Why it is important to do this review

The decision to start enteral tube feeding is emotive, controversial and influenced by complex ethical issues (The 2002). The decision to intervene differs with clinical need, local practice and physician and carer preference, and whether there is an advance directive or advance care plan in place. Common justifications given may include the prolongation of life by correcting malnutrition, reducing the risk of aspiration and pressure ulcers, pneumonia and other infections and/or the optimising of quality of life by promoting physical comfort.

However, it has not been established whether enteral tube feeding achieves any of these outcomes and may in contrast cause harm. For instance while inadequate intake of food is thought to lead to distressing hunger and thirst, data suggest that among cognitively intact patients refusal of food and water in the context of terminal illness is not painful (McCann 1994). In a prospective, longitudinal uncontrolled study of patients with severe dementia conducted in the Netherlands in 2000, researchers found that the mean level of discomfort (dyspnoea, restlessness, and physicians' observations of pain and dehydration, mostly in those who remained awake) was highest at the time of the decision not to start enteral feeding and decreased in the days thereafter (Pasman 2005). Some studies suggest that enteral tube feeding may have an effect opposite to that desired and actually increase mortality, morbidity and reduce quality of life. It may worsen urinary and faecal incontinence which is associated with an increase risk of pressure ulcers. It may increase pulmonary secretions. PEG is an invasive surgical procedure with significant risk of post-operative adverse events including aspiration pneumonia, oesophageal perforation, migration of the tube, haemorrhage and wound infection (Abuksis 2000). It may cause agitation leading to the patient requiring physical or chemical restraint to avoid self-extubation, and this may be seen as a violation of patients' right to dignity. There are also issues of whether informal carers who give consent are duly informed both of the benefits and potential harms of intervention and of alternatives to optimise quality of life. Ethical issues include whether life in advanced dementia should be artificially prolonged and what is considered to constitute "euthanasia" in terms of giving or withholding treatment.

Despite these issues and many discussion papers questioning the utility of enteral tube feeding in advanced dementia, it remains a common intervention. In one survey conducted between 2001 and 2002, of Israeli and Canadian hospital patients with end-stage dementia, 24% (92/2287) were fed by nasogastric tube or gastrostomy (Clarfield 2006). In a larger survey, using data from the US in 1999, 34% of 186,835 nursing home residents with advanced cognitive impairment had a feeding tube (Mitchell 2003), although it has been found to be less likely to occur in certain groups of patients with severe dementia. In particular, in a prospective longitudinal uncontrolled study conducted in the Netherlands in

2000, it was found that decisions not to start enteral tube feeding were made most often in severely demented, female patients with an acute intercurrent illness (Pasman 2005). However, It remains possible that, with the expected increase in people with advanced dementia, enteral tube feeding will become increasingly common.

OBJECTIVES

To evaluate the outcome of enteral tube nutrition for older people with advanced dementia who develop problems with eating and swallowing or who have poor nutritional intake.

METHODS

Criteria for considering studies for this review

Types of studies

We planned to include a broad range of controlled comparison studies: RCTs, controlled clinical trials, controlled before and after studies and interrupted time series studies. In the absence of such experimental studies we included observational studies if they used, to compare outcomes, a control group.

Such studies could compare artificial nutrition with no intervention or "usual treatment or care", in any healthcare setting (including acute hospitals, nursing and residential homes and the community), published in any language, and for which adequate information was provided or could be obtained from the researchers.

Types of participants

Participants per protocol were adults all aged 50 and over of either sex who had poor nutritional intake or had developed problems with eating and swallow and where a majority of the study sample had a medical diagnosis of primary degenerative dementia made according to validated diagnostic criteria such as DSM-IV or ICD-10 (APA 1994; WHO 1993) and with advanced cognitive impairment defined by a recognised and validated tool, such as stage 7A or above on the Functional Assessment stage (FAST) tool (Reisberg 1994), or any other validated measure or by clinical assessment. As we envisaged per protocol that there would be limited studies that included samples where all had advanced dementia, we also included studies where the majority, over 50%, had advanced dementia. Other diagnoses included patients with other cognitive degenerative diseases. Dementias included Alzheimer's disease, vascular dementia or mixed dementia, Lewy body dementia or frontotemporal lobar degeneration (FTLD). Patients may have resided at home, in the community or in any healthcare setting.

Types of interventions

Studies were included if they evaluated the effectiveness of enteral tube feeding via a nasogastric tube or via a tube passed by percutaneous endoscopic gastrostomy (PEG) to deliver artificial nutrition.

Interventions of oral supplementation of vitamins and or minerals were not included.

Comparative interventions included usual treatment or wait list groups.

Types of outcome measures

Primary outcomes

The primary outcomes were mortality (measured by length of survival post-intervention) and quality of life (measured by a validated quality of life scale or tool).

Secondary outcomes

The secondary outcome measures included improvement of nutritional or functional parameters, prevention or healing of pressure ulcers, and change in behavioural and psychiatric symptoms of dementia if these were measured with validated tools.

Adverse events evaluated included: aspiration pneumonia, local complications (i.e. local bleeding or infection), systemic complications (i.e. fluid imbalance or overload), urinary or faecal incontinence or constipation.

Search methods for identification of studies

Electronic searches

See Cochrane Dementia and Cognitive Improvement Group methods used in reviews.

The Specialized Register of the Cochrane Dementia and Cognitive Improvement Group (CDCIG) was searched on 18 April 2008 for all years up to December 2005. This register contains records from the following major healthcare databases: *The Cochrane Library*, MEDLINE, EMBASE, PsycINFO, CINAHL and LILACs, and many ongoing trial databases and other grey literature sources. The following search terms were used: enteral nutrition OR nutritional support OR percutaneous feeding OR artificial feeding OR artificial hydration OR endoscopic gastrostomy OR tube feeding OR peg OR enteral feeding OR stomach tube OR forced feeding OR percutaneous feeding OR artificial nutrition OR nutritional support OR feeding methods OR tube.

The Cochrane Library, MEDLINE, EMBASE, PsycINFO, CINAHL and LILACS were searched separately on 18 April 2008 for records added to these databases after December 2005 to April 2008. The search terms used to identify relevant controlled trials on dementia, Alzheimer's disease and mild cognitive impairment for the Group's Specialized Register can be found in the Group's module on *The Cochrane Library*. These search terms were combined with the following search terms and adapted for each database, where appropriate: enteral nutrition OR nutritional support OR percutaneous feeding OR artificial feeding OR artificial hydration OR endoscopic gastrostomy OR tube feeding OR peg OR enteral feeding OR stomach tube OR forced feeding OR percutaneous feeding OR artificial nutrition OR nutritional support OR feeding methods OR tube.

To view search strategies used for each source, see additional Table 1.

On 18 April 2008, the Specialized Register consisted of records from the following databases:

Healthcare databases

- *The Cochrane Library*: (2006, Issue 1);
- MEDLINE (1966 to 2006/07, week 5);
- EMBASE (1980 to 2006/07);

- PsycINFO (1887 to 2006/08, week 1);
- CINAHL (1982 to 2006/06);
- SIGLE (Grey Literature in Europe) (1980 to 2005/03);
- LILACS: Latin American and Caribbean Health Science Literature (http://bases.bireme.br/cgi-bin/wxislind.exe/iah/online/?IsisScript=iah/iah.xis&base=LILACS&lang=i&form=F) (last searched 29 August 2006).

Conference proceedings

- ISTP (http://portal.isiknowledge.com/portal.cgi) (Index to Scientific and Technical Proceedings) (to 29 August 2006);
- INSIDE (BL database of Conference Proceedings and Journals) (to June 2000);.

Theses

- Index to Theses (formerly ASLIB) (http://www.theses.com/) (UK and Ireland theses) (1716 to 11 August 2006);
- Australian Digital Theses Program (http://adt.caul.edu.au/): (last update 24 March 2006);
- Canadian Theses and Dissertations (http://www.collectionscanada.ca/thesescanada/index-e.html): 1989 to 28 August 2006);
- DATAD - Database of African Theses and Dissertations (http://www.aau.org/datad/backgrd.htm);
- Dissertation Abstract Online (USA) (http://wwwlib.umi.com/dissertations/gateway) (1861 to 28 August 2006).

Ongoing trials

UK

- National Research Register (http://www.update-software.com/projects/nrr/) (last searched issue 3/2006);
- ReFeR (http://www.refer.nhs.uk/ViewWebPage.asp?Page=Home) (last searched 30 August 2006);
- Current Controlled trials: Meta Register of Controlled trials (mRCT) (http://www.controlled-trials.com/) (last searched 30 August 2006) :
- ISRCTN Register - trials registered with a unique identifier
- Action medical research
- Kings College London
- Laxdale Ltd
- Medical Research Council (UK)
- NHS Trusts Clinical Trials Register
- National Health Service Research and Development Health Technology Assessment Programme (HTA)
- National Health Service Research and Development Programme 'Time-Limited' National Programmes
- National Health Service Research and Development Regional Programmes
- The Wellcome Trust
- Stroke Trials Registry (http://www.strokecenter.org/trials/index.aspx) (last searched 31 August 2006);

Netherlands

Nederlands Trial Register (http://www.trialregister.nl/trialreg/index.asp) (last searched 31 August 2006);

USA/International

- ClinicalTrials.gov (http://www.ClinicalTrials.gov) (last searched 31 August 2006) (contains all records from http://clinicalstudies.info.nih.gov/);
- IPFMA Clinical trials Register: www.ifpma.org/clinicaltrials.html. The Ongoing Trials database within this Register searches http://www.controlled-trials.com/isrctn, http://www.ClinicalTrials.gov and http://www.centerwatch.com/. The ISRCTN register and Clinicaltrials.gov are searched separately. Centerwatch is very difficult to search for our purposes and no update searches have been done since 2003.
- The IFPMA Trial Results databases searches a wide variety of sources among which are:
- http://www.astrazenecaclinicaltrials.com (seroquel, statins)
- http://www.centerwatch.com
- http://www.clinicalstudyresults.org
- http://clinicaltrials.gov
- http://www.controlled-trials.com
- http://ctr.gsk.co.uk
- http://www.lillytrials.com (zyprexa)
- http://www.roche-trials.com (anti-abeta antibody)
- http://www.organon.com
- http://www.novartisclinicaltrials.com (rivastigmine)
- http://www.bayerhealthcare.com
- http://trials.boehringer-ingelheim.com
- http://www.cmrinteract.com
- http://www.esteve.es
- http://www.clinicaltrials.jp

This part of the IPFMA database is searched and was last updated on 4 September 2006:

Lundbeck Clinical Trial Registry (http://www.lundbecktrials.com) (last searched 15 August 2006);

Forest Clinical trial Registry (http://www.forestclinicaltrials.com/) (last searched 15 August 2006).

The search strategies used to identify relevant records in MEDLINE, EMBASE, PsycINFO, CINAHL and LILACS can be found in the Group's module on *The Cochrane Library.*

Searching other resources

We attempted to contact experts in the field to identify any further trial evaluations that were not identified in the main search, and we checked the reference lists and undertook forward citation searches of included studies and relevant literature reviews identified by the above methods.

Data collection and analysis

Selection of studies

In accordance with the defined inclusion criteria, citations were screened by one of the review authors (BC). Where it was not possible to accept or reject, the full text of the citation was obtained for further evaluation.

Following screening, the full text of eligible citations was assessed for inclusion independently by two of the review authors (BC and

ES). If any differences of opinion existed they were resolved by consensus with the other review author (LJ). If resolution was not possible, we attempted to contact the authors for clarification. Justification for excluding studies at this stage was documented.

Quality assessment

Two review authors (BC and ES) planned to independently assess the quality of randomization of included trials using the Cochrane Collaboration guidelines (Higgins 2008):

- Grade A: Randomization; placebo-controlled; concealed allocation - adequate concealment
- Grade B: Concealment method not clearly defined
- Grade C: Inadequate concealment; no randomization.

We recognise that this system may not be entirely relevant for this review, as once allocated, blinding may or may not be possible.

We planned also to assess for each study:

- 1. recruitment and attrition bias
- 2. performance and detection bias.

We planned also to asses whether intention to treat analyses were performed.

For identified observational studies we assessed methodological quality using the Newcastle-Ottawa Scale (Wells 2008). This scale as reported in the Cochrane Handbook was identified in a review of instruments for assessing the methodological quality of non-randomized studies of interventions as one of the most useful tools. This tool contains items in three domains on:

- Selection. Whether case is adequately defined and representative and how controls (if there is a control group) were selected and defined.
- Comparability of cohort and controlling factors or control group.
- Exposure. On ascertainment and response rate.

The quality of included studies was tabulated.

Data extraction

A data extraction form was designed for the review. Where possible, the following information was obtained for each study:

- The number of patients eligible, number randomized (if a RCT), and reasons why were patients not included in the trial.
- The number of patients evaluated at follow-up(s) and what the follow-up time points were.
- Patient characteristics including age, sex, co-morbidities, diagnosis and type of dementia, advanced directive status, type of health care or community setting, stage of disease when enteral feeding was considered and reason for enteral feeding.
- Trial design features on masking, whether parallel or cross-over, features of randomisation, and sample size calculation.
- Artificial nutrition intervention including mode and reason for intervention. The need to restrain the patient.
- Comparison intervention including duration and mode.
- Outcome data at all time points including how it was measured, and the mean or categorical scores of the main and other outcomes.
- Presence of pressure ulcers.
- Complications such as bleeding at the site of insertion.
- Urinary or faecal incontinence or constipation.
- Quality of life and how this was measured.
- Other behavioural and psychiatric symptoms of dementia and the scales used to measure this.

Data were independently extracted by one reviewer (BC) and checked by a second reviewer (ES) and if necessary it was planned, in the case of any disagreement or discrepancy to be reviewed by the third reviewer (LJ). Where information was lacking, we attempted to make contact with trial authors or trial sponsors.

Data analysis

Measures of treatment effect

Studies measuring treatment effect were either dichotomous data, continuous or survival analysis.

Dichotomous data

It was planned that where dichotomous data were reported in a RCT, odds ratios (ORs) and their 95% confidence intervals (CI) would be generated.

Continuous data

It was planned that effect measures for ordinal data reported in a RCT would be assessed as continuous data. The weighted mean difference (WMD) would be generated for ordinal data where the data were provided as a mean and standard deviation. For survival time a hazard ratio with a 95% confidence interval would be calculated.

Missing data

Where data were missing we attempted to contact trial authors. For RCTs identified we planned to use continuous outcomes in which standard deviations (SDs) were not reported, and if no information was available from the authors, that the SDs would be calculated via the standard error of the mean (SEM).

Drop-outs

As drop-outs were potentially more likely to have a negative outcome in this review, it was planned that they would not be included in the main analysis. Instead they would be included, if possible, in any subgroup analysis.

Meta-analysis

It was planned that if data from RCTs were of sufficient quality and sufficiently similar (in terms of patient population, diagnostic criteria, intervention, outcome measure, length of follow-up and type of analysis) they would be combined in a meta-analysis to provide a pooled effect estimate. A fixed-effects model would be used in the first instance. If there was no statistical heterogeneity, a random-effects model would be used to check the robustness of the fixed-effect model. If statistical heterogeneity was observed, the random-effects model would be used *a priori*.

Statistical heterogeneity would be assessed between trials using the chi-squared statistic and I-squared statistic (a chi-squared P value of less than 0.05 or an I-squared value equal to or more than 50% would be considered indicative of heterogeneity).

If heterogeneity was identified, subgroup analysis would be undertaken to explore the lack of homogeneity.

To explore clinical heterogeneity in any meta-analysis and to investigate the effect modification of participants and treatment types, we planned to perform the following subgroup analyses:

Participants

(1) Gender: male or female
(2) Type of dementia whether Alzheimer's disease, vascular dementia, Lewy Body or a rarer syndrome.
(3) Indication for enteral feeding (if data available), including recurrent aspiration pneumonia, abnormal swallowing evaluations, abnormal nutritional parameters, preference of family or carers and advanced directives.
(4) Health care setting or community.
(5) Drop-outs. Responders and remitters to treatment were calculated on the intention-to-treat (ITT) basis. Where participants had withdrawn from the trial before the endpoint, it was assumed they will have experienced the negative outcome by the end of the trial (e.g. failure to respond to treatment). When there was missing data and the method of "last observation carried forward" (LOCF) was used to do an ITT analysis, then the LOCF data was used, with due consideration of the potential bias and uncertainty introduced.

Intervention

Type of enteral feeding intervention. We compared modes of administration i.e. nasogastric feeding versus PEG.

Sensitivity analysis

We planned to perform a sensitivity analyses in order to explore the influence of the following factors by:
1. Excluding unpublished studies (if there were any)
2. Taking account of study quality (low, moderate, or high risk of bias)
3. Excluding studies using the following filters:
(a) diagnostic criteria used for dementia
(b) source of funding (industry versus other)
(c) scales used for measuring effect (validated versus other).

It was planned that outcome data from non-RCT designs would inform this review if no similar interventions had been evaluated under RCT conditions. Presentation of any such data followed the recommendations by the Cochrane EPOC group. Comparison data for each design were reported separately. Results were presented using/calculating a standard method of presentation where possible. Consideration was undertaken of outcome heterogeneity associated with study design.

Publication bias

We planned to explore if sufficient RCTs identified publication bias by using funnel plots.

RESULTS

Description of studies

See Characteristics of included studies ; Characteristics of excluded studies

Results of the search

On 18 April 2008 searches were performed in seven healthcare databases as well as databases containing conference proceedings, theses and trial registers. The total number of hits retrieved (after de-duplication) was 452. To view search strategies used and hits retrieved for each source see Table 1.

Included studies

Study methodologies

No randomized controlled trials were identified. Seven observational controlled cohort studies were identified, six of which included the primary outcome of mortality (Alvarez-Fernandez 2005; Jaul 2006; Meier 2001; Mitchell 1997; Murphy 2003; Nair 2000). The seventh study evaluated nutritional parameters and adverse effects (Peck 1990). The commonest methodology used was that of case note review or analysis of an existing data set comparing those who did and did not receive enteral feeding (Mitchell 1997; Murphy 2003; Peck 1990; Jaul 2006). Three studies used a prospective methodology (Alvarez-Fernandez 2005; Meier 2001; Nair 2000). One study randomly selected controls (Peck 1990).

Participants and setting

The majority of studies were set in the United States (five studies; Meier 2001; Mitchell 1997; Murphy 2003; Nair 2000; Peck 1990) with others in Spain (Alvarez-Fernandez 2005), and Israel (Jaul 2006). Study populations were mainly recruited from in-patient/ tertiary hospital populations (Alvarez-Fernandez 2005; Jaul 2006; Meier 2001; Murphy 2003; Nair 2000) or nursing homes (Mitchell 1997; Peck 1990). The selected studies gave a total sample of 1821 (409 who received enteral feeding and 1467 comparison subjects), however these numbers were mainly influenced by the study of Mitchell 1997 et al with 1386 subjects (135 with enteral feeding and 1251 comparison subjects). The age of subjects ranged from 63 to 107 years and the mean in all studies was over 82 years (two studies did not give this information (Jaul 2006; Murphy 2003)). Study subjects were predominately female, the proportion ranging from 47% (Jaul 2006) to 92.5% (Alvarez-Fernandez 2005), the study by Murphy 2003, which was conducted in a USA Veterans hospital, was all male.

Diagnosis of dementia

Only one study used validated diagnostic criteria (DSM-IV) for the diagnosis of advanced dementia (Alvarez-Fernandez 2005). In two of the other studies, patients were described as having "advanced dementia" and this was then staged, most commonly using the FAST scale (Reisberg 1994) at a severity level of 6d and above (urinary incontinence) (Alvarez-Fernandez 2005; Meier 2001). Peck 1990 used an MMSE score of <23 and the sample will therefore have included participants with various levels of severity of dementia. The Cognitive Performance Scale (Morris 1990), at a cut off of 5 or less (severe cognitive impairment), was used to define subjects with advanced dementia in the studies by Mitchell 1997 and Jaul 2006 used the "cognitive ability" items for self-care activities from the Disability Rating Scale, a scale designed to rate disability in patients with severe head trauma (Rappaport 1982). In one study, patients were described as having "advanced dementia" but no information was given regarding diagnostic criteria or severity staging for dementia (Murphy 2003). In one of the other studies the degree of dementia was not stated but inclusion criteria included documented inadequacy of oral

intake because of cognitive impairment (Nair 2000). None of the studies gave information on diagnostic sub-types of dementia i.e. the proportion of patients with Alzheimer's disease or vascular dementia. In the sixth study, Mitchell 1997, all patients had severe cognitive impairment measured by the Cognitive Performance Scale and of these 72% were reported to have dementia. It is not clear whether the others in the sample had cognitive decline that was caused by other conditions or if they did have a diagnosis of dementia that had not been recorded on the minimum data set referenced for the study. In the study by Jaul 2006, 68% had dementia. In two other studies not all in the control group had dementia, in the study by Peck 1990, 71% had dementia and in the study by Nair 2000 it is unclear. Additionally, the study by Peck 1990 included patients with dementia in the less advanced stages using an MMSE cut off score of 23. It is not clear what proportion of patients within this group had a diagnosis of severe dementia.

Consent

Meier 2001 and Alvarez-Fernandez 2005 obtained consent from a family member, carer or surrogate decision maker. Murphy 2003 undertook a retrospective case note review and they obtained approval from local institutional review board to review patients records. Mitchell 1997 used data from an existing large data set, thus consent and ethics committee institutional review board approval were not obtained. The studies by Peck 1990, Jaul 2006 and Nair 2000 do not contain any information on these issues.

Indication for enteral feeding

Details of the clinical indications for enteral feeding were given in four studies. The commonest indication in the study by Jaul 2006 was "neurologic deficiency (72%) followed by refusal to eat (13%), decreased level of consciousness (8%) and "other" causes (7%). In Nair 2000, the inclusion criterion was a documented inadequacy of oral intake because of cognitive impairment. Peck 1990 gave weight loss (44%) as the commonest indication, followed by refusal to eat (23%), dysphagia (17%) and stroke (15%). Mitchell 1997 examined risk factors for feeding tube placement, rather than clinical indication, in their cohort and in the study by Murphy 2003 all subjects had documented dysphagia. In Nair 2000 all subjects had an inadequate oral intake.

Interventions

In three studies, the intervention was PEG feeding (Meier 2001; Murphy 2003; Nair 2000), one study examined nasogastric feeding (Alvarez-Fernandez 2005) and two studies a combination of interventions; Jaul 2006, 62 patients with NGT, 7 with PEG and Peck 1990, 39 subjects with NGT, 9 with gastrostomy and 4 with jejunostomy. Mitchell 1997 examined "feeding tube placement" but the type is not clearly specified. However, since this study was conducted in the USA it is likely that the very large majority of participants had a gastrostomy or jejunostomy tube as this is usual local practice.

Excluded studies

Nine studies were excluded at full text. Most were excluded as they included patients with a range of conditions with no separate analysis for those in groups where the majority had dementia.

Risk of bias in included studies

All studies have a high risk of bias by the nature of their research design. All studies under-reported key methodological components. In two studies not all participants had dementia (Jaul 2006; Mitchell 1997) and in two other studies it is not clear whether any of the control group had dementia (Nair 2000, Peck 1990). None of the studies reported comparability on a range key characteristics between those in the intervention group and comparison groups. See Table 2 (Newcastle-Ottawa Quality Assessment Scale Cohort Studies_. All studies were further limited in range of their evaluation of enteral feeding outcomes.

Effects of interventions

Primary outcomes

Mortality

Six studies using a range of analysis methods evaluated mortality outcomes. In the study by Jaul 2006, median survival in patients with nasogastric tubes was significantly increased (250 days) compared to those feeding orally (40 days) (log-rank test $P < 0.001$). Cox regression also suggested an increased mortality risk with oral feeding (unadjusted hazard ratio 2.86, 95% CI 1.5 to 5.45), however this association became non-significant after controlling for co-morbidities (dementia, stroke, persistent vegetative state and peripheral vascular disease), adjusted hazard ratio 1.55 (95% CI 0.5 to 1.9), suggesting that the higher mortality in patients with NG feeding could be explained by differing co-morbidity. No other study found a significant association between decreased mortality risk and enteral feeding.

Murphy 2003 used Kaplan-Maier techniques to compare median survival times. They found no significant impact on median survival with PEG fed patients surviving 59 days (range 3 to 365) compared to 60 days (range 2 to 229) with no enteral feeding (log-rank test, $P = 0.37$). Mitchell 1997 found no association between feeding tube status in survival in the unadjusted model (relative risk 1.06, 95% CI, 0.81 to 1.39) or the model adjusted for potential confounders (age <87 years, aspiration, chewing or swallowing problems, stroke, functional impairment, no dementia, pressure sores and resuscitation status) where the relative risk was 0.90 (95% CI, 0.67 to 1.21). Findings from Meier 2001 were similar and median survival times for those with feeding tubes was 195 days (range 21 to 405) and those without feeding tubes 189 days (4 to 1502). Cox analysis (adjusted for a wide range of potential confounders, dementia stage, sex, age, prior hospitalisations, prior pneumonia, degree of involvement of surrogate decision maker, long-term primary care physician, pressure ulcers, residence at home vs. nursing home) gave a hazard ratio for mortality of those who had a feeding tube present on acute admission of 1.20 (95% CI, 0.5 to 2.8) and those who had a feeding tube placed during admission of 0.97 (95% CI, 0.5 to 1.9). Alvarez-Fernandez 2005 found an increased unadjusted mortality risk associated with having a permanent nasogastric tube (risk ratio 3.53, 95% CI, 1.5 to 8.30). In Nair 2000, mortality at six months was higher in patients who had a PEG (44% vs 26%, $P = 0.03$).

Quality of life

None of the studies stated that they measured quality of life, although one reported that over a six month period 71% of 52 patients needed to be physically restrained to prevent extubation,

compared to 55% of those who were not enterally fed. This difference was not statistically significant (Peck 1990).

Secondary outcomes

Nutritional parameters

A range of nutritional parameters was considered by three of the studies: weight, BMI, albumin, haematocrit and cholesterol. Jaul 2006 found that nasogastric feeding had no effect on weight or body mass index. In the study by Peck 1990 48% of those fed by nasogastric tube gained >5 lb compared to 17% in the comparison group. Enteral feeding had no beneficial impact on albumin levels. Jaul 2006 found no significant difference in albumin between nasogastric tube-fed patients (median albumin 29 g/L) and those fed orally (median albumin 31 g/L). Albumin levels significantly decreased in patients who were fed by nasogastric tube (3.29 g/dL) compared to 3.66 g/dL in orally fed patients (Student's t-test, P = 0.043)(Alvarez-Fernandez 2005). This was also found in Nair 2000, where controls had a higher serum albumin than the patients (3.32 ± 0.44 g/dl vs 2.86 ± 0.5 g/dl, P = 0.001). Nasogastric feeding had no significant effect on haematocrit, cholesterol (Alvarez-Fernandez 2005) or haemoglobin levels (Jaul 2006).

Functional parameters

These were not examined as an outcome in any of the studies.

Pressure ulcers

Two studies compared the prevalence of decubitus (pressure) ulcers between those fed enterally and those fed orally. Peck 1990 found that the prevalence of decubitus ulcers in those fed orally was 14% compared to 21% in those fed enterally (nasogastric feeding 20%, gastrostomy 22% and jejunostomy 25%), this difference was non-significant. Jaul 2006 reported that by the end of the study period 42% of those fed orally and 21% of those fed by nasogastric tube had pressure sores (Fisher's exact test, P = 0.065). There was a significant difference in the mean number of pressure sores per patient (0.97 per tube fed patient, compared with 1.92 per orally fed patient, Student's t-test P = 0.03).

Behavioural and psychiatric symptoms of dementia

These were not examined as an outcome in any of the studies.

Adverse events

None of the studies states *a priori* the aim to report on adverse events including incidence of aspiration pneumonia, local complications i.e. local bleeding or infection, systemic complications (i.e. fluid imbalance or overload) or urinary or faecal incontinence or constipation. Two studies do report adverse events. In one, at six months, 58% of enterally fed patients had aspiration pneumonia (54% of those with nasogastric feeding, 67% with gastrostomy and 75% with jejunostomy) compared to 17% of those fed orally (X^2 test P ≤ 0.01 comparison between tube fed and not) and 21% decubitus ulcers compared to 14% who were fed orally (X^2 test P 1.08 a not significant comparison between tube fed and not) Peck 1990. Murphy 2003 reported that one patient of the 23 (4.3%) who had a PEG inserted developed an intra-abdominal abscess resulting in sepsis and death.

DISCUSSION

We found inconclusive evidence that enteral tube feeding provides any benefit in dementia patients in terms of survival time, mortality risk, quality of life, nutritional parameters, physical functioning, and improvement or reduced incidence of pressure ulcers. We found no evaluations on effect on quality of life, physical functionality or behavioural or psychiatric symptoms of dementia. There was little information on adverse events for these invasive procedures, although in one study a patient died after developing sepsis from an abdominal abscess following a PEG insertion. It was notable that the majority of the studies were carried out in the USA and that the patient populations were heterogenous in terms of demographics, place of residence and dementia diagnosis. Only one study used validated diagnostic criteria for dementia, and no studies gave information on the subtypes of dementia. This is particularly relevant as there is an established association between stroke and increased risk for the placement of feeding tubes (Martino 2005) and this will have an impact on outcomes. Disease duration in dementia is notoriously difficult to measure as the disease onset is slow and insidious, no studies were able to control for this. Severity of dementia may be a useful proxy for this, however measures of severity of dementia were also lacking in most studies, thus making it difficult to ascertain both how well matched comparison groups were and the morbidity of the population being studied.

Methodological issues

Ethically and practically, it would be extremely challenging to conduct randomized controlled trials for these interventions. The principle methodology used in included studies was that of a cohort design comparing groups of patients who did and did not receive the intervention. Thus, investigators were unable to be blind to the intervention and there was no evidence of allocation concealment. Selection bias is inevitable and this is associated with the ethical issues surrounding the intervention, for example in one study only people with surrogate decision makers available were recruited (Meier 2001), in another only those recruited with the consent of their family doctor participated (Alvarez-Fernandez 2005). However, it should be noted that this situation is not dissimilar to that which occurs with fully randomized controlled trials involving patients with dementia and their carers.

In these cohort studies "intervention" and "control" groups were not well matched (Peck 1990); information necessary to make judgments regarding this was not given (Alvarez-Fernandez 2005; Jaul 2006; Meier 2001, Murphy 2003,Nair 2000) and differences between comparison groups not controlled for (Peck 1990).

In Mitchell 1997 they correct in their analysis for key confounders. But many of the conclusions of the included studies could also be explained by the problem of confounding-by-indication. For example, the presence of pressure ulcers could be an indication of more severe debility, which might be associated with increased tube feeding. This would explain a higher prevalence of pressure ulcers in tube-fed patients compared with the control group.

We found that mortality was the most common outcome, given in six of seven studies. Few studies measured a full range of clinically relevant outcomes and this may be due to the retrospective nature of some data collection or the use of existing data sets. Of note, there were no attempts to measure quality of life, physical

function, behavioural and psychiatric disorders of dementia, and no objective assessment of discomfort or pain.

Numbers receiving the intervention were small, ranging from 14-135 (median 52) and thus studies may have been underpowered to detect differences between "control" and intervention groups. We were unable to pool data and conduct meta-analysis or examine bias using funnel plots because there were no randomized controlled trials.

If randomized controlled trials of this intervention are difficult, how may these methodological challenges be resolved? One study in our review (Murphy 2003) compared subjects who had surrogates to give consent for enteral feeding versus those who did not as a comparison group. Unfortunately there was limited information regarding the "control" group (whose surrogates refused consent) so it is not clear how well matched they are in terms of age, social class or severity of dementia. If this information were available in future studies this recruitment strategy for comparison/control groups may enable us to give more valid information regarding outcomes.

Pooling data from cohort studies or multi-centre studies may overcome issues with sample size, particularly if a standardised range of outcome data is collected, including those of most relevance to families, carers and patients, for example, quality of life, function and the use of physical and "chemical" restraints. There should also be standardised documentation regarding the indication for feeding tube placement and adverse events.

More accurate definition of the patient group in terms of dementia type, using validated diagnostic criteria such as DSM-IV (APA 1994) or ICD-10 (WHO 1993), and appropriate severity measures for severe dementia i.e. the FAST scale, would also allow more valid comparisons to be made. Several studies included patients with unspecified diagnoses or dementia of unspecified severity and such heterogeneity in included populations limits the interpretation of the findings of this review. Some studies i.e. Mitchell 1997 attempted to control for co-morbidities and data on the number of co-morbidities and their severity would allow for better control of potential confounders. More work is required on the risks and benefits of different types of enteral feeding so that comparisons can be made between nasogastric, PEG and jejunostomy techniques. Finally, because of the legal, social and cultural issues surrounding these interventions, and the variety of settings in which these patients are cared for (at home, residential home, acute hospitals), more data are required from a range of countries and different types of institutions.

Ethical considerations

Enteral tube feeding in advanced dementia is an emotive issue; there remain concerns amongst carers, the public and professionals about "starving to death" frail older people with advanced dementia. This may lead to placement of a feeding tube despite evidence that such intervention may not be effective or beneficial. This is compounded by differing ethical and legal frameworks even within the same country, for example, individual US states have highly variable rates of feeding tube placement because of different federal laws and varying religious beliefs. In addition, factors such as age, gender and ethnicity may affect the course of disease in dementia and the conduct of decision making surrounding interventions (Pasman 2005; Thune-Boyle 2009). Although no data are available from this review to inform the effects of such variations, in clinical practice they are likely to be of importance to attitudes to enteral tube feeding.

Dementia is a neurodegenerative syndrome surrounded by diagnostic uncertainty and often not perceived to be a terminal illness, despite evidence to the contrary (Meier 2001). Evidence from other terminal illnesses suggests that refusal of food and water is not painful (McCann 1994; Meier 2001). More robust evidence on how these interventions impact on quality of life would give more context to the ethical considerations.

Lack of insight and capacity to make autonomous decisions are hallmarks of severe dementia and such patients inevitably are unable to give informed consent for these procedures. This highlights the potential role of advance care planning and decision making to maximise the delivery of high quality and appropriate care to individual patients within this vulnerable group.

AUTHORS' CONCLUSIONS

Implications for practice

Despite the large number of patients receiving this intervention there is insufficient evidence for the effectiveness of enteral feeding for older people with advanced dementia on survival, quality of life, nutrition and pressure ulcers, function and behavioural or psychiatric symptoms of dementia.

Implications for research

Future studies should include larger sample sizes with better matching of control and intervention groups, more data on potential confounders and more precise diagnosis of the type and severity of dementia. Clinically important outcomes such as quality of life should be considered as well as nutritional status and survival. The most appropriate research method would be prospective, comprehensive data collection on very large samples.

This could be through prescription databases or nursing home 'minimum dataset' data. The emotive ethical issues mean that this is an important public health issue. Well-designed, large scale data collection projects in countries where the practice is widespread are therefore needed. Consideration should be given to mandatory reporting requirements.

ACKNOWLEDGEMENTS

We would like to acknowledge the contributions of the consumer reviewers, Jane Perrotta and U. Hla Htay and the peer reviewers of the review's protocol and the review, as well as the advice and help of the Rupert McShane, Helen Collins, other members of the editorial team, and the information specialist, Anna Noel-Storr of the Cochrane Dementia and Cognitive Improvement Group.

REFERENCES

References to studies included in this review

Alvarez-Fernandez 2005 *{published data only}*

Alvarez-Fernandez B, Garcia-Ordonez MA, Martinez-Manzanares C, Gomez-Huelgas R. Survival of a cohort of elderly patients with advanced dementia: nasogastric tube feeding as a risk factor for mortality. *International Journal of Geriatric Psychiatry* 2005;**20**:363-70.

Jaul 2006 *{published data only}*

Jaul E, Singer P, Calderon-Margalit R. Tube feeding in the demented elderly with severe disabilities. *IMAJ* 2006;**8**:870-4.

Meier 2001 *{published data only}*

Meier DE, Ahronheim JC, Morris J, Baskin-Lyons S, Morrison RS. High short-term mortality in hospitalized patients with advanced dementia: Lack of benefit of tube feeding.. *Archives of Internal Medicine* 2001;**161**:594-59.

Mitchell 1997 *{published data only}*

Mitchell SL, Kiely DK, Lipsitz LA. The risk factors and impact on survival of feeding tubes placement in nursing home residents with severe cognitive impairment. *Archives of Internal Medicine* 1997;**157**:327-32.

Murphy 2003 *{published data only}*

Murphy LM, Lipman TO. Percutaneous endoscopic gastrostomy does not prolong survival in patients with dementia. *Archives of Internal Medicine* 2003;**163**:1351-33.

Nair 2000 *{published data only}*

Nair S, Hertan H, Pitchumoni CS. Hypoalbuminaemia is a poor predictor of survival after percutaneous endoscopic gastrostomy in elderly patients with dementia. *The American Journal of Gastroenterology* 2000;**95**:133-6.

Peck 1990 *{published data only}*

Peck A, Cohen CE, Mulvhill MN. Long term enteral feeding of aged demented nursing home patients. *Journal of the American Geriatrics Society* 1990;**38**:1195-8.

References to studies excluded from this review

Berlowitz 1997 *{published data only}*

Berlowitz DR, Brandeis GH, Anderson J, Brand HK. Predictors of pressure ulcer healing among long-term residents. *Journal of the American Geriatrics Society* 1997;**45**:30-4.

Callahan 2000 *{published data only}*

Callahan CM, Haag KM, Weinberger M, Tierney WM, Buchanan NN, Stump TE, et al. Outcomes of percutaneous endoscopic gastrostomy among older adults in a community setting. *Journal of the American Geriatrics Society* 2000;**48**:1048-54.

Ciocon 1988 *{published data only}*

Ciocon JQ, Silverstone FA, Graver M, Foley CJ. Tube feedings in elderly patients. *Archives of Internal Medicine* 1988;**148**:429-33.

Feinberg 1996 *{published data only}*

Feinberg MJ, Knebel J, Tully J. Prandial aspiration and pneumonia in an elderly population followed over 3 years. *Dysphagia* 1996;**11**:104-9.

Fox 1995 *{published data only}*

Fox KA, Mularski RA, Sarfati MR, Brooks ME, Warneke JA, Hunter GC, et al. Aspiration pneumonia following surgically placed feeding tubes. *American Journal of Surgery* 1995;**170**:564-7.

Henderson 1992 *{published data only}*

Henderson CT, Trumbore LS, Mobarhan S, Benya R, Miles TP. Prolonged tube feeding in long-term care, nutritional status and clinical outcomes. *Journal of the American College of Nutrition* 1992;**11**:309-25.

Kaw 1994 *{published data only}*

Kaw M, Sekas G. Long-term follow-up of consequences of percutaneous endoscopic gastrostomy tubes in nursing home patients. *Digestive Diseases and Sciences* 1994;**39**:738-43.

Langmore 2002 *{published data only}*

Langmore SE, Skarupski KA, Park PS, Fries BE. Predictors of aspiration pneumonia in nursing home residents. *Dysphagia* 2002;**17**:298-307.

Loser 1998 *{published data only}*

Loser C, Wolters S, Folson UR. Enteral long-term nutrition via percutaneous endoscopic gastrostomy in 210 patients. *Digestive Diseases and Sciences* 1998;**43**:2549-57.

Additional references

Abuksis 2000

Abuksis G, Mor M, Segal N, Shemesh I, Plout S, Sulkes J, et al. Percutaneous endoscopic gastronomy: High mortality rates in hospitalized patients. *American Journal of Gastroenterology* 2000;**95**(1):128-32.

APA 1994

American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. American Psychiatric Association. 4th Edition. Washington, DC: APA, 1994.

Clarfield 2006

Clarfield AM, Monette J, Bergman H, Monette M, Ben-Israel Y, Caine Y, Charles J, Gordon M, Gore B. Enteral feeding in end-stage dementia: a comparison of religious, ethnic, and national differences in Canada and Israel. *Journal of Gerontology* 2006;**61A**:621-627.

Ferri 2005

Ferri CP, Prince M, Brayne C, Brodaty H, Fratiglioni L, Ganguli M, et al. Global prevalence of dementia: a Delphi consensus study. *Lancet* 2005;**366**:2112.

Finucane 1999

Finucane TE, Christmas C, Travis K. Tube feeding in patients with advanced dementia: a review of the evidence. *JAMA* 1999;**282**(14):1365-70.

Hebert 2003

Hebert LE, Scherr PA, Bienias JL, Bennett DA, Evans DA. Alzheimer disease in the US population. *Archives of Neurology* 2003;**60**:1119-22.

Hendrie 1998

Hendrie HC. Epidemiology of dementia and Alzheimer's disease. *American Journal of Geriatric Psychiatry* 1998;**6**:S3-18.

Higgins 2008

Higgins JPT, Green S, editors. Cochrane Handbook for Systematic Reviews of Interventions Version 5.0.0 [updated February 2008]. The Cochrane Collaboration, 2008. Available from www.cochrane-handbook.org.

Kawas 1998

Kawas CH. Alzheimer's disease. Principles of geriatric medicine and gerontology. 4th Edition. New York: McGraw-Hill, 1998.

Martino 2005

Martino R, Foley N, Bhogal S, Diamant N, Speechley M, Teasell R. Dysphagia after stroke. *Stroke* 2005;**36**:2756-63.

McCann 1994

McCann RM, Hall WJ, Groth-Juncker A. Comfort care for terminally ill patients. The appropriate use of nutrition and hydration. *JAMA* 1994;**272**:1271-5.

Mitchell 2003

Mitchell SL, Teno JM, Roy J, Kabumoto G, Mor V. Clinical and organizational factors associated with feeding tube use among nursing home residents with advanced cognitive impairment. *JAMA* 2003;**290**(1):73-80.

Morris 1990

Morris JN, Hawes C, Fries BE, et al. Designing the National Assessment Instrument for Nursing Homes. *Gerontologist* 1995;**35**:293-307.

Morris 1993

Morris JC. The Clinical Dementia Rating (CDR): current version and scoring rules. *Neurology* 1993;**43**:2414-4.

NIH 1999

National Institute of Health. Progress report on Alzheimer's disease. Report nr 99-4664.. Washington, DC: US Department of Health and Human Services, 1999.

Njegovan 2001

Njegovan V, Hing MM, Mitchell SL, Molnar FJ. The hierarchy of functional loss associated with cognitive decline in older persons. *Journals of Gerontology A. Biological Science and Medical Science* 2001;**56**(10):638-43.

Pasman 2005

Pasman HRW, Onwuteaka-Philipsen BD, Kriegsman DMW, Ooms ME, Ribbe MW, van der Wal G. Discomfort in Nursing Home Patients With Severe Dementia in Whom Artificial Nutrition and Hydration Is Forgone. *Archives of Internal Medicine* 2005;**165**:1729-35.

Rappaport 1982

Rappaport M, Hall KM, Hopkins K, Belleza T, Cope DN. Disability rating scale for severe head trauma patients: coma to community. *Archives of Physical Medicine and Rehabilitation* 1982;**63**:118-23.

Reisberg 1994

Reisberg B, Sclan SG, Franssen E, Kluger A, Ferris S. Dementia staging in chronic care populations. *Alzheimer's Disease and Associated Disorders* 1994;**8**(Suppl 1):S188-205.

Small 1999

Small W. Dementia. Geriatric review syllabus. 4th Edition. Dubuque, IA: Kendall Hunt, 1999.

Stevens 2002

Stevens T, Livingston G, Kitchen G, Manela M, Walker Z, Katona C. Islington study of dementia subtypes in the community. *British Journal of Psychiatry* 2002;**180**:270-6.

The 2002

The A, Pasman R, Onwuteaka-Philipsen B, Ribbe M, van der Wal G. Withholding the artificial administration of fluids and food from elderly people with dementia: ethnographic study. *BMJ* 2002;**325**:1326-31.

Thune-Boyle 2009

Thuné-Boyle ICV, Sampson EL, Jones L, King M, Tookman A, Lee D, Blanchard MR. Challenges to improving end of life care of people with advanced dementia in the UK. Dementia 2009; Vol. In Press.

WHO 1993

World Health Organisation. The ICD-10 classification of mental and behavioural disorders: Diagnostic criteria for research. Geneva: World Health Organisation, 1993.

Wolfson 2001

Wolfson C, Wolfson DB, Asgharian M, M'Lan CE, Ostbye T, Rockwood K, et al. A reevaluation of the duration of survival after the onset of dementia. *New England Journal of Medicine* 2001;**344**:1111-16.

Xie 2008

Xie J, Brayne C, Matthew FE. Medical Research Council Cognitive Function and Ageing Study collaborators. *BMJ* 2008;**336**:258-62.

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Alvarez-Fernandez 2005

Methods	Observational prospective cohort study. Median follow up of 30 months
Participants	67 Spanish community based patients aged 65 years or older (mean age 82.2 years plus or minus 6.7 years) with advanced dementia defined by DSM-IV and stage 7A or above on FAST. Not stated reason for tube feeding. Unclear if those who were tube feed were comparable to those not tube feed. 92.5 % female.
Interventions	14/67 were nasogastric tube fed.
Outcomes	Univariate analysis with log rank test was used to identify factors predicting mortality. Those variables found to be related with survival were included in a cox proportional hazards model. The final model included the following factors; pneumonia during previous year (RR 3.7, P = 0.001), the presence of permanent nasogastric tube (RR 3.5, P = 0.003) and serum albumin level lower then 3.4g/dl (RR 2.9, P = 0.028).
Notes	Limitations: Unclear how comparable those tube fed compared to those not tube fed. Small number tube feed.

Jaul 2006

Methods	Observational prospective cohort study. Followed up for 17 months.
Participants	88 Israeli psychogeriatric inpatients aged 79 ± 9 years. Not all patients were demented (in the tube fed group 68% had dementia). There were significantly more patients in the tube feeding group that were demented (P value 0.002), female (P value 0.019) and the group was older (P value 0.009).
Interventions	62 were fed by nasogastric tube, and 26 orally fed. Indications for tube feeding included difficulty swallowing, refusal to eat and decreased level of consciousness.
Outcomes	Outcomes measured at follow-up were pressure ulcers, survival time and mortality. In the tube fed group 21% had pressure ulcers at follow-up, in the orally fed group 42% had. During follow up 25 (40.3%) of the tube feeding group died. The median survival time was 250 days, survival in the orally fed group was 40 days.
Notes	Limitations: both groups contained a mixed group of psychogeriatric patients limiting strength of any analysis.

Meier 2001

Methods	Prospective observational cohort study. Follow up to potentially 5 years.
Participants	99 American inpatients with advanced dementia (defined as FAST stage 6d or greater) and an available surrogate decision maker (to make decision on patient's behalf on participating in study). Median age 84 years (range 63-100). 81% were female, 15 had advanced directives.
Interventions	Tube feeding of which at least 51 patients had a PEG inserted. Since this study was conducted in the USA it is likely that the majority of participants had a gastrostomy or jejunostomy tube as this is usual local practice.

Meier 2001 *(Continued)*

	17% admitted to hospital with tube already in place, new tube placed in 50% (51/99), 31% left hospital without a feeding tube. Reason for tube not stated.
Outcomes	In stepwise logistic regression tube feeding was not associated with survival (P = 0.90).
Notes	Limitations: unclear how comparable were demented patients who were tube fed with those that weren't.

Mitchell 1997

Methods	Prospective observational cohort study. Follow up to 24 months
Participants	1386 American nursing home residents 65 or older with recent progression to severe cognitive impairment, using a score of 5 or less at baseline but who progressed at some point during the next 24 months to a score of 6 on the Cognitive Performance Scale. Researchers state that although the majority of cognitive disability in the group was likely to be caused by dementia, other conditions may have caused the residents decline in cognitive status. Median age 87 years, range 65-107. 75.6% female.
Interventions	135/1386 Patients fed via feeding tube placement were compared with those who did not have a tube.
Outcomes	Survival analysis: after adjusting for potential confounders (age <87 years, aspiration, chewing or swallowing problems, stroke, functional impairment, no dementia, pressure ulcers and DNR status) feeding tube placement was not significantly associated with survival (RR 0.90, 95% CI 0.67 to 1.21).
Notes	Limitations: It is not established that all patients have dementia, and it is not established how similar the groups were.

Murphy 2003

Methods	Retrospective observational cohort study. Follow up to 2 years.
Participants	All consultations for PEG tube placement over 24 months in patients with dementia. Male patients with advanced dementia (as documented in the medical notes), dysphagia and life expectancy considered to be at least 30 days and no contraindication to conscious sedation and no other disease contributing to dysphagia. Age of patients not provided.
Interventions	Percutaneous endoscopic gastrostomy (PEG) was performed in 23 patients. In 18 patients who met the medical criteria the surrogate decision maker refused placement. No details per group on baseline demographics are provided.
Outcomes	A Kaplan-Meier survival curve was used to compare median survival between patients who received a PEG tube and patients where PEG tube placement was refused. The median survival for 23 patients who underwent PEG was 59 days and in 18 patients who did not undergo PEG was 60 days, P value 0.37. There was one major complication in the group that under went PEG - an intra-abdominal abscess, resulting in sepsis and death.
Notes	Lack of clarity on how comparable the two groups were

Nair 2000

Methods	Observational prospective cohort with control group. Follow-up 180 days
Participants	American hospital patients. Intervention: 55 elderly patients with dementia and inadequate oral intake (because of their cognitive impairment) referred for PEG placement. 42/55 female. In those at end of study had died the mean age was 82.8 years and in those alive the mean was 83.8 years. Control: Included 33 patients from the geriatric division who did not have a PEG. The patients in the control group and the intervention group were comparable in age and gender
Interventions	Percutaneous endoscopic gastrostomy
Outcomes	Survival benefit. Chi squared test and Fisher exact test. Mortality at 6 months was higher in patients who had a PEG (44% vs 26%, P = 0.03)
Notes	It is not reported whether patients in the control group have dementia

Peck 1990

Methods	Observational retrospective cohort with control group. Follow-up 6 months.
Participants	American nursing home patients. 52 intubated patients with dementia (Mini Mental Status Examination) MMS scores of zero) were compared with 52 non-intubated patients of mixed diseases. In this group 71% were demented (scoring less than 23 on the MMS), and had resided in the nursing facility for a shorter time (mean 36 months compared to 66). In the intubated group the mean age was 87 years, and 45/52 were female.
Interventions	Long term enteral feeding (nasogastric, gastrostomy and jejunostomy tubes - does not state number of patients per mode of feeding), 26/52 had been in place for more than a year (range 1 month to 6.4 years). Reasons for feeding were weight loss 23/52 (44%), refusal to eat 12/52 (23%), dysphagia 9/52 (17%) and stroke 8/52 (15%).
Outcomes	In the tube fed group at 6 months: 25/52 (48%) increased in weight, 58% had episodes of aspiration pneumonia, 21% decubitus ulcers, and 71% were restrained to prevent extubation.
Notes	Limitation: non intubated group were not comparable on disease.

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Berlowitz 1997	No separate analysis on included patients with dementia
Callahan 2000	Compared dementia with other illness groups
Ciocon 1988	No separate analysis on included patients with dementia
Feinberg 1996	No separate analysis on included patients with dementia
Fox 1995	No separate analysis on included patients with dementia

Study	Reason for exclusion
Henderson 1992	No separate analysis on included patients with dementia
Kaw 1994	No separate analysis on included patients with dementia
Langmore 2002	No separate analysis on included patients with dementia
Loser 1998	No separate analysis on included patients with dementia

ADDITIONAL TABLES

Table 1. Search strategies and numbers retrieved

Source searched	Search strategy	Hits retrieved
Medline (Ovid SP)	1. dement$.mp.	174
	2. alzheimer$.mp.	
	3. dementia/	
	4. alzheimer disease/	
	5. enteral nutrition/	
	6. nutritional support/	
	7. percutaneous feeding.mp.	
	8. artificial feeding.mp.	
	9. artificial hydration.mp.	
	10. endoscopic gastrostomy.mp.	
	11. tube feeding.mp.	
	12. peg.mp.	
	13. enteral feeding.mp.	
	14. stomach tube$.mp.	
	15. forced feeding.mp.	
	16. percutaneous feeding.mp.	
	17. artificial nutrition.mp.	
	18. nutritional support.mp.	
	19. enteral nutrition.mp.	
	20. feeding methods.mp.	
	21. tube$.mp.	
	22. 1 or 2 or 3 or 4	
	23. 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21	

Table 1. Search strategies and numbers retrieved *(Continued)*

	24. 22 and 23	
	25. randomized controlled trial.pt.	
	26. controlled clinical trial.pt.	
	27. randomized.ab.	
	28. randomly.ab.	
	29. trial.ab.	
	30. groups.ab.	
	31. survey$.tw.	
	32. evaluat$.tw.	
	33. 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32	
	34. humans.sh.	
	35. 33 and 34	
	36. 24 and 35	
Embase (Ovid SP)	1. dement$.mp.	337
	2. alzheimer$.mp.	
	3. dementia/	
	4. alzheimer disease/	
	5. enteral nutrition/	
	6. nutritional support/	
	7. percutaneous feeding.mp.	
	8. artificial feeding.mp.	
	9. artificial hydration.mp.	
	10. endoscopic gastrostomy.mp.	
	11. tube feeding.mp.	
	12. peg.mp.	
	13. enteral feeding.mp.	
	14. stomach tube$.mp.	
	15. forced feeding.mp.	
	16. percutaneous feeding.mp.	
	17. artificial nutrition.mp.	
	18. nutritional support.mp.	
	19. enteral nutrition.mp.	
	20. feeding methods.mp.	
	21. tube$.mp.	

Table 1. Search strategies and numbers retrieved *(Continued)*

	22. 1 or 2 or 3 or 4	
	23. 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21	
	24. 22 and 23	
	25. randomized controlled trial.sh.	
	26. controlled clinical trial.sh.	
	27. randomized.tw.	
	28. randomly.ab.	
	29. trial.ab.	
	30. groups.ab.	
	31. survey$.tw.	
	32. evaluat$.tw.	
	33. stud$.tw.	
	34. 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33	
	35. 34 and 24	
Cinahl (Ovid SP)	1. dement$.mp.	47
	2. alzheimer$.mp.	
	3. dementia/	
	4. alzheimer disease/	
	5. enteral nutrition/	
	6. nutritional support/	
	7. percutaneous feeding.mp.	
	8. artificial feeding.mp.	
	9. artificial hydration.mp.	
	10. endoscopic gastrostomy.mp.	
	11. tube feeding.mp.	
	12. peg.mp.	
	13. enteral feeding.mp.	
	14. stomach tube$.mp.	
	15. forced feeding.mp.	
	16. percutaneous feeding.mp.	
	17. artificial nutrition.mp.	
	18. nutritional support.mp.	
	19. enteral nutrition.mp.	
	20. feeding methods.mp.	

Table 1. Search strategies and numbers retrieved *(Continued)*

	21. tube$.mp.	
	22. 1 or 2 or 3 or 4	
	23. 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21	
	24. 22 and 23	
	25. clinical trials/	
	26. randomized controlled trial.tw.	
	27. randomized.ab.	
	28. randomly.ab.	
	29. trial.ab.	
	30. groups.ab.	
	31. survey$.tw.	
	32. evaluat$.tw.	
	33. 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32	
	34. 24 and 33	
PsycInfo (Ovid SP)	1. dement$.mp.	38
	2. alzheimer$.mp.	
	3. dementia/	
	4. alzheimer disease/	
	5. enteral nutrition/	
	6. nutritional support/	
	7. percutaneous feeding.mp.	
	8. artificial feeding.mp.	
	9. artificial hydration.mp.	
	10. endoscopic gastrostomy.mp.	
	11. tube feeding.mp.	
	12. peg.mp.	
	13. enteral feeding.mp.	
	14. stomach tube$.mp.	
	15. forced feeding.mp.	
	16. percutaneous feeding.mp.	
	17. artificial nutrition.mp.	
	18. nutritional support.mp.	
	19. enteral nutrition.mp.	
	20. feeding methods.mp.	

Table 1. Search strategies and numbers retrieved *(Continued)*

	21. tube$.mp.	
	22. 1 or 2 or 3 or 4	
	23. 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21	
	24. 22 and 23	
	25. clinical trials/	
	26. randomized controlled trial.tw.	
	27. randomized.ab.	
	28. randomly.ab.	
	29. trial.ab.	
	30. groups.ab.	
	31. survey$.tw.	
	32. evaluat$.tw.	
	33. 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32	
	34. 24 and 33	
The Cochrane Library	1. dementia (In All Text)	14
	2. alzheimer* (In All Text)	
	3. "enteral nutrition" (In All Text)	
	4. "nutritional support" (In All Text)	
	5. "percutaneous feeding" (In All Text)	
	6. "artificial feeding" (In All Text)	
	7. "artificial hydration" (In All Text)	
	8. "endoscopic gastrostomy" (In All Text)	
	9. "tube feeding" (In All Text)	
	10. peg (In All Text)	
	11. "enteral feeding" (In All Text)	
	12. "stomach tub*" (In All Text)	
	13. "forced feeding" (In All Text)	
	14. "percutaneous feeding" (In All Text)	
	15. "artificial nutrition" (In All Text)	
	16. "nutritional support" (In All Text)	
	17. "feeding methods" (In All Text)	
	18. tube* (In All Text)	
	19. #1 OR #2	

Table 1. Search strategies and numbers retrieved *(Continued)*

	20. #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 21. #19 AND #20	
LILACs	dementia and (enteral nutrition OR nutritional support OR percutaneous feeding OR artificial feeding OR artificial hydration OR endoscopic gastrostomy OR tube feeding OR peg OR enteral feeding OR stomach tube OR forced feeding OR percutaneous feeding OR artificial nutrition OR nutritional support OR enteral nutrition OR feeding methods OR tube)	2
SR CDCIG	enteral nutrition OR nutritional support OR percutaneous feeding OR artificial feeding OR artificial hydration OR endoscopic gastrostomy OR tube feeding OR peg OR enteral feeding OR stomach tube OR forced feeding OR percutaneous feeding OR artificial nutrition OR nutritional support OR enteral nutrition OR feeding methods OR tube	19
ClinicalTrials.gov	dementia and (enteral nutrition OR nutritional support OR percutaneous feeding OR artificial feeding OR artificial hydration OR endoscopic gastrostomy OR tube feeding OR peg OR enteral feeding OR stomach tube OR forced feeding OR percutaneous feeding OR artificial nutrition OR nutritional support OR enteral nutrition OR feeding methods OR tube)	1
mRCT	(dementia or alzheimer%) AND (enteral or feeding or nutrition)	0

Table 2. Newcastle-Ottawa Quality Assessment Scale Cohort Studies

Reference	Representative of the exposed cohort	Selection of the non exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohort on the basis of design or analysis	Ascertainment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow-up of cohorts
Alvarez-Fernandez 2005	Yes	Drawn from the same community	Secure record	Yes	Unclear	Record linkage	Yes	Complete
Jaul 2006	Somewhat representative	Drawn from the same community	Secure record	Yes	No	Record linkage	Yes	Complete
Meier 2001	Yes	Unclear	Secure record	No	Unclear	Record linkage	Yes	Complete
Mitchell 1997	Yes	Drawn from the same community	Secure record	Yes	Unclear	Record linkage	Yes	Unclear
Murphy 2003	Somewhat representative	Drawn from the same community	Secure record	Yes	Unclear	Record linkage	Yes	Complete
Nair 2000	Yes	Unclear	Secure record	Yes	No	Record linkage	Yes	Subjects lost to follow-up unlikely (as few) to introduce bias
Peck 1990	Yes	Drawn from the same community	Secure record	No	No	Record linkage	Yes	Complete

CONTRIBUTIONS OF AUTHORS

ELS: All correspondence; drafting of review versions, selection of trials and interpretation of data analysis.

BC: Drafting of review versions, selection of trials, extraction of data; entry of data and interpretation of data analysis.

LJ: Drafting of review versions, selection of trials.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- Marie Curie Cancer Care, UK.
- Barnet Enfield and Haringey Mental Health Trust, UK.

External sources

- No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

No randomized controlled trials were found and the identified studies included a highly heterogenous population and range of outcomes, thus we were unable to conduct any of the planned analyses including meta-analysis, sensitivity analysis or identification of bias.

INDEX TERMS

Medical Subject Headings (MeSH)

*Enteral Nutrition [mortality]; Dementia [*complications] [mortality]; Malnutrition [*prevention & control]; Pressure Ulcer [epidemiology]; Treatment Outcome

MeSH check words

Aged; Humans