Enteral tube feeding for people with severe dementia (Review)


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Enteral tube feeding for people with severe dementia

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ABSTRACT

Background
The balance of benefits and harms associated with enteral tube feeding for people with severe dementia is not clear. An increasing number of guidelines highlight the lack of evidenced benefit and potential risks of enteral tube feeding. In some areas of the world, the use of enteral tube feeding is decreasing, and in other areas it is increasing.

Objectives
To assess the effectiveness and safety of enteral tube feeding for people with severe dementia who develop problems with eating and swallowing or who have reduced food and fluid intake.

Search methods
We searched ALOIS, the Cochrane Dementia and Cognitive Improvement Group’s register, MEDLINE, Embase, four other databases and two trials registers on 14 April 2021.

Selection criteria
We included randomised controlled trials (RCTs), or controlled non-randomised studies. Our population of interest was adults of any age with a diagnosis of primary degenerative dementia of any cause, with severe cognitive and functional impairment, and poor nutritional intake. Eligible studies evaluated the effectiveness and complications of enteral tube feeding via a nasogastric or gastrostomy tube, or via jejunal post-pyloric feeding, in comparison with standard care or enhanced standard care, such as an intervention to promote oral intake. Our primary outcomes were survival time, quality of life, and pressure ulcers.

Data collection and analysis
Three review authors screened citations and two review authors assessed full texts of potentially eligible studies against inclusion criteria. One review author extracted data, which were then checked independently by a second review author. We used the 'Risk Of Bias In Non-randomised Studies of Interventions' (ROBINS-I) tool to assess the risk of bias in the included studies. Risk of confounding was assessed against a pre-agreed list of key potential confounding variables. Our primary outcomes were survival time, quality of life, and pressure ulcers. Results were not suitable for meta-analysis, so we presented them narratively. We presented results separately for studies of
Enteral tube feeding for people with severe dementia

What is tube feeding?

Somebody who can’t eat or drink through their mouth may be given liquid food through a tube into their stomach. This is called enteral tube feeding. The tube passes through their nose into their stomach (a nasogastric tube), or is inserted into the stomach through a small cut in their belly (percutaneous endoscopic gastrostomy or PEG).

Main results

We found no eligible RCTs. We included fourteen controlled, non-randomised studies. All the included studies compared outcomes between groups of people who had been assigned to enteral tube feeding or oral feeding by prior decision of a healthcare professional. Some studies controlled for a range of confounding factors, but there were high or very high risks of bias due to confounding in all studies, and high or critical risks of selection bias in some studies.

Four studies with 36,816 participants assessed the effect of PEG feeding on survival time. None found any evidence of effects on survival time (low-certainty evidence).

Three of four studies using mixed or unspecified enteral tube feeding methods in 310 participants (227 enteral tube feeding, 83 no enteral tube feeding) found them to be associated with longer survival time. The fourth study (1386 participants: 135 enteral tube feeding, 1251 no enteral tube feeding) found no evidence of an effect. The certainty of this body of evidence is very low.

One study of PEG feeding (4421 participants: 1585 PEG, 2836 no enteral tube feeding) found PEG feeding increased the risk of pressure ulcers (moderate-certainty evidence). Two of three studies reported an increase in the number of pressure ulcers in those receiving mixed or unspecified enteral tube feeding (234 participants: 88 enteral tube feeding, 146 no enteral tube feeding). The third study found no effect (very-low certainty evidence).

Two studies of nasogastric tube feeding did not report data on survival time or pressure ulcers.

None of the included studies assessed quality of life.

Only one study, using mixed methods of enteral tube feeding, reported on pain and comfort, finding no difference between groups. In the same study, a higher proportion of carers reported very heavy burden in the enteral tube feeding group compared to no enteral tube feeding.

Two studies assessed the effect of nasogastric tube feeding on mortality (236 participants: 144 nasogastric group, 92 no enteral tube feeding). One study of 67 participants (14 nasogastric, 53 no enteral tube feeding) found nasogastric feeding was associated with increased mortality risk. The second study found no difference in mortality between groups. The certainty of this evidence is very low. Results on mortality for those using PEG or mixed methods of enteral tube feeding were mixed and the certainty of evidence was very low. There was some evidence from two studies for enteral tube feeding improving nutritional parameters, but this was very low-certainty evidence. Five studies reported a variety of harm-related outcomes with inconsistent results. The balance of evidence suggested increased risk of pneumonia with enteral tube feeding.

None of the included studies assessed behavioural and psychological symptoms of dementia.

Authors’ conclusions

We found no evidence that tube feeding improves survival; improves quality of life; reduces pain; reduces mortality; decreases behavioural and psychological symptoms of dementia; leads to better nourishment; improves family or carer outcomes such as depression, anxiety, carer burden, or satisfaction with care; and no indication of harm. We found some evidence that there is a clinically significant risk of pressure ulcers from enteral tube feeding. Future research should focus on better reporting and matching of control and intervention groups, and clearly defined interventions, measuring all the outcomes referred to here.

Plain Language Summary

Enteral tube feeding for people with severe dementia

What are the advantages and problems of tube feeding people with severe dementia?

Key messages

Tube feeding may not increase the length of time people with severe dementia live compared to no tube feeding. The risk of developing a pressure sore is probably higher with a feeding tube than with no tube. No studies looked at quality of life. We need more and better studies to investigate tube feeding people with severe dementia. Future studies should focus on a broader range of outcomes including, pain, quality of life and the impact on carers.

What is tube feeding?

Somebody who can’t eat or drink through their mouth may be given liquid food through a tube into their stomach. This is called enteral tube feeding. The tube passes through their nose into their stomach (a nasogastric tube), or is inserted into the stomach through a small cut in their belly (percutaneous endoscopic gastrostomy or PEG).
Why is this important for people with dementia?

People with dementia often have difficulties eating and drinking. During the early stages of dementia, they may forget to eat, chew food without swallowing, or be confused at mealtimes. Some people experience changes in the taste and smell of food. In the later stages of dementia, people often have difficulties swallowing. It can be difficult to ensure they receive appropriate food and fluids.

People with severe dementia need full-time care, and it is often their families who care for them. It is difficult to decide whether or not to tube-feed someone with dementia because the feeding tube can be uncomfortable or even painful, and may cause other unwanted effects such as pneumonia, worsen bowel or bladder control, as well as bleeding, swelling and infection. People with severe dementia may be confused or distressed by the tube and may try to remove it.

What did we want to find out?

We wanted to know whether tube feeding helps people with severe dementia who have problems with eating and swallowing.

We were interested in the effect of tube feeding on:

- how long people lived;
- their quality of life (well-being); and
- the development or healing of pressure sores (also known as bed sores).

What did we do?

We searched for studies that investigated whether:

- PEG compared to no tube;
- a nasogastric tube compared to no tube; or
- PEG, nasogastric and other types of tube feeding compared to no tube

was effective and whether tube feeding caused any unwanted effects in adults of any age with severe dementia and poor intake of food and drink.

We compared and summarised the results of the studies and rated our confidence in the evidence, based on factors such as study methods and sizes.

What did we find?

We included 14 studies that included 49,714 participants. Of these, 6203 were tube-fed and 43,511 were not. Participants with no feeding tube were given standard care or standard care with extra treatments to encourage eating and drinking.

Main results

In people with severe dementia, compared to no tube feeding:

- PEG may make no difference to how long people live (4 studies, 36,816 people), and leads to a small increase in the chance of developing pressure sores (1 study, 4421 people). We don’t know if nasogastric tube feeding increases the length of time people live or increases their chance of developing pressure sores, because none of our included studies gave information about these points. Studies of people with either PEG or nasogastric tubes showed tube feeding may increase the length of time people live (4 studies, 1696 people), and may slightly increase the chance of developing pressure sores (3 studies, 351 people).

None of our included studies reported quality of life.

What are the limitations of the evidence?

We have moderate confidence in our finding that pressure ulcers were more common in people who were fed with a PEG tube. However, we have little to very little confidence for our other findings.

Three main factors reduced our confidence in the evidence. Firstly, people in the studies were not randomly placed into different treatment groups. This means that differences between the groups could be due to differences between people rather than between the treatments. However, due to ethical considerations it would be very difficult to do this in future studies. Secondly, results were very inconsistent across the different studies. Finally, some studies were very small.

The results of further research could differ from the results of this review.

How up to date is this evidence?

The evidence is up to date to 14 April 2021.
### Summary of findings 1. PEG compared to no enteral tube feeding for people with severe dementia

**Patient or population:** people with severe dementia  
**Setting:** all settings  
**Intervention:** PEG  
**Comparison:** no enteral tube feeding

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Impact</th>
<th>Nº of participants (studies)</th>
<th>Certainty of the evidence (GRADE)</th>
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</thead>
</table>
| Survival time<sup>a</sup> | 2 studies reported no benefits to median survival times (59 days vs 60 days, and 195 days vs 189 days).  
Follow-up: 18 months (Ticinesi 2016), 12 months (Teno 2012a).  
Follow-up timing is not specified in 2 studies (Meier 2001; Murphy 2003) | 36,816 (4 studies) | ⊕⊕⊝ ⊝ ⊝ ⊝ LOW<sup>b</sup> |
| Mortality<sup>c</sup> | 2 studies reported mortality with mixed findings. 1 study reported no evidence of a difference in mortality after 180 days between groups (52% vs 50%). 1 study reported higher 18-month mortality in participants receiving the intervention (70% vs 40%).  
Follow-up: 180 days (Hwang 2014), 18 months (Ticinesi 2016) | 6445 (2 studies) | ⊕⊕⊝⊝ ⊝ ⊝ ⊝ VERY LOW<sup>b,d</sup> |
| Quality of life | Not measured | - | - |
| Pressure ulcers<sup>e</sup> | 1 study found PEG feeding was associated with an increase in risk of developing pressure ulcers (OR 2.27, 95% CI 1.95 to 2.65)  
Follow-up: within 30 days (Teno 2012b) | 4421 (1 study) | ⊕⊕⊕⊝ MODERATE<sup>f</sup> |
| Pain and comfort | Not measured | - | - |
| Improvement of nutritional status | Not measured | - | - |

<sup>a</sup>The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

CI: confidence interval; RR: risk ratio; OR: odds ratio

**GRADE Working Group grades of evidence**

- **High certainty:** we are very confident that the true effect lies close to that of the estimate of the effect.  
- **Moderate certainty:** we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.  
- **Low certainty:** our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.  
- **Very low certainty:** we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of the effect.
Survival time measured via retrospective medical notes review, interviews with caregivers, and minimum data set (MDS).

Downgraded by two levels due to serious risk of bias; participants not randomly assigned to ‘intervention’ and ‘no intervention’ groups so not possible to control for all confounders; risk of confounding may be present; not all studies controlled for all important confounders. One study has critical risk of bias in selection of participants into the study.

Mortality reported from MDS and interviews with caregivers.

Downgraded by one level due to inconsistency of findings reported.

Pressure ulcers reported from MDS, original outcome measure not known. Assessed with: stage 2 or higher.

Downgraded by one level due to moderate risk of bias in confounding; participants not randomly assigned to ‘intervention’ and ‘no intervention’ groups so not possible to control for all confounders; risk of confounding may be present. However, propensity score matching was used to control for confounding and selection bias in this study, and this is a large sample.

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### Summary of findings 2. Nasogastric tubes compared to no enteral tube feeding for people with severe dementia

#### Nasogastric tubes compared to no enteral tube feeding for people with severe dementia

**Patient or population:** people with severe dementia  
**Setting:** all settings  
**Intervention:** nasogastric tubes  
**Comparison:** no enteral tube feeding  

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Impact</th>
<th>№ of participants (studies)</th>
<th>Certainty of the evidence (GRADE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Survival time</td>
<td>Not measured</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
| Mortality<sup>a</sup>  
Follow-up: every 3 months (participants were enrolled between 1 February 1999 and 2 June 1999 and followed until 15 July 2001 (Álvarez-Fernández 2005), with a median follow-up of 832 days); 12 months (Chou 2020). | 2 studies reported mixed evidence. 1 study reported an increased unadjusted mortality risk associated with having a permanent nasogastric tube (RR 3.33, 95% CI 1.5 to 8.30). 1 study reported no difference in mortality between groups (adjusted OR = 2.38, 95% CI 0.58 to 9.70). | 236 (2 studies) | ⊕⊕⊕⊝ VERY LOW b,c |
| Quality of life | Not measured | - | - |
| Pressure ulcers | Not measured | - | - |
| Pain and comfort | Not measured | - | - |
| Improvement of nutritional parameters (nutrition)<sup>d</sup>  
Follow-up: baseline only from previous 12 months (Álvarez-Fernández 2005) | 1 study showed a reduction in albumin levels in the nasogastric tube group (3.29 g/dL) compared to orally fed participants (3.66 g/dL). No evidence of an effect was seen for haematocrit, cholesterol or changes in anthropometric data (arm circumference, tricipital skinfold or muscle area of the arm). | 67 (1 study) | ⊕⊕⊕⊝ VERY LOW b,c |

<sup>a</sup>The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

CI: confidence interval; RR: risk ratio; OR: odds ratio

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**GRADE Working Group grades of evidence**

**High certainty:** we are very confident that the true effect lies close to that of the estimate of the effect.  
**Moderate certainty:** we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
**Low certainty:** our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

**Very low certainty:** we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

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\(^a\)Mortality method of data collection not reported.

\(^b\)Downgraded by one level due to inconsistency of findings reported.

\(^c\)Downgraded by two levels due to serious risk of bias: participants not randomly assigned to 'intervention' and 'no intervention' groups so not possible to control for all confounders, and there was limited controlling for confounding with not all important confounders controlled for. There was critical risk of bias in selection of participants.

\(^d\)Nutritional parameters were evaluated from anthropometric and laboratory data.

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**Summary of findings 3. Mixed (nasogastric or PEG) or unspecified enteral tube feeding for people with severe dementia**

**Mixed (nasogastric or PEG) or unspecified enteral tube feeding for people with severe dementia**

**Patient or population:** people with severe dementia

**Setting:** all settings

**Intervention:** any enteral feeding

**Comparison:** no enteral tube feeding

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Impact</th>
<th>Nr of participants (studies)</th>
<th>Certainty of the evidence (GRADE)</th>
</tr>
</thead>
</table>
| Survival time\(^d\) | 3 studies observed longer survival times in intervention group:  
- 1 study reported median survival of 695 days in intervention group compared to 75 days for no tube feeding group.  
- 1 study reported average survival of 237 days for intervention group compared to 184 days for no tube feeding group.  
- 1 study reported median survival of 23 months compared to 2 months in those without a tube.  
In contrast, 1 study found no evidence of improved survival times with enteral feeding (RR 0.90, 95% CI 0.67 to 1.21). | 1696 (4 studies) | ☐☐☐☐ VERY LOW \(^b,c\) |
| Mortality\(^d\) | 1 study reported no evidence of a difference between groups for mortality at 22 months (42% vs 27%). | 234 (2 studies) | ☐☐☐☐ VERY LOW \(^b,e\) |
| Quality of Life | Not measured. | - | - |
| Pressure ulcers\(^f\) | 2 studies reported an increase in number of pressure ulcers in the intervention group (2.74 vs 1.31, and 26% vs. 12%). 1 study reported no difference in pressure ulcer prevalence between those who had enteral tube feeding (34%) vs. those who had no enteral tube feeding (38%). | 351 (3 studies) | ☐☐☐☐ VERY LOW \(^b,e\) |
### Pain and comfort

| No follow-up (Bentur 2015) | 1 study reported no evidence of a difference between groups for CAD-EOLD scores (29 vs. 32). | 117 (1 study) | ☬☹☹☹ VERY LOW e,i |

### Improvement of nutritional parameters (Nutrition)

| Follow-up: every 6 months (Arinzon 2008) | 1 study reported improvement in blood count, renal function tests and electrolytes, hydration status, serum osmolarity and in serum proteins, but not in serum cholesterol and CRP levels. | 167 (1 study) | ☬☹☹☹ VERY LOW e,i |

*The risk in the intervention group*(and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; RR: risk ratio; OR: odds ratio

### GRADE Working Group grades of evidence

- **High certainty**: we are very confident that the true effect lies close to that of the estimate of the effect.
- **Moderate certainty**: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
- **Low certainty**: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
- **Very low certainty**: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

### CRP: C-reactive protein

- Survival time measured via questionnaires with medical staff, MDS, interviews with caregivers.
- Downgraded by one level due to inconsistency of findings reported.
- Downgraded by two levels due to serious risk of bias, participants not randomly assigned to “intervention” and “no intervention groups” so not possible to control for all confounders, risk of confounding may be present, not all studies control for all important confounders. There was critical risk of bias in selection of participants in two studies.
- Mortality method of data collection not reported.
- Downgraded by two levels due to serious risk of bias, participants not randomly assigned to “intervention” and “no intervention groups” so not possible to control for all confounders, risk of confounding may be present, study did not control for confounders. There was critical risk of bias in selection of participants.
- Pressure ulcers measured according to 2007 National pressure Ulcer Advisory Panel’s staging system, and not reported.
- Downgraded by two levels due to serious risk of bias, participants not randomly assigned to “intervention” and “no intervention groups” so not possible to control for all confounders, risk of confounding may be present, no studies controlled for confounders. There was critical risk of bias in selection of participants in all studies.
- Pain and comfort measured using the Comfort Assessment in Dying End-Of-Life in Dementia (CAD-EOLD) scale.
- Downgraded by one level due to imprecision, based on single study of small sample size.
- Nutritional parameters measured using laboratory investigation and anthropometric assessment.
BACKGROUND
Description of the condition

Dementia is a syndrome of cognitive decline that leads to impairment in two or more cognitive domains, including memory, executive functions, attention, language, and visuospatial abilities (Bayer 2010). The cognitive impairment causes functional decline, interfering with an individual's ability to conduct activities of daily living (World Health Organization 2018). Most dementias are caused by progressive neurodegenerative conditions. The most common cause of dementia is Alzheimer's disease, followed by vascular dementia (World Health Organization 2012). Mixed dementias (with more than one underlying cause) are also common (Alzheimer's Disease International 2009; Livingston 2013). The progression of dementia is highly variable between individuals and is often complicated by other health conditions. Prognosis is difficult to predict. Median survival has been estimated at 4.1 years (Xie 2008).

Survival times from the point of diagnosis in primary care are estimated to be 6.7 years in those aged 60 to 69 years, dropping to 1.9 years in those diagnosed aged 90 years and over (Rait 2010). Dementia is associated with the fastest rise in serious health-related suffering, and the number of people living with dementia requiring palliative care is expected to increase four-fold by 2060 (Sleeman 2019).

Currently, an estimated 50 million people live with dementia worldwide, and this is expected to rise to 152 million in 2050 (World Health Organization 2019). In 2015 there were an estimated 9.9 million new diagnoses of dementia globally each year, equating to a new person receiving the diagnosis every 3.2 seconds (Alzheimer’s Disease International 2015). The numbers of people living with dementia are higher in East Asia than anywhere else in the world (9.8 million), followed by Western Europe (7.5 million), South Asia (5.1 million), and North America (4.8 million) (Alzheimer’s Disease International 2015). This trend suggests that, by 2050, there will be a 264% increase of people living with dementia in low-income countries, 223% in lower middle-income countries, 227% in upper middle-income countries, and 116% in high-income countries (Alzheimer's Disease International 2015; Matthews 2013).

People living with dementia become increasingly reliant on those around them, usually family members, for support with activities of daily living. In the early stages, most types of dementia are characterised by changes in memory and other higher cognitive functions, such as communication (e.g. difficulty finding the right words), disorientation, and difficulty with household tasks (Bayer 2010). Symptoms progress differently in each person, but generally, the person with dementia will become increasingly forgetful and need help with personal care and communication. He or she may also develop changes in behaviour, such as disinhibition or aggression, or mental health symptoms such as hallucinations. In the severe stages, a person living with dementia becomes completely reliant on others. Common symptoms in severe dementia include immobility, double incontinence, agitation, and pain (Samson 2018). Nutritional status can impact on the incidence, progression, and severity of pressure ulcers, which can be common among older adults and those with severe dementia.

Difficulties with eating are common among people with dementia (Mitchell 2016; Samson 2018); these may be noticed before a formal diagnosis is made. It can be hard for people with dementia to maintain their weight or to drink enough. During the early stages of dementia, problems may be caused by the person forgetting to eat, chewing food without swallowing, or becoming disoriented at mealtimes. There may be changes in how food and the dining environment is perceived, including altered taste and smell of food, which may make it unappetising (Kai 2015). In the later stages of dementia, people may develop physical difficulties swallowing; for example, difficulties managing the food properly once it is in the mouth (oral phase dysphagia), or food or drink going down the 'wrong way' into the lungs (aspiration) when swallowing (pharyngeal phase dysphagia) (Volkert 2015). They may also lose the automatic swallowing reflex. Cohort studies have found up to 86% of people living with advanced dementia will have difficulties with eating or swallowing in the last six months of life (Mitchell 2016). Swallowing difficulties may be more problematic among people with vascular dementia, where there is a greater risk of stroke, but there is little literature on the prevalence of swallowing difficulties by dementia type.

Swallowing difficulties may not always indicate the terminal stages of dementia. Over 91% of people with dementia will be living with at least one co-morbid or concurrent long-term health condition (Browne 2017), including stroke (Bunn 2014), which could affect swallowing abilities in the earlier stages of dementia. Acute illness - for example, infections such as pneumonia or urinary tract infections (UTI) - may also temporarily impair swallowing ability.

Description of the intervention

Whether or not to intervene by feeding artificially via an enteral tube (passed through the nose or abdomen) is a common clinical dilemma facing those who care for people with severe dementia (Brooke 2015; Davies 2016; Davies 2018; De 2019; Mathew 2016; Watt 2019).

In this Cochrane Review, we define 'enteral tube feeding' as the administration of food via a nasogastric tube, via a percutaneous endoscopic gastrostomy (PEG) tube or via jejunal post-pyloric feeding. We exclude intravenous administration of fluids from this review because this is more commonly used as a short-term intervention during episodes of acute physical illness.

How the intervention might work

In nasogastric feeding, the tube is passed through the nose and down to the stomach via the oesophagus. In PEG, the feeding tube is passed through an endoscope, down the oesophagus and into the stomach. It is then guided out through an incision in the abdominal wall. Jejunal post-pyloric feeding is a method of feeding directly into the small bowel where the feeding tube is passed through the nose, oesophagus, stomach, and into the jejunum. Enteral tube feeding may be perceived to be a method of managing malnutrition and weight loss, reducing the risk of aspiration associated with oral feeding, preventing pressure ulcers through improving nutritional status, or simply increasing quality of life and comfort. Alternatively, enteral tube feeding may be a temporary intervention while managing intercurrent physical illness, such as pneumonia and other infections, where swallowing may be temporarily impaired.

Why it is important to do this review

Difficulties with eating and drinking are challenging for all those involved, including the person living with dementia, their family,
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The decision to intervene with enteral tube feeding is complex and emotive (Braun 2005; Volkert 2015). In most societies, providing food or feeding someone is seen as a sign of care and has ‘symbolic significance’ (Volkert 2015). Not providing food or nutrition can be seen as a symbol of neglect, allowing the person to go hungry or ‘starve to death’ (Hoefer 2000). There is additional complexity because people with severe dementia lack the capacity to make this decision for themselves. Depending on the laws in their country, it may then be made in their ‘best interests’ by others. The use of enteral tube feeding has implications for the dignity and personhood of the individual. Professionals and family carers may have conflicting concerns regarding using tube feeding. They may think it can prolong life, increase nutritional status, and prevent complications (Punchik 2018; Snyder 2013). Families may perceive that a lack of enteral tube feeding when someone cannot swallow or eat causes starvation, and not intervening may be considered a form of euthanasia (Gil 2018).

The evidence about effects of enteral tube feeding is contradictory and long-term use of this intervention is not encouraged. Previous studies, including the earlier Cochrane Review, found no evidence that enteral tube feeding was effective for increasing survival, improving quality of life, improving nutritional parameters (measured with blood tests), or decreasing pressure ulcers (American Geriatrics Society 2014; Sampson 2009).

There is evidence that enteral tube feeding may increase mortality and morbidity, and reduce quality of life (Cintrá 2014). Studies have demonstrated that enteral tube feeding is associated with increased discomfort, aspiration pneumonia, and worsening of urinary and faecal incontinence (Cloonan 1988; Finucane 1996; Odom 2003). Incontinence increases pressure ulcer risk, and there is also evidence that enteral tube feeding increases the risk of pressure ulcers and does not aid the healing process (Teno 2012d). Finally, nasal necrosis is associated with prolonged use of nasogastric tubes (Lai 2001).

PEG surgical procedures are invasive, may cause distress and discomfort, and risk bowel perforation, localised bleeding, inflammation, and infection. A study of deaths following PEG tube insertion in 719 people with predominantly neurological diagnoses in the UK found that 2% died on the day the PEG was inserted and 43% died within seven days. In 19% of cases, the procedure was regarded as futile by an expert panel (Johnston 2008). PEG can be particularly problematic for someone with dementia who may not recognise the device, may be distressed by it, and may attempt to remove the tube. To reduce this risk, individuals may need to be restrained either physically (e.g. through the use of ‘mittens’) or chemically (e.g. through sedation). Others, however, have argued that the evidence of harm is unclear, and that PEG may not increase mortality in people with dementia (Brooke 2015).

Although there are increasing numbers of recommendations that highlight the lack of evidenced benefit and potential risks for enteral tube feeding (American Geriatrics Society 2014; Sampson 2009; Van der Steen 2014), debate continues on this issue (Van der Steen 2014). An absence of evidence does not mean the intervention may not be effective or appropriate for some people, and ruling out this intervention for all people with severe dementia prevents clinicians from delivering individually-tailored care (Regnard 2010). Trends in practice in this area vary in different parts of the world. For example, there is decreasing use of enteral tube feeding in the UK and the USA (Mitchell 2016), but there appears to be increasing use in other countries, such as Taiwan (Chang 2016).

Policy and guidance documents, including a decision aid developed as part of the 2018 dementia guideline published by the National Institute for Health and Care Excellence (NICE) in the UK (NICE 2018), have been based on a Cochrane Review that is 12 years old (Sampson 2009). With more studies published in the intervening years, the current review - which focuses on severe dementia in all ages - will impact clinical and policy practice.

OBJECTIVES

To assess the effectiveness and safety of enteral tube feeding for people with severe dementia who develop problems with eating and swallowing or who have reduced food and fluid intake.

METHODS

Criteria for considering studies for this review

Types of studies

We included any randomised controlled trials (RCTs), controlled non-randomised studies that compared enteral tube feeding with no intervention, or usual treatment or care, or with another active intervention. Studies could be conducted in any healthcare setting (including acute hospitals), long-term care settings (nursing, residential or other care homes), or in participants’ own homes.

Types of participants

We included adults of any age and gender with: (a) a clinical diagnosis of primary degenerative dementia of any cause made according to validated diagnostic criteria, such as Diagnostic and Statistical Manual 5th edition (DSM-5) (APA 2013) or International Classification of Diseases 10th edition (ICD-10) (World Health Organization 1993); (b) severe cognitive and functional impairment, defined either by a recognised and validated tool (e.g. stage 7A or above on the Functional Assessment Staging Tool (FAST) tool (speak five to six words during day, doubly incontinent) (Reisberg 1994), Clinical Dementia Rating (CDR) Scale score of 3 (no significant function, severe memory loss, oriented to person only, unable to make judgements or solve problems, requires much help with personal care, frequent incontinence) (Hughes 1982), Cognitive Performance Scale score 5 or 6 (based on scores for decision making, memory, eating performance and ability to make self understood) (Morris 1994)), or by clinical assessment; and (c) a report of poor nutritional intake.
We included studies with a mixed population where a separate analysis was conducted on those with severe dementia, or where the mixed population included 50% or more with severe dementia.

**Types of interventions**

Eligible interventions were enteral tube feeding via a nasogastric tube, via a gastrostomy tube, or via jejunal post-pyloric feeding to deliver nutrition. We excluded studies of oral dietary supplementation. Comparators could include no intervention or standard care, waiting list, or enhanced standard care, including another active intervention to promote oral intake (e.g. provision of finger food or a textured, modified diet).

**Types of outcome measures**

**Primary outcomes**

This review focused on three primary outcomes:

- survival time (measured by the time-to-event post-intervention);
- quality of life (measured by a recognised and validated quality of life scale or tool, such as the quality of life in late-stage dementia (QUALID) scale (Weiner 2000), or the Dementia Quality of Life scale (Dem-QoL) (Smith 2007));
- pressure ulcers.

**Secondary outcomes**

Secondary outcomes were:

- pain and comfort measured with validated scales;
- mortality;
- behavioural and psychological symptoms of dementia (indicators of distress), measured using a validated scale (e.g. the Neuropsychiatric Inventory (NPI)) (Cummings 1997);
- nutritional parameters (e.g. albumin levels);
- family carer outcomes, such as depression, anxiety, carer burden, satisfaction with care, or increased sense of competence measured using validated scales (e.g. Hospital Anxiety and Depression Scale (Zigmond 1983), Beck Depression Inventory (Beck 1996), Zarit Burden Interview (Zarit 1980), Sense of Competence Questionnaire (Schepers 2012), Satisfaction With Care at the End Of Life in Dementia (SWC-EOLD)) (Volicer 2001);
- harm-related outcomes (adverse events) such as:
  - aspiration pneumonia;
  - gastrointestinal and urinary symptoms (e.g. constipation, reflux, urinary/faecal incontinence);
  - local bleeding;
  - infections;
  - systemic complications (e.g. fluid imbalance or overload);
  - feeding tube problems (i.e. blocking or need for tube to be re-sited).

**Search methods for identification of studies**

**Electronic searches**

We searched ALOIS (www.medicine.ox.ac.uk/alois), which is the Cochrane Dementia and Cognitive Improvement Group's Specialised Register on 14 April 2021.

ALOIS is maintained by the Information Specialists of the Cochrane Dementia and Cognitive Improvement Group. It contains studies in the areas of dementia (prevention and treatment), mild cognitive impairment, and cognitive improvement. The studies are identified from:

- monthly searches of a number of major healthcare databases: MEDLINE, Embase, CINAHL (Cumulative Index to Nursing and Allied Health Literature), PsycINFO, and LILACS (Latin American and Caribbean Health Science Information database);
- monthly searches of a number of trial registers: ISRCTN; UMIN (Japan’s Trial Register); the World Health Organization (WHO) portal (which covers ClinicalTrials.gov, ISRCTN, the Chinese Clinical Trials Register, the German Clinical Trials Register, the Iranian Registry of Clinical Trials, the Netherlands National Trials Register, and others);
- quarterly searches of the Cochrane Library’s Central Register of Controlled Trials (CENTRAL);
- six-monthly searches of a number of grey literature sources: ISI Web of Knowledge Conference Proceedings; Index to Theses; Australasian Digital Theses.

To view a list of all sources searched for ALOIS, see About ALOIS on the ALOIS website (alois.medsci.ox.ac.uk/).

Details of the search strategies used for the retrieval of reports of trials from the healthcare databases, CENTRAL, and conference proceedings can be viewed in the ‘Methods used in reviews’ section within the editorial information about the Cochrane Dementia and Cognitive Improvement Group.

In addition, we searched MEDLINE, Embase, and PsycINFO, all via Ovid SP, CINAHL via EBSCOhost, Web of Science’s Core Collection via ISI Web of Science, LILACS via BIREME, ClinicalTrials.gov at www.clinicaltrials.gov and the World Health Organization’s meta trials register ICTRP at apps.who.int/trialsearch.aspx. We searched these sources on 13 December 2019 and 14 April 2021 to ensure that we captured non-RCTs, controlled before-and-after studies, and interrupted time-series studies. The search strategies and the number of hits retrieved can be seen in Appendix 1 and see Figure 1.
There were no language restrictions on the search.
Searching other resources
We contacted experts in the field by posting calls for evidence to identify any further trial evaluations that were not identified in the citation databases searches. We searched the conference proceedings of the European Association for Palliative Care, and International Psychogeriatrics Association Conference. We screened reference lists of included articles and tracked citations.

Data collection and analysis
Selection of studies
Three review authors (YB-M, AF, ND) screened all citations. Each review author independently classified the citations into three groups: ‘exclude’, ‘potentially relevant’ or ‘unsure’. We excluded papers classified by two review authors as ‘exclude’. We retrieved the full-text versions of all ‘potentially relevant’ and ‘unsure’ citations for definitive assessment of eligibility. One review author (YBM, ND) conducted a comprehensive assessment of the full texts against the inclusion criteria. A second review author (ND, ELS, YBM) checked the decisions. We resolved any disagreements through discussion, involving another review author (VV) if necessary. We documented our justification for excluding studies at the full-text stage and illustrated the study selection process in a PRISMA diagram.

Data extraction and management
We designed a data extraction form for the review. Where possible, we obtained the following information for each included study.

- The number of eligible participants and reasons why participants were not included in the study.
- The number of participants evaluated at follow-up(s) and what the follow-up time points were.
- Participant characteristics including age, sex, co-morbidities, diagnosis and type of dementia, advance decision or proxy decision maker status, type of healthcare or community setting, stage of disease when enteral tube feeding or other intervention was considered, and reason for enteral tube feeding or other intervention.
- Study design features.
- Enteral nutrition intervention including dosage, duration, and mode, including the need to restrain the participant.
- Comparison intervention, including duration and mode.
- Outcome data at all time points, including how outcome was measured, and the mean or categorical scores of the primary and secondary outcomes.

For non-randomised studies, we followed guidance from the Cochrane Handbook for Systematic Reviews of Interventions (Reeves 2020), and also extracted, where possible:

- information on study design, using the checklist from the Cochrane Non-Randomised Studies Methods Group (NRSMG) (Reeves 2017). This tool aims to identify key design features, such as presence of comparator group, participant/cluster allocation, what parts of the study were prospective, what variables were included, and whether comparability between groups was assessed. We recorded this information in a table (Table 1);
- data on confounding factors considered and methods used to control for confounding. We used the ‘Risk Of Bias In Non-randomised Studies of Interventions’ (ROBINS-I) tool as a template for this information (Sterne 2019);
- comparability of groups on confounding factors considered;
- data about multiple effect estimates (both unadjusted and adjusted estimates, if available).

One review author (ND, VV, ELS, KM, CS, AF, or BC) extracted data, which was checked by a second review author (ND, ELS, or VV). In the case of any disagreement or discrepancy, a third review author was consulted. The third review author was selected according to the expertise required to make the relevant decision.

Assessment of risk of bias in included studies
Two review authors (ND, VV or ELS) independently assessed the risk of bias related to study design or conduct in each of the outcomes in the summary of findings tables for each of the included studies, using the ROBINS-I tool (Sterne 2019). We resolved disagreements by consensus (Higgins 2020).

We assessed the risk of bias associated with factors pre-intervention (bias due to confounding and selection of participants), at intervention (information bias) and post-intervention (bias due to confounding, selection, information, and reporting). We judged the risk of bias in each domain and the overall risk of bias for each outcome in each study based on ROBINS-I guidance (Sterne 2019). We used the following overall risk of bias criteria.

- Low risk of bias: the study is judged to be at low risk of bias for all domains.
- Moderate risk of bias: the study is judged to be at low or moderate risk of bias for all domains.
- Serious risk of bias: the study is judged to be at serious risk of bias in at least one domain, but not at critical risk of bias in any domain.
- Critical risk of bias: the study is judged to be at critical risk of bias in at least one domain.
- No information: there is no clear indication that the study is at serious or critical risk of bias and there is a lack of information in one or more key domains of bias.

For some non-RCT study designs, we used additional guidance from the Cochrane Effective Practice and Organisation of Care (EPOC) group (EPOC 2017).

We incorporated the results of the risk of bias assessment into the review through systematic narrative description and commentary about each item, and reported these per outcome per study in Table 2; Table 3; Table 4; Table 5; Table 6; Table 7; Table 8; Table 9; Table 10; Table 11; Figure 2; Figure 3; Figure 4; Figure 5; Figure 6; Figure 7; Figure 8; Figure 9; Figure 10; Figure 11.
Figure 2. ROBINS-I assessments for: PEG Tube versus no enteral tube for people with severe dementia. Outcome: survival time

<table>
<thead>
<tr>
<th>Study</th>
<th>D1</th>
<th>D2</th>
<th>D3</th>
<th>D4</th>
<th>D5</th>
<th>D6</th>
<th>D7</th>
<th>Overall</th>
</tr>
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<tbody>
<tr>
<td>Teno 2012a</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Murphy 2003</td>
<td>x</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>?</td>
<td>+</td>
<td>+</td>
<td>x</td>
</tr>
<tr>
<td>Ticinesi 2016</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>x</td>
<td>+</td>
<td>+</td>
<td>x</td>
</tr>
<tr>
<td>Meier 2001</td>
<td>-</td>
<td>!</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>!</td>
</tr>
</tbody>
</table>

Domains:
D1: Bias due to confounding.
D2: Bias due to selection of participants.
D3: Bias in classification of interventions.
D4: Bias due to deviations from intended interventions.
D5: Bias due to missing data.
D6: Bias in measurement of outcomes.
D7: Bias in selection of the reported result.

Judgement:
- Critical
- Serious
- Moderate
- Low
- No information
Figure 3. ROBINS-I assessments for: PEG tube versus no enteral tube for people with severe dementia. Outcome: pressure ulcers

<table>
<thead>
<tr>
<th>Study</th>
<th>D1</th>
<th>D2</th>
<th>D3</th>
<th>D4</th>
<th>D5</th>
<th>D6</th>
<th>D7</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Teno 2012b</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>X</td>
<td>+</td>
<td>-</td>
</tr>
</tbody>
</table>

Domains:
D1: Bias due to confounding.
D2: Bias due to selection of participants.
D3: Bias in classification of interventions.
D4: Bias due to deviations from intended interventions.
D5: Bias due to missing data.
D6: Bias in measurement of outcomes.
D7: Bias in selection of the reported result.

Judgement
- Serious
- Moderate
+ Low

Figure 4. ROBINS-I assessments for: PEG tube versus no enteral tube for people with severe dementia. Outcome: mortality

<table>
<thead>
<tr>
<th>Study</th>
<th>D1</th>
<th>D2</th>
<th>D3</th>
<th>D4</th>
<th>D5</th>
<th>D6</th>
<th>D7</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ticinesi 2018</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>X</td>
<td>+</td>
<td>+</td>
<td>X</td>
</tr>
<tr>
<td>Hwang 2014</td>
<td>X</td>
<td>X</td>
<td>+</td>
<td>+</td>
<td>?</td>
<td>+</td>
<td>+</td>
<td>X</td>
</tr>
</tbody>
</table>

Domains:
D1: Bias due to confounding.
D2: Bias due to selection of participants.
D3: Bias in classification of interventions.
D4: Bias due to deviations from intended interventions.
D5: Bias due to missing data.
D6: Bias in measurement of outcomes.
D7: Bias in selection of the reported result.

Judgement
- Serious
- Moderate
+ Low
? No information
Figure 5. ROBINS-I assessments for: nasogastric tube versus no enteral tube for people with severe dementia. Outcome: mortality

Figure 6. ROBINS-I assessments for: nasogastric tube versus no enteral tube for people with severe dementia. Outcome: nutritional parameters
Figure 7. ROBINS-I assessments for: mixed (nasogastric or PEG) or unspecified enteral tube feeding for people with severe dementia. Outcome: survival time

<table>
<thead>
<tr>
<th>Study</th>
<th>D1</th>
<th>D2</th>
<th>D3</th>
<th>D4</th>
<th>D5</th>
<th>D6</th>
<th>D7</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Takenoshita 2017</td>
<td>X</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>?</td>
<td>+</td>
<td>+</td>
<td>X</td>
</tr>
<tr>
<td>Takayama 2017</td>
<td>X</td>
<td>!</td>
<td>+</td>
<td>+</td>
<td>?</td>
<td>+</td>
<td>+</td>
<td>!</td>
</tr>
<tr>
<td>Mitchell 1997</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Cintra 2014</td>
<td>X</td>
<td>!</td>
<td>-</td>
<td>+</td>
<td>?</td>
<td>+</td>
<td>+</td>
<td>!</td>
</tr>
</tbody>
</table>

Domains:
- D1: Bias due to confounding.
- D2: Bias due to selection of participants.
- D3: Bias in classification of interventions.
- D4: Bias due to deviations from intended interventions.
- D5: Bias due to missing data.
- D6: Bias in measurement of outcomes.
- D7: Bias in selection of the reported result.

Judgement:
- Critical
- Serious
- Moderate
- Low
- No information
Figure 8. ROBINS-I assessments for: mixed (nasogastric or PEG) or unspecified enteral tube feeding for people with severe dementia. Outcome: pressure ulcer

<table>
<thead>
<tr>
<th>Study</th>
<th>D1</th>
<th>D2</th>
<th>D3</th>
<th>D4</th>
<th>D5</th>
<th>D6</th>
<th>D7</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bentur 2015</td>
<td>✗</td>
<td>!</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>✗</td>
<td>+</td>
<td>✗ !</td>
</tr>
<tr>
<td>Arinzon 2008</td>
<td>✗</td>
<td>!</td>
<td>+</td>
<td>+</td>
<td>?</td>
<td>-</td>
<td>+</td>
<td>✗ !</td>
</tr>
<tr>
<td>Cintra 2014</td>
<td>✗</td>
<td>!</td>
<td>-</td>
<td>+</td>
<td>?</td>
<td>X</td>
<td>+</td>
<td>✗ !</td>
</tr>
</tbody>
</table>

Domains:
D1: Bias due to confounding.
D2: Bias due to selection of participants.
D3: Bias in classification of interventions.
D4: Bias due to deviations from intended interventions.
D5: Bias due to missing data.
D6: Bias in measurement of outcomes.
D7: Bias in selection of the reported result.

Judgement
- Critical
- Serious
- Moderate
- Low
- No information

Figure 9. ROBINS-I assessments for: mixed (nasogastric or PEG) or unspecified enteral tube feeding for people with severe dementia. Outcome: pain and comfort

<table>
<thead>
<tr>
<th>Study</th>
<th>D1</th>
<th>D2</th>
<th>D3</th>
<th>D4</th>
<th>D5</th>
<th>D6</th>
<th>D7</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bentur 2015</td>
<td>✗</td>
<td>!</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>✗</td>
<td>+</td>
<td>✗ !</td>
</tr>
</tbody>
</table>

Domains:
D1: Bias due to confounding.
D2: Bias due to selection of participants.
D3: Bias in classification of interventions.
D4: Bias due to deviations from intended interventions.
D5: Bias due to missing data.
D6: Bias in measurement of outcomes.
D7: Bias in selection of the reported result.

Judgement
- Critical
- Serious
- Low
We identified the most important confounders for all outcomes before completing risk of bias assessments, as part of the ROBINS-I process, with discussions amongst the clinical members of the research team and experts. These confounders were: age, gender, ethnicity, co-morbidities, dementia severity, usual place of residence, frailty, presence of advance directive or Do Not Attempt Cardiopulmonary Resuscitation (DNACPR) order, presence of pressure ulcers (not when assessing outcomes of pressure ulcers), function in activities of daily living (ADL), and body mass index (BMI).
Measures of treatment effect

We report study results organised by mode of enteral tube feeding and comparator evaluated. We used the following measures of treatment effects.

- Dichotomous data: for dichotomous data we extracted or calculated relative risks (RRs) or odds ratios (ORs) and their 95% confidence intervals (CIs). Because we did not calculate any pooled effect estimates, we did not calculate numbers needed to treat for an additional beneficial outcome (NTNB) or numbers needed to treat for an additional harmful outcome (NTNH) for our primary outcomes, as planned in the review protocol.
- Continuous data: for effects measured as ordinal data, we treated these as continuous data. We planned to extract or calculate the mean difference (MD) from the means and standard deviations (SD), if sufficient data were given.
- Time-to-event data: we extracted hazard ratios (HRs) and their 95% CIs. If these were not reported, we estimated them from other reported statistics (Parmar 1998), or if this was not possible, we reported a summary statistic of the survival time data in each group.

Unit of analysis issues

In our handling of included studies, we considered issues that may impact on findings, using guidance from the Cochrane Handbook for Systematic Reviews of Interventions (Deeks 2020). No unit of analysis issues were encountered. In all studies, the unit of analysis was individual participants who did, or did not, receive enteral tube feeding.

Dealing with missing data

Given the nature of the population, we anticipated a significant amount of missing data as a result of attrition due to participants' death. We did not undertake any imputation for missing participant data.

For studies using continuous outcomes in which SDs were not reported, and we were unable to calculate the SD from the standard error of the mean (SEM), we planned to calculate or impute this using relevant data to be combined in a meta-analysis.

We did not exclude studies on the basis of missing data.

Assessment of heterogeneity

We assessed clinical heterogeneity between studies, considering differences in outcomes, outcome measures, intervention characteristics (e.g. type, timing) and co-morbidities. We did not conduct any meta-analyses and therefore did not use any statistical tests of heterogeneity.

Assessment of reporting biases

Because we did not conduct any meta-analyses, we were unable to use funnel plots to assess for possible reporting biases.

Data synthesis

We did not conduct any meta-analyses, due to limited evidence as a result of only one study providing evidence for many of the outcomes in the comparisons, or different outcomes and diversity in methodology when more than one study provided evidence. Instead, we undertook a narrative synthesis of the included studies, following the 'Synthesis without meta-analysis (SWIM) in systematic reviews: reporting guideline' (Campbell 2020).

Due to the heterogeneity in the data, interventions and outcomes, it was feasible only to describe results; we were not able to do any additional analysis such as combining P values, or calculating summary statistics of intervention effect estimates (for example, median, interquartile range).

Subgroup analysis and investigation of heterogeneity

Where we identified heterogeneity in a meta-analysis, we planned to undertake subgroup analyses to investigate its possible sources. Subgroup analysis explores whether the overall effect varies with different trial populations, and with the nature and content of the interventions. In this update, we planned the following subgroup analysis.

- Delivery method (e.g. nasogastric, PEG, or jejunal post-pyloric feeding).
- Type of dementia disease (e.g. Alzheimer’s, vascular dementia).
- Clinical setting (e.g. care home or hospital).

Due to the absence of meta-analysis, formal subgroup analysis was not possible. However, we explored the effects of nasogastric and PEG enteral tube feeding in separate narrative comparisons.

Sensitivity analysis

We did not conduct any sensitivity analyses.

Summary of findings and assessment of the certainty of the evidence

We include a summary of findings table for each of three comparisons, to present the main findings in a tabular format, including the certainty of evidence using the GRADE approach. We summarise the effect estimates from each study, the quantity and overall certainty of evidence for all primary outcomes and key secondary outcomes.

The three comparisons are:

- PEG tube feeding compared to no enteral tube feeding;
- nasogastric tube feeding compared to no enteral tube feeding;
- mixed (nasogastric or PEG) or unspecified enteral tube feeding compared to no enteral tube feeding.

We present these outcomes in the summary of findings tables, regardless of the availability of data:

- survival time;
- quality of life;
- pressure ulcers;
- mortality;
- nutritional parameters;
- pain and comfort.

Two review authors (a combination of ND, ELS and VV) independently assessed the certainty of the evidence for all outcomes using the GRADE approach. We used the guidelines provided in Chapter 14 of the Cochrane Handbook for Systematic Reviews of Interventions (Schünemann 2020).
The GRADE system uses the following criteria for assigning a certainty level to a body of evidence (Schünemann 2020).

- High: randomised trials; or double-upgraded observational studies.
- Moderate: downgraded randomised trials; or upgraded observational studies.
- Low: double-downgraded randomised trials; or observational studies.
- Very low: triple-downgraded randomised trials; or downgraded observational studies; or case series/case reports.

The GRADE approach uses five considerations (study limitations, consistency of effect, imprecision, indirectness, and publication bias) to assess the certainty of the body of evidence for each outcome. The GRADE system uses the following criteria for assigning grade of evidence.

- High: we are very confident that the true effect lies close to that of the estimate of the effect.
- Moderate: we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of effect, but there is a possibility that it is substantially different.
- Low: our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.
- Very low: we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

Factors that may decrease the certainty level of a body of evidence are:

- limitations in the design and implementation of available studies suggesting high likelihood of bias;
- indirectness of evidence (indirect population, intervention, control, outcomes);
- unexplained heterogeneity or inconsistency of results (including problems with subgroup analyses);
- imprecision of results (wide CIs);
- high probability of publication bias (0.7854 to 1.1359).

Factors that may increase the certainty level of a body of evidence are:

- large magnitude of effect;
- all plausible confounding would reduce a demonstrated effect or suggest a spurious effect when results show no effect;
- dose-response gradient.

We decreased the grade rating by one (-1) or two (-2) (up to a maximum of -3 to ‘very low’) if we identified:

- serious (-1) or very serious (-2) limitations to study quality;
- important inconsistency (-1);
- some (-1) or major (-2) uncertainty about directness;
- imprecise or sparse data (-1);
- high probability of reporting bias (-1).

In certain circumstances, we adjusted the overall rating for a particular outcome as recommended by GRADE guidelines (Guyatt 2013).

RESULTS
Description of studies

Results of the search

Our electronic database search identified a total of 8009 records. The research team found one additional reference. The total number of records after de-duplication was 5862. The Cochrane Dementia and Cognitive Improvement Group’s information specialist performed a first assessment, removing obviously irrelevant records. This left 652 records for the author team to assess. We identified a further eight duplicates and excluded 513 citations based on title and abstract. We identified 18 conference abstracts for which we were unable to obtain enough information to make a decision on eligibility (by searching for further citations and attempting to contact authors); we placed these in the category ‘Awaiting classification’. We examined 118 records in full text. We identified fourteen studies (19 records, five of these were earlier conference abstracts: Cintra 2013; Meier 2000; Teno 2011; Teno 2012c; Ticinesi 2015) for inclusion after full-text screening. Figure 1 describes the study identification process.

Included studies

See the Characteristics of included studies.

Design

None of the included studies were RCTs. We used the checklist from the Cochrane Non-Randomised Studies Methods Group (NRSMG) to describe the design of the included studies (Reeves 2017); see Table 1 for details of the checklist signalling questions.

The intervention and comparator were allocated to individuals in all studies.

Outcome data were available after intervention or comparator only for most studies (Arinzon 2008; Bentur 2015; Chou 2020; Cintra 2014; Hwang 2014; Meier 2001; Mitchell 1997; Murphy 2003; Takayama 2017; Teno 2012a; Teno 2012b; Ticinesi 2016). In two studies, outcome data were available both before (once) and after intervention or comparator (Takenoshita 2017; Álvarez-Fernández 2005).

In all studies, the intervention effect was estimated by the difference between groups of individuals receiving the intervention or those receiving the comparison.

Five studies controlled for confounding (Meier 2001; Mitchell 1997; Teno 2012a Teno 2012b; Ticinesi 2016), with a further five studies controlling for some but not all important confounders relevant to the outcomes, as detailed in the methods section of this review (Álvarez-Fernández 2005; Cintra 2014; Chou 2020; Takayama 2017; Takenoshita 2017). Hwang 2014 does not explicitly state in the paper which covariates were included in their propensity scoring used to control for bias. Three did not control for confounding for any outcomes measured (Arinzon 2008; Bentur 2015; Murphy 2003).
Participants in all studies were allocated to the intervention as a result of a clinical decision by a healthcare decision maker or practitioner.

In only one study were actions or choices - leading to an individual or cluster becoming a member of a group - carried out after the study was designed (Meier 2001). Therefore in the majority of studies participants were already allocated to receive the intervention or not before the study started. In three studies, pre-intervention characterisation of individuals was carried out after the study was designed (Álvarez-Fernández 2005, Takenoshita 2017, Ticinesi 2016), and in nine studies, assessment of outcomes was completed after the study was designed (Álvarez-Fernández 2005; Arinzon 2008; Bentur 2015; Chou 2020; Cintra 2014; Meier 2001; Takayama 2017; Takenoshita 2017; Ticinesi 2016). These descriptions give as an indication of when the intervention was implemented.

Finally, no studies measured both potential confounders and outcome variables before the intervention. Six studies measured neither before the intervention (Álvarez-Fernández 2005; Arinzon 2008; Bentur 2015; Chou 2020; Cintra 2014; Murphy 2003), seven measured only potential confounders (Hwang 2014; Meier 2001; Mitchell 1997; Takayama 2017; Teno 2012a; Teno 2012b; Ticinesi 2016), and one measured only outcome variables before the intervention (Takenoshita 2017).

Participants and settings

Demographics

Sample sizes of included studies ranged from 41 (Murphy 2003), to 36,492 participants (Teno 2012a). Of the 49,714 participants in the included studies, 6203 received enteral tube feeding and 43,511 were comparison participants.

As would be expected from this population, most study participants were female, with proportions of females in cohorts ranging from 53.4% (Takenoshita 2017), to 95.2% (Álvarez-Fernández 2005). Murphy 2003 was conducted in a veterans’ hospital and all study participants were male. Age of study participants, where given, ranged from 63 to 100 years, and the mean age in all studies was over 76 years.

Settings

Six studies were from the USA (Hwang 2014; Meier 2001; Mitchell 1997; Murphy 2003; Teno 2012a; Teno 2012b), two from Israel (Arinzon 2008; Bentur 2015), two from Japan (Takayama 2017; Takenoshita 2017), and one study each from Brazil (Cintra 2014), Italy (Ticinesi 2016), Spain (Álvarez-Fernández 2005) and Taiwan (Chou 2020).

Study settings may be described according to where the enteral feeding was initiated (for PEG feeding, usually an acute general hospital because of the nature of the intervention) and by where participants were followed up for outcome assessment.

Eight studies described cohorts where enteral feeding, usually by PEG tube insertion, was initiated in acute general hospitals (Hwang 2014; Meier 2001; Mitchell 1997; Murphy 2003; Teno 2012a; Teno 2012b; Ticinesi 2016). Participant follow-up data were then obtained following discharge to a care home in four studies (Hwang 2014; Mitchell 1997; Teno 2012a; Teno 2012b). Ticinesi 2016 followed up 48% of participants in their own homes and 52% in nursing homes after acute hospital PEG tube insertion. Chou 2020 followed up participants in their own home. Meier 2001 followed up participants during the acute hospital admission until discharge or death in hospital. Murphy 2003 describe a cohort where enteral feeding was initiated in an acute hospital but does not give information on where participants were followed up.

Arinzon 2008 recruited and followed up participants from skilled nursing facilities or long-term care wards. Cintra 2014 recruited participants from a range of services, including outpatient clinics, community care units and an acute general hospital. Participants were recruited and followed up in long-term psychogeriatric hospitals in the studies by Takayama 2017 and Takenoshita 2017. Participants were recruited from their own homes or nursing homes by Álvarez-Fernández 2005 and Bentur 2015.

Diagnosis and severity of dementia

Twelve of the fourteen studies did not report or refer to a dementia diagnosis using validated criteria. One study, Álvarez-Fernández 2005, made a diagnosis of dementia using the Diagnostic and Statistical Manual of Mental Disorders Criteria (4th edition) (DSM-IV) (APA 2000). In Takenoshita 2017, all participants with Alzheimer’s disease were diagnosed according to National Institute on Ageing and Alzheimer’s Association (NIA-AA) criteria (McKhann 2011); participants with vascular dementia using the American Heart Association and American Stroke Association (AHA-ASA) criteria (Gorelick 2011); and all other participants diagnosed using International Classification of Diseases 10th edition (ICD-10) criteria (World Health Organization 1993).

Most studies reported dementia by severity. The Cognitive Performance Scale (CPS) and the Functional Assessment Staging Test (FAST) were the most common scales used across studies. Four studies defined severe cognitive impairment as stage 6 or a recent transition to stage 6 on the CPS (Hwang 2014; Mitchell 1997; Teno 2012a; Teno 2012b). Five studies used a score on the FAST scale of 6d (Meier 2001), 6e or above (Takayama 2017), and 7a or above (Álvarez-Fernández 2005; Chou 2020; Cintra 2014).

Bentur 2015 used the Global Deterioration Scale (GDS), and included family carers of people living with advanced dementia of GDS stage 6 or above. Finally, one study used a combination of measures to define severe dementia: Ticinesi 2016 used a FAST score above 5 and a Clinical Dementia Rating (CDR) score above 1.

Some studies did not use a validated measure for stage of dementia. Arinzon 2008 reported severe cognitive impairment with participants recruited from two psychiatric wards of terminal (advanced vascular and degenerative type dementia) elderly participants. Takenoshita 2017 did not define severe dementia in their methods but reported in their results severity using the FAST and CDR scales. All participants scored either 2 or 3 on CDR and 6e or above on the FAST scale. Murphy 2003 used ‘advanced dementia’, as recorded in medical notes.

Interventions

Six studies investigated the impact of PEG tubes compared with no intervention (Hwang 2014; Meier 2001; Murphy 2003; Teno 2012a; Teno 2012b; Ticinesi 2016).
Five studies compared more than one enteral feeding method to no intervention. Takenoshita 2017 included 46 participants (20 fed via PEG and 26 via nasogastric tube); Takayama 2017 included 102 participants with dementia (42 fed via PEG and 60 via nasogastric tube); Arinzon 2008 included 57 participants (15 fed via PEG and 42 via nasogastric tube); Bentur 2015 included 30 participants in the intervention group (15 fed via PEG and 15 via nasogastric tube); and Cintra 2014 included 31 participants with “alternative feeding” - 28 via nasogastric tube and 3 unspecified.


One study did not report the method of enteral tube feeding used (Mitchell 1997).

**Indication for tube feeding**

Six studies did not report indications for tube feeding (Álvarez-Fernández 2005; Bentur 2015; Chou 2020; Hwang 2014; Meier 2003; Mitchell 1997). In Takayama 2017, the indication was a physician’s opinion that the participant could not live without long-term tube feeding. One study reported the indication to be difficulty with eating, swallowing or dysphagia (Murphy 2003). Similarly, Teno 2012a and Teno 2012b cited the need for “support with eating”. Takenoshita 2017 reported difficulty with eating orally for 12 weeks before a physician judged long-term artificial nutrition was needed for survival. Other studies reported several indications for tube feeding. Ticinesi 2016 gave eating problems due to dysphagia or refusal to eat, leading to failure to target nutritional needs, as inclusion criteria. In Arinzon 2008, the most frequent indications were weight loss (40%), stroke with impaired oral intake (32%), refusal to eat (28%), vegetative state (12%), advanced stage of Parkinson’s disease (9%), and malignancy (5%). Finally, in Cintra 2014, reduced swallowing ability (41.9%) was the most common indication, followed by aspiration pneumonia (35.5%).

**Excluded studies**

We excluded 99 studies at full-text stage (see Characteristics of excluded studies): 46 included participants that did not have severe dementia or did not specify severity; 22 included participants with a range of conditions and no separate analysis of those with severe dementia; 8 editorials and commentaries did not provide primary data; 9 had the wrong comparator group; 10 were of the wrong study design; 3 had the wrong intervention; and 1 was the wrong indication.

**Risk of bias in included studies**

We have produced tables and figures recording risk of bias assessments for each comparison’s outcomes, for the relevant studies. These details are in: Table 2; Table 3; Table 4; Table 5; Table 6; Table 7; Table 8; Table 9; Table 10; Table 11; Figure 2; Figure 3; Figure 4; Figure 5; Figure 6; Figure 7; Figure 8; Figure 9; Figure 10; and Figure 11. Many studies do not report on how they measured several outcomes. For example, pressure ulcers were reported by stage but studies often did not show how they were measured or what standardised measure was used (Bentur 2015). Teno 2012b reported that a nurse recorded these from medical records but it is unclear what measurement was used. Harm was not measured using a standardised measure but through clinical reports or incidents. We did not include harm and family outcomes in the summary of findings tables, and therefore have not reported a ROBINS-I risk of bias for these outcomes.

**Bias due to confounding**

We judged the risk of bias due to confounding to be moderate to serious across all outcomes and studies. No studies were randomised and so all were at risk of baseline confounding. Five studies attempted to control for most of the important confounders, as identified in the methods section:

- Meier 2001 controlled for: dementia stage, sex, age, prior hospitalisations, prior pneumonia, degree of involvement of surrogate decision maker, long-term primary care physician, presence of pressure ulcer, presence of a feeding tube, and residence at home versus nursing home;
- Mitchell 1997 controlled for: aged less than 87 years, aspiration, chewing or swallowing problems, stroke, functional impairment, no dementia, pressure ulcers, and do not resuscitate (DNR) status;
- Teno 2012a controlled for: socio-demographic variables, evidence of advance care planning including advance directives, DNR orders, do not hospitalise (DNH) orders, any feeding restrictions, pertinent medical diagnoses from the Minimum Data Set (MDS), clinical conditions including dehydration, inability to consume food or fluids, fever, wound infection, weight loss, swallowing problems, chewing problems, syringe feeding, mechanically altered diet, dietary supplementation, BMI, presence of a pressure ulcer, functional status and disease severity including activities of daily living (ADL) score, and two models that predict mortality (Advanced Dementia Prognostic Tool score and Changes in Health, End-stage disease and Symptoms and Signs score);
- Teno 2012b controlled for: age, sex, race, marital status, education, evidence of advance-care planning, DNR and DNH orders, feeding restrictions, medical diagnoses (e.g. cancer, clostridium difficile diarrhoea, stroke, hip fracture, diabetes), clinical conditions (including dehydration, inability to consume food or fluids, fever, wound infection, weight loss, swallowing problems, chewing problems, syringe feeding, mechanically altered diet, dietary supplementation), BMI, measures of functional status and disease severity including ADL score, and two models that predict mortality (the Advanced Dementia Prognostic Tool (ADEP'T) score and Changes in Health, End-stage disease and Symptoms and Signs (CHESS) score);
- Ticinesi 2016 controlled for: age, dementia stage, type of dementia, comorbidities and setting of living at follow-up (community versus nursing home).

Five studies controlled for only some confounders but not all important confounders relevant to the outcomes, as detailed in the methods section, of this review:

- Álvarez-Fernández 2005 controlled for pneumonia in previous year, presence of permanent nasogastric tube, and serum albumin level;
- Chou 2020 controlled for ADL, age, BMI, sex, feeding status, pressure ulcers, Norton scale score (assessing risk of pressure ulcers);
Enteral tube feeding for people with severe dementia (Review)

Bias in measurement of outcomes
No outcome assessors were blinded to the intervention status. However, where measurements were objective - including survival time, mortality and laboratory data for nutritional outcomes - we judged the risk of bias in this domain to be low. More subjective outcomes were at higher risk of bias across all studies. Bentur 2015 used reports by family carers for all outcome measures in their study (pressure ulcers and pain), which presents a risk of bias from selective recall and delays in the recall period.

Bias in selection of reported results
All outcomes across all studies were at low risk of bias due to selection of reported results. Study authors did not use multiple outcome measurements for the same outcome or conduct multiple analyses of the intervention-outcome relationship.

Effects of interventions
See: Summary of findings 1 PEG compared to no enteral tube feeding for people with severe dementia; Summary of findings 2 Nasogastric tubes compared to no enteral tube feeding for people with severe dementia; Summary of findings 3 Mixed (nasogastric or PEG) or unspecified enteral tube feeding for people with severe dementia

We were not able to perform meta-analyses in this review for several reasons. Overall, there was limited evidence, such that only one study provided evidence for many of the outcomes in the comparisons. For outcomes where more than one study provided evidence, we did not conduct meta-analyses due to different outcome measures being reported and diversity in study methods.

For pressure ulcer outcomes, where more than one study provided data, we did not perform meta-analyses due to different effect measures being reported (e.g. average number of pressure ulcers, prevalence of 3rd or 4th grade pressure ulcers, and prevalence).

For survival time outcomes, where more than one study provided data, the studies reported different effect measures. Where median survival time was reported in multiple studies, there was insufficient detail for data pooling. For two studies reporting regression analyses, there was heterogeneity in the confounders used in the analysis.

Bias in selection of participants
We judged there to be a range of risks of bias in selection of participants among studies, ranging from low to critical risk of bias. Many studies selected participants who were already having enteral tube feeding (the intervention of interest) before the start of the study (n = 8) (Álvarez-Fernández 2005; Arinzon 2008; Bentur 2015; Chou 2020; Cintra 2014; Hwang 2014; Meier 2001; Takayama 2017). For these studies, it is possible that people in the intervention group were more ill at the start of the study than those in the control group. Two studies excluded participants if there had been mention of a feeding tube in the clinical records six months prior to start of data collection (Teno 2012a; Teno 2012b). Selecting participants based on the intervention status and characteristics prior to the start of the intervention may have influenced the outcomes, and therefore poses a critical risk of selection bias. Two of these studies attempted to account for selection bias, through the use of propensity score matching (Hwang 2014; Teno 2012b), and we therefore classified them as being at serious risk of bias in selection of participants into the study.

Bias due to misclassification of interventions
The risk of bias due to misclassification of interventions was generally low as it was easy to determine in most studies whether participants were receiving enteral tube feeding or not. Similarly, bias due to deviations from the intended intervention was low for all outcomes across studies, as no deviations were reported or expected with this type of intervention. Four studies investigated a mix of enteral tube feeding methods, with some participants receiving nasogastric and others PEG feeding (Arinzon 2008; Bentur 2015; Takayama 2017 Takehoshita 2017). These studies reported which participants received which intervention, although only one such study reported separate analyses by type of enteral tube feeding (Takayama 2017). Two studies, it was unclear which type of enteral feeding intervention the participants received (Mitchell 1997; Cintra 2014). We considered these two studies to be at higher risk of bias due to misclassification of intervention.

Bias due to missing data
In most studies, there was no information to assess risk of bias due to missing data. Ticinesi 2016 do not state whether all outcome data for all outcomes were available, but it is unlikely that they were. The trial excluded participants who died or whose family carer could not be contacted. Chou 2020 excluded participants who had missing information, but do not specify how many or what information was missing.

• Cintra 2014 controlled for sex, feeding route, duration of diagnosis, duration of dysphagia, FAST classification, calf perimeter, presence of pressure ulcers, number of pressure ulcers, arterial hypertension, diabetes, place of recruitment and story of hospital admission. However, these were only controlled for in the survival outcome and not pressure ulcer outcome;
• Takehoshita 2017 controlled for peripheral venous nutrition or tube feeding, age, sex, and comorbidity scores;
• Takayama 2017 controlled for age, gender, diagnosis of dementia, and method of artificial nutrition.

One study, Hwang 2014, did not explicitly state in the paper which covariates were included in their propensity scoring used to control for bias. Three studies did not control for confounding for any outcomes measured (Arinzon 2008; Bentur 2015; Murphy 2003).

Summary of bias
Summarising our risk of bias judgements by outcome, we considered that pain outcomes were at overall critical risk of bias (Bentur 2015); pressure ulcer outcomes were at critical (Arinzon 2008; Bentur 2015; Cintra 2014) or serious (Teno 2012b) risk; and all nutrition outcomes were at critical risk (Álvarez-Fernández 2005; Arinzon 2008). Survival outcome measures were a mixture of moderate (Mitchell 1997; Takehoshita 2017), serious (Murphy 2003; Ticinesi 2016), and critical (Cintra 2014; Meier 2001; Takayama 2017; Teno 2012a) risks of bias. Mortality outcomes were at serious (Hwang 2014; Ticinesi 2016) or critical (Álvarez-Fernández 2005; Arinzon 2008; Chou 2020; Cintra 2014) risk of bias.
Mortality outcomes, where more than one study provided data, were reported at diverse time points. Therefore, we could not combine results due to methodological diversity.

The effects of the interventions are reported as fully as possible. We report OR, RR or HR with CIs directly from the included studies; we did not conduct additional analyses. No studies reported on quality of life or behavioural and psychological symptoms of dementia (BPSD).

**Comparison 1: PEG versus no enteral tube feeding**

See Summary of findings 1.

**Survival time**

Based on data from four studies of 36,816 participants, PEG tube placement may have little or no effect on survival time compared to no enteral feeding.

In a study of 41 participants (23 PEG group, 18 no enteral tube feeding), median survival with PEG feeding was 59 days (interquartile range [IQR] 2 to 365 days) versus 60 days (IQR 2 to 229 days) without PEG feeding, not adjusting for any confounders (Murphy 2003). In a study of 99 participants (68 PEG group, 31 no enteral tube feeding), Meier 2001 found median survival time with PEG feeding was 195 days (range 21 to 1405 days) compared to 189 days (range 4 to 1502 days) in those with no feeding tube, not adjusting for any confounders. In a study of 36,492 participants (1956 PEG group, 34,536 no enteral tube feeding), Álvarez-Fernández 2005 found there was an increased unadjusted mortality risk associated with having a permanent nasogastric tube, compared with a “non-permanent” tube (RR 3.53, 95% CI 1.5 to 8.30), not adjusting for any confounders.

Ticinesi 2016 grouped findings by Clinical Dementia Rating (CDR) score (CDR 3 and CDR 4 or 5) in a study of 184 participants (54 PEG, 130 no enteral tube feeding). Mean survival time was 0.66 ± (SD) 0.09 years in the PEG group, and 1.28 ± (SD) 0.08 years in the oral nutrition group. It is unclear from this data whether PEG improves survival. PEG may decrease survival time in those with a CDR score of 3, adjusted in multivariate Cox regression for age, sex, type of dementia, Charlson Comorbidity Index and setting of discharge (HR 3.21, 95% CI 1.25 to 8.26), and have little or no effect on survival time in those with a CDR score of 4 or 5 (HR 1.27, 95% CI 0.51 to 3.18).

We judged the certainty of evidence to be low. We downgraded the certainty of evidence by two levels due to very serious risk of bias. There was a high risk of bias due to confounding in all studies: participants were not randomly assigned to intervention or comparator groups, and not all studies controlled for important confounders. Furthermore, we judged one study to be at critical risk of bias for selection of participants into the study, and three studies at low risk (Table 2).

**Pressure ulcers**

One study of 4421 participants (1585 PEG group, 2836 no enteral tube feeding) found that PEG feeding probably increases the risk of pressure ulcers compared with no tube feeding (adjusted OR 2.27, 95% CI 1.95 to 2.65) (Teno 2012b). This study used propensity score matching to attempt to minimise selection bias due to differences in risk factors between those who received a PEG tube and those who did not. Factors included in the propensity score matching were: socio-demographic and care planning variables, co-morbidities, clinical factors, measures of functional status and disease severity, and scores on two models that predict mortality (see Table 3 for details). We judged the certainty of the outcome to be moderate, downgrading one level due to moderate risk of bias. Participants were not randomly assigned to intervention and comparator groups, so a risk of confounding is present. However, this was a large study, which attempted to control for a wide range of potential confounders.

**Mortality**

Evidence on mortality comparing PEG with no enteral feeding was inconsistent. Based on data from two studies of 6445 participants, we are uncertain whether PEG feeding has an effect on mortality when compared to no enteral feeding.

In a study of 6261 participants (1924 PEG group, 4337 no enteral feeding), mortality after 180 days was similar between participants with (51.9%) and without (49.8%) PEG tubes (Hwang 2014). However, the covariates used for propensity score matching were derived from the literature but not explicitly stated in the paper, so we cannot assess the level of selection bias.

In a study of 184 participants (54 PEG group, 130 no enteral feeding), Ticinesi 2016, after adjusting for age and sex in multivariate Cox regression, found mortality at 18 months was increased in participants with PEG (70%) versus those using oral nutrition (40%).

We judged the certainty of evidence to be very low. We downgraded the certainty of evidence by two levels because of very serious risk of bias. None of the studies were randomised and so a risk of confounding is present, and not all studies controlled for all important confounders. We also downgraded the evidence by one level because of serious inconsistency in the findings (Table 4).

**Harm-related outcomes**

In a study of 41 participants (23 PEG group, 18 no enteral tube feeding), Murphy 2003 found 4% of those with PEG developed an intra-abdominal abscess, not adjusting for any confounders.

**Comparison 2: nasogastric tube versus no enteral tube feeding**

See Summary of findings 2.

**Mortality**

Evidence on mortality comparing nasogastric tube with no enteral feeding was inconsistent. Based on two studies of 236 participants (144 nasogastric group, 92 no enteral tube feeding), we are uncertain whether nasogastric tube placement increased mortality compared with no tube feeding.

In a study of 169 participants (130 nasogastric group, 39 advanced hand feeding), Chou 2020 found no difference in mortality between the nasogastric tube or advanced hand feeding (no enteral tube feeding) groups, adjusted for ADL, age, BMI, sex, feeding status, pressure ulcers, or Norton scale score (adjusted OR 2.38, 95% CI 0.58 to 9.70).

In a study of 67 participants (14 nasogastric group, 53 no enteral tube feeding), Álvarez-Fernández 2005 found there was an increased unadjusted mortality risk associated with having a permanent nasogastric tube, compared with a “non-permanent” tube (RR 3.53, 95% CI 1.5 to 8.30), not adjusting for any confounders.
We judged the certainty of evidence to be very low. We downgraded the certainty of evidence by two levels because of very serious risk of bias due to confounding. Participants were not randomly assigned to intervention and comparator groups and there was limited controlling for confounding, with not all important confounders controlled for. We also downgraded by one level due to serious inconsistency in the findings (Table 5).

**Nutritional parameters**

Based on one study of 67 participants (14 nasogastric group, 53 no enteral tube feeding), we are uncertain whether nasogastric tube placement improves nutritional parameters (nasogastric group albumin levels 3.29 g/dL, compared to 3.66 g/dL in orally fed participants) (Álvarez-Fernández 2005). There were also no important between-group differences in haematocrit, cholesterol or changes in anthropometric data (arm circumference, tricipital skinfold or muscle area of the arm). There was no adjusting for confounders. We judged the certainty of evidence to be very low. We downgraded the certainty of evidence by two levels because of very serious risk of bias due to confounding. Participants were not randomly assigned to intervention and comparator groups, and there was limited controlling for confounding, with not all important confounders controlled for. We also downgraded by one level due to imprecision, as this result is based on one very small study (Table 6).

**Harm-related outcomes**

Based on one study of 169 participants (130 nasogastric group, 39 advanced hand feeding (no enteral tube feeding)), nasogastric tube feeding may increase the risk of pneumonia compared to advanced hand feeding (48% and 26%, respectively) (Chou 2020). Adjusting for age, sex, feeding status, pressure sores, ADL, and serum albumin levels, nasogastric tube feeding did not decrease risk of pneumonia compared to advanced hand feeding (adjusted OR 2.20, 95% CI 0.92 to 5.30).

**Comparison 3: Mixed (nasogastric or PEG) or unspecified enteral tube feeding versus no enteral feeding**

See **Summary of findings 3**.

**Survival time**

Evidence on survival time for this comparison was inconsistent. Based on data from four studies of 1696 participants, we are uncertain whether mixed or unspecified enteral tube feeding improves survival compared with no enteral feeding.

In a study of 58 participants (46 enteral tube feeding group, 12 no enteral tube feeding), Takenoshita 2017 found that minority enteral tube feeding survived for 23 months, versus 2 months for no enteral feeding. In further unadjusted analysis (Cox proportional hazards regression), Takenoshita 2017 showed longer survival for PEG tube feeding (HR 9.8, 95% CI 3.6 to 27.0). In a study of 185 participants (150 enteral tube feeding group, 35 no enteral tube feeding), Takayama 2017 found a median survival time for mixed enteral tube feeding of 695 days versus 75 days with no enteral feeding, adjusted for age, gender, and dementia diagnosis.

In a study of 67 participants (31 enteral tube feeding group, 36 no enteral tube feeding), Cintra 2014 found an average survival of 236.7 days (95% CI 203.0 to 270.4) for mixed or unspecified enteral tube feeding, and 184.0 days (95% CI 127.2 to 240.8) for oral feeding. This study did not adjust for all important confounders, as identified in the methods of this review.

After controlling for a range of potential confounding factors (age < 87 years, aspiration, chewing or swallowing problems, stroke, functional impairment, no dementia, pressure ulcers, and DNR status), Mitchell 1997, in a study of 1386 participants (135 enteral tube feeding group, 1251 no enteral tube feeding), found no evidence for improved survival time with enteral tube feeding (RR for PEG feeding 0.90, 95% CI 0.67 to 1.21).

We judged the certainty of the evidence to be very low. We downgraded the certainty of evidence by two levels because of very serious risk of bias due to confounding. Participants were not randomly assigned to intervention and comparator groups and there was limited controlling for confounding, with not all important confounders controlled for. There was also critical risk of bias in selection of participants in two studies. We also downgraded certainty by one level because of serious inconsistency in the findings (see Table 7).

**Pressure ulcers**

Evidence on pressure ulcers for this comparison was inconsistent. Based on data from three studies of 351 participants which examined the association between tube feeding and the presence of pressure ulcers, we are uncertain whether mixed or unspecified enteral tube feeding increases pressure ulcers.

In a study of 67 participants (31 enteral tube feeding group, 36 no enteral tube feeding), Cintra 2014 found tube feeding was associated with more pressure ulcers (tube feeding 2.74 average number of pressure ulcers per participant versus oral feeding 1.31 average number of pressure ulcers per participant), and a higher prevalence of 3rd or 4th grade pressure ulcers (tube feeding 25.8% versus oral feeding 8.3%). They did not adjust for all important confounders (see Table 7). In a study of 117 participants (30 enteral tube feeding group, 87 no enteral tube feeding), Bentur 2015 found no important effect on pressure ulcer prevalence between those with (34.2%) and those without (37.9%) feeding tubes; there was no adjustment for confounders. Finally, in a study of 167 participants (57 enteral tube feeding group, 110 no enteral tube feeding), Arinzon 2008 found that enteral feeding was associated with a higher prevalence of pressure ulcers (tube feeding 26% versus oral feeding); there was no adjustment for confounders.

We judged the certainty of the evidence to be very low. We downgraded the certainty of evidence by two levels because of very serious risk of bias due to confounding. Participants were not randomly assigned to intervention and comparator groups, and there was limited controlling for confounding, with not all important confounders controlled for. There was also serious risk of bias in selection of participants in all studies. We also downgraded certainty by one level because of serious inconsistency in the findings (see Table 8).

**Pain and comfort**

We are uncertain if mixed or unspecified enteral tube feeding improves pain and comfort. This is based on one study of 117 participants (30 enteral tube feeding group, 87 no enteral tube feeding) (Bentur 2015). This study found no evidence of a difference for overall scores on the Comfort Assessment in Dying End-Of-Life...
in Dementia (CAD-EOLD) scale between those with feeding tubes (28.9) and those without feeding tubes (32.2) (Bentur 2015). There were lower scores on the well-being subscale of the CAD-EOLD in feeding tube users than non-users (5.2 versus 6.93). There was no adjustment for confounders.

We judged the certainty of the evidence to be very low. We downgraded the certainty of evidence by two levels because of very serious risk of bias due to confounding. Participants were not randomly assigned to intervention and comparator groups, and there was limited controlling for confounding, with not all important confounders controlled for. There was also critical risk of bias in selection of participants. We also downgraded certainty by one level due to imprecision as this result is based on one small study (see Table 9).

**Mortality**

From two studies of 234 participants, we are uncertain if mixed or unspecified enteral tube feeding increases mortality. In a study of 167 participants (57 enteral tube feeding group, 110 no enteral tube feeding), there was no difference between groups for mortality at 22 months (42% for those with enteral feeding compared to 27% of controls) (Arinzon 2008). There was no adjustment for confounders.

In a study of 67 participants (31 enteral tube feeding group, 36 no enteral tube feeding), Cintra 2014 found an adjusted RR of mortality of 2.3 (95% CI 1.158 to 4.667) for mixed or unspecified enteral tube feeding. The study did not adjust for all important confounders, as identified in the methods of this review.

We judged the certainty of the evidence to be very low. We downgraded the certainty of evidence by two levels because of very serious risk of bias due to confounding. Participants were not randomly assigned to intervention and comparator groups, and there was limited controlling for confounding, with not all important confounders controlled for. There was also critical risk of bias in selection of participants in both studies. We also downgraded certainty by one level because of serious inconsistency in the findings (see Table 10).

**Nutritional parameters**

Based on one study of 167 participants (57 enteral tube feeding group, 110 no enteral tube feeding), we are uncertain if mixed or unspecified enteral tube feeding affects nutritional parameters and laboratory results (blood count (haemoglobin and lymphocyte count), renal function tests and electrolytes, hydration status, serum osmolality, serum proteins, serum cholesterol), or lowers BMI (21.98 in enteral tube feeding versus 23.23 in the comparator group after 3 months) (Arinzon 2008). There was no adjusting for confounders. We judged the certainty of the evidence to be very low. We downgraded the certainty of evidence by two levels because of serious risk of bias of confounding. Participants were not randomly assigned to intervention and comparator groups, and there was limited controlling for confounding, with not all important confounders controlled for. There was also critical risk of bias in selection of participants. We downgraded the evidence further by one level to very low, due to imprecision, as it is based on one small study (see Table 11).

**Family carer outcomes**

In a study of 117 participants (30 enteral tube feeding group, 87 no enteral tube feeding), Bentur 2015 explored how enteral feeding in people with dementia still living in their own homes may impact on outcomes for family carers. A higher proportion of carers of people with feeding tubes (44%) reported very heavy burden compared to 19% of those caring for people without feeding tubes. Similar proportions of carers from the enteral feeding and no enteral feeding groups were possibly depressed (51.7% versus 57.5%). There was no adjusting for confounders.

**Harm-related outcomes**

Evidence on harm-related outcomes for this comparison was inconsistent. Based on data from three studies of 292 participants, mixed or unspecified enteral tube feeding may increase harm-related outcomes. In a study of 167 participants (57 enteral tube feeding group, 110 no enteral tube feeding), Arinzon 2008 found 61% of those with enteral feeding experienced at least one major complication or symptom related to nutrition. Cases of pneumonia were higher in the enteral tube feeding group compared to the control group (47% versus 24%). The study also described complications of enteral feeding: 4% experienced re-feeding syndrome, and 13% of those with PEG developed an abscess at the stoma site. There was no adjusting for confounders. In a study of 67 participants (31 enteral tube feeding group, 36 no enteral tube feeding), Cintra 2014 found diagnoses of aspiration pneumonia were higher in the enteral tube feeding group (58.1%) compared to the oral feeding group (25%), and the risk was twice as high in the enteral tube feeding group (RR 2.32, 95% CI 1.22 to 4.40). There was no adjusting for confounders. Finally, in a study of 58 participants (46 enteral tube feeding group, 12 no enteral tube feeding), Takenoshita 2017 found no evidence of a difference between those with enteral tube feeding and those without in bouts of pneumonia and days of antibiotic use. There was no adjusting for confounders.

**DISCUSSION**

This is an update of the 2009 Cochrane Review on enteral tube feeding for older people with dementia (Sampson 2009). For this update, we identified 14 studies, none of which were randomised controlled trials.

**Summary of main results**

We did not conduct any meta-analyses, due to limited evidence as a result of only one study providing evidence for many of the outcomes in the comparisons, or different outcomes and diversity in methodology when more than one study provided evidence. Ultimately, we found no evidence of a positive impact of feeding tubes. We found one study showing a clinically significant risk of pressure ulcers in people with severe dementia fed via enteral tube feeding (Teno 2012b).

We found no conclusive evidence that enteral tube feeding provides benefit for people with severe dementia in terms of survival and mortality. Risk of having or developing a pressure ulcer appears to be higher with enteral feeding tubes. There is limited, very low-quality evidence that enteral tube feeding may improve some nutritional parameters. However, these studies have a high risk of bias and BMI does not increase with tube feeding. No studies evaluated the impact of enteral tube feeding on quality of life.
or behavioural and psychological symptoms of dementia (BPSD). Only one study measured comfort and pain using the CAD-EOLD scale (Bentur 2015), and found that on the well-being subscale (which includes serenity, peace, and calm), those with enteral tubes had lower well-being scores. No studies evaluated pain using a standardised measure of pain. Only one study reported on impact on family carers (Bentur 2015), finding a higher burden and potential feelings of depression in family carers of those living at home with enteral tube feeding. Only one study explicitly stated an aim to evaluate harm-related outcomes (Takenoshita 2017), and reported the prevalence of pneumonia. Two other studies reported on harm-related outcomes (Arinzon 2008; Cintra 2014), including pneumonia, re-feeding syndrome, abscess, and positioning or replacement of tubes.

Overall completeness and applicability of evidence

Although we found no RCTs, there are many more studies in this updated review than were identified in the previous review (Sampson 2009). For ethical reasons, it is also not possible to conduct RCTs in this population (e.g. people with severe dementia, as opposed to older people).

Most studies were conducted in the USA. Few participants in the studies had young onset dementia and most studies focused on older people (over 65 years of age). Only three studies report the subtypes of dementia (Takayama 2017; Takenoshita 2017; Ticinesi 2016).

The included studies reported severity of dementia using a range of measures. The categorisation of severe dementia varied across studies, making comparison of studies and participants difficult. A previous review, defining end of life in dementia and severe dementia, has highlighted this variation as a challenge (Browne 2021). This review focused on severe dementia. However, many studies did not describe the severity of dementia, and were therefore excluded. Many excluded studies had a mixed sample of people with and without dementia. We set an inclusion criterion that at least 50% of the study sample should be people with dementia, or data for those with dementia should be available separately.

We had planned subgroup analysis by type of dementia, delivery method, and clinical setting; however, meta-analysis was not possible. The nature of the evidence means it is not possible to draw strong conclusions.

Quality of the evidence

It is both ethically and practically challenging to conduct a randomised controlled trial for enteral tube feeding in people with severe dementia. All included studies were observational non-randomised studies. All studies and outcomes had moderate, serious, or critical risk of bias due to confounding, with many not controlling for important factors such as age, gender, ethnicity, comorbidities, and frailty. It is impossible to blind researchers to the intervention, leading to potential bias in outcome measurements. However, where measurements were objective, such as survival time, mortality, or laboratory data for nutritional outcomes, we judged this risk to be low. Finally, due to the nature of these studies, there was a high risk of bias as participants were mostly assigned to intervention and non-intervention groups before studies commenced.

In some studies, the intervention was not always clear (i.e. PEG or nasogastric tube), such as in Mitchell 1997, which just specified 'tube feeding', and Cintra 2014, which specified that 28 participants had nasogastric tubes and the other three participants received an unspecified type of enteral tube feeding. Four other studies did not separate analysis on participants who received either PEG or nasogastric tube (Arinzon 2008; Bentur 2015; Takayama 2017; Takenoshita 2017).

Five studies controlled for confounding (Meier 2001; Mitchell 1997; Teno 2012a; Teno 2012b; Ticinesi 2016). However, five studies controlled for only some confounders, but not all important confounders relevant to the outcomes, as detailed in the methods section of this review (Álvarez-Fernández 2005; Chou 2020; Cintra 2014; Takayama 2017; Takenoshita 2017). The Hwang 2014 study report did not explicitly state which covariates were included in their propensity scoring used to control for bias. Three studies did not control for confounding for any outcomes measured (Arinzon 2008; Bentur 2015; Murphy 2003). Conclusions from these studies could therefore be explained by the problem of confounding by indication. For example, gender and age could be a prognostic factor for survival. Similarly, pressure ulcers could possibly indicate greater dependency and need, which could be associated with tube feeding. Hence, a higher proportion of pressure ulcers in the intervention compared to control groups may be expected.

The most common outcome measure was survival time in eight studies, followed by mortality (six studies), pressure ulcers (four studies), and nutrition (two studies). Pain was reported once; however, this was as part of the CAD-EOLD scale, which is not specifically a measure of pain, but of overall comfort. No studies reported on BPSD or quality of life. Five studies reported harm; however, this was mixed in how it was reported and what was classified as harm. Many reports of harm included pressure ulcers and mortality, which are considered as separate outcomes for our review.

Sample sizes ranged from 41 (Murphy 2003), to 36,492 participants (Teno 2012a), with some studies underpowered to detect a difference between intervention and control groups. Smaller samples were from cohort studies, and larger samples were from large, routinely-collected minimum data sets in the USA.

Most studies included only people with severe dementia. However, one study consisted of a mixed sample, and therefore this limits the interpretation from this study (Mitchell 1997). Many studies used different scores on the same measurement scales as an indication of severe dementia, making comparisons difficult. It would be helpful if future studies were to use standardised cut-offs for defining severe dementia. Finally, studies should also clearly define dementia using validated diagnostic criteria, such as the DSM-5, to allow more valid comparisons and conclusions to be made.

According to the GRADE criteria, we considered the overall certainty of the evidence to be low or very low for all outcomes - due to risk of bias, imprecision, and inconsistency across studies - except for pressure ulcers in the PEG versus no enteral tube feeding comparison, which we considered moderate certainty.

We acknowledge that many of our included studies were not originally formulated with a systematic review of effectiveness in...
Enteral tube feeding for people with severe dementia (Review)

Mind. We are applying GRADE ratings to non-interventional studies and could only conduct a narrative description of our findings.

Potential biases in the review process

This review was conducted following guidance from the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2020), thereby minimising the introduction of bias during the review process. We consulted Cochrane methodology teams for support and advice when completing narrative summary of findings tables and the ROBINS-I risk of bias.

Agreements and disagreements with other studies or reviews

This is an update of the 2009 Cochrane Review of enteral tube feeding for older people with dementia (Sampson 2009). The earlier version of the review identified seven controlled cohort studies, and also found inconclusive evidence regarding the effect of enteral tube feeding on survival time, mortality, nutritional parameters, physical functioning and pressure ulcers, and no evidence about quality of life, physical functioning or BPSD. This updated review has added findings using a validated scale for comfort (CAD-EOLD).

There are two recent non-Cochrane reviews regarding enteral feeding for people with dementia (Jiaopo 2019; Lee 2020). Ijaopo 2019 completed a review identifying similar studies and reached similar conclusions about the quality of the evidence and effectiveness of enteral tube feeding in people with advanced dementia. They also highlighted the negative impact on pressure ulcers and the potential benefits for nutritional parameters. They concluded that tube feeding does not stop dementia progression nor prevent imminent death. A meta-analysis from Lee 2020 indicated that enteral tube feeding was associated with increased mortality rate, with PEG showing higher mortality rates compared to no tube feeding. Tube feeding did not prolong survival, supporting most of the studies in the current review. They reported that people with advanced dementia with tube feeding had significantly higher risks of pneumonia and pressure ulcers, again supporting the findings of the current review. Tube feeding did not improve nutritional status, including albumin levels, haemoglobin levels, and cholesterol, which aligns with mixed findings in the current review. However, Lee 2020 conducted a meta-analysis despite the fact that studies were heterogeneous and may not have been suitable for pooling.

Authors' Conclusions

Implications for practice

We found no evidence of benefit of enteral tube feeding on increasing survival time, reducing pain and increasing comfort, reducing mortality, and improving nutritional status. This is based on low- and very low-certainty evidence which is at risk of bias. There is evidence of clinically significant risk for pressure ulcers from enteral tube feeding, based on moderate-certainty evidence. There are no data on quality of life and BPSD.

Implications for research

Future research should focus on better reporting and matching of control and intervention groups, clearly-defined interventions (e.g. not mixing PEG and nasogastric in the intervention groups), recording of the subtypes of dementia, and consistent reporting on both the severity of dementia and settings as these may have an effect on the outcomes. Studies need to evaluate the impact of tube feeding on quality of life, BPSD, family carer outcomes (including depression and burden of care) and pain, all of which are clinically important. There is a need for better use of validated instruments with all measures. We believe that quality of life is important even at the advanced stages of dementia, and should be measured using validated tools for this population.

The evidence particularly points to the increase in pressure ulcers due to enteral tube feeding and this should be explored further.

Moving forward, routine data collected from hospitals where PEG tubes are placed may provide useful insights.

Due to the ethical constraints of conducting randomised controlled trials with this intervention and population, the best method continues to be prospective comprehensive data collection on very large samples. This is particularly important where the use of these interventions is favoured, including in Japan and Taiwan (Anantapong 2020; Barrado-Martin 2021b; Chang 2016).

Acknowledgements

We thank peer reviewers Joanne Brooke, Efrat Gil and a third reviewer (who wishes to remain anonymous), and consumer reviewer Roberta McKee-Jackson for their comments and feedback on the review.
Enteral tube feeding for people with severe dementia (Review)

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**CHARACTERISTICS OF STUDIES**

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

**Álvarez-Fernández 2005**

**Study characteristics**

**Methods**
Observational study: the intervention was allocated to individuals, with outcome data available before (once) and after the intervention/comparator (different individuals).

The effect of the intervention was estimated by difference between groups (of individuals receiving either intervention or comparator).

The researchers did not aim to control for confounding; they only controlled for pneumonia and albumin.

Groups of individuals were allocated to the intervention as a result of clinical decision by a healthcare decision maker or practitioner.

Assessment of outcomes was not carried out after the study was designed.

**World Health Organization 2019**

**Xie 2008**

**Zarit 1980**

**Zigmond 1983**

**References to other published versions of this review**

**Sampson 2008**

**Sampson 2009**
Neither characterisation of individuals before the intervention, nor actions and choices leading to an individual becoming a member of a group, were carried out after the study was designed. Potential confounders (with the exception of pneumonia and albumin) and outcome variables were not measured before the intervention.

Participants
67 community-based participants, living at home or in nursing homes, 65 years old or over with a diagnosis of dementia defined by DSM-IV and staged as FAST 7A or greater. 14 received permanent NGT feeding, 53 received oral feeding or non-permanent NGT feeding.

Participants were excluded if: 1) in a biologically terminal state, 2) had cancer, 3) had any acute process, 4) had a severe organ failure, or 5) had dementia due to a non-degenerative cause.

Interventions
Intervention: permanent NGT feeding
Reasons for the use of enteral nutrition were not reported.
Comparison: non-permanent NGT feeding

Outcomes
Reported by family:
1. duration of dementia at baseline;
2. mortality every 3 months at follow-up (from 01.02.1999 until 15.07.2001);
3. date of death at follow-up, as reported by family, family doctor or death certificate.

Nutritional parameters at baseline as reported by researcher:
1. tricipital skinfold thickness;
2. arm circumference;
3. the muscle area of the arm.

Mortality every 3 months at follow-up, time from recruitment.

Notes
26 participants were excluded during recruitment.
Participation involved a baseline clinical evaluation and blood test (48 hours after clinical evaluation) and 3-monthly follow-up.
Follow-up completed up to 24 months after recruitment.
Limited comparisons of permanent use of NGT versus non-permanent NGT.
Unclear sources of funding or conflicts of interest.

Arinzon 2008

Study characteristics

Methods
Observational study: the intervention was allocated to individuals, with outcome data available after the intervention/comparator only (different individuals).

The effect of the intervention was estimated by difference between groups (of individuals receiving either intervention or comparator).

The researchers did not aim to control for confounding.

Groups of individuals were allocated to the intervention as a result of clinical decision by a healthcare decision maker or practitioner.

Assessment of outcomes was carried out after the study was designed.
Neither characterisation of individuals before the intervention, nor actions and choices leading to an individual becoming a member of a group, were carried out after the study was designed.

Neither potential confounders nor outcome variables were measured before the intervention.

Study period was between 01 March 2001 and 31 December 2002.

Participants
- 167 participants with advanced vascular and degenerative type of dementia in 3 psychogeriatric wards.
- 57 participants received enteral nutrition (42 via NGT and 15 via PEG), 110 participants formed the control group.

Details on inclusion and exclusion criteria were not provided.

Interventions
- Intervention: enteral feeding via NGT or PEG. The most frequent indications for the use of enteral nutrition were weight loss, stroke with impaired oral intake, refusal to eat, vegetative state, advanced stage of Parkinson's disease, and malignancy.
- Comparison: oral nutritional support, 76% required oral supplementation via Ensure.

Outcomes
- Nutritional parameters at baseline and every 6 months thereafter:
  1. blood tests
  2. anthropometric measurements

Mortality from recruitment.

Adverse events as having experienced at least one major complication or symptom related to nutrition, or pneumonia.

Notes
- Unclear when nutritional parameters measurements stopped and who completed anthropometric measurements.
- No funding stated. Declared no conflict of interests.

Study characteristics

Methods
- Observational study: the intervention was allocated to individuals, with outcome data available after the intervention/comparator only (different individuals).

The effect of the intervention was estimated by difference between groups (of individuals receiving either intervention or comparator).

The researchers did not aim to control for confounding.

Groups of individuals were allocated to the intervention as a result of clinical decision by a healthcare decision maker or practitioner.

Assessment of outcomes was carried out after the study was designed.

Neither characterisation of individuals before the intervention, nor actions and choices leading to an individual becoming a member of a group were carried out after the study was designed.

Neither potential confounders nor outcome variables were measured before the intervention.

The study was conducted among participants with dementia who were members of the second largest Preferred-Provider Organization in Israel, who lived in one of the 3 largest districts where this organisation worked in the last 3 months of 2012.
### Bentur 2015 (Continued)

#### Participants
117 family carers of participants with advanced dementia, stage 6 or above on GDS.

Included participants living with dementia were based in the community or had been living in the community. Both current family carers and bereaved in the past 3 to 6 months were included.

Exclusion criteria were not reported.

30 participants were feeding-tube users, 37 were non-users.

#### Interventions
Intervention: tube feeding (15 participants via PEG, 15 participants via NGT). Family carers answered a questionnaire.

Reasons for the use of tube feeding were not reported.

Comparison: no tube feeding.

#### Outcomes
All outcomes were cross sectional, it was not reported when the intervention was given and when the assessment was done.

Pressure ulcers as reported by family carers via questionnaire.

Related to the family carer:
1. symptom management end-of-life in dementia (SM-EOLD) scale,
2. comfort assessment in dying end-of-life in dementia (CAD-EOLD) scale,
3. satisfaction with end-of-life care end-of-life in dementia (SWC-EOLD) scale,
4. Agency for Healthcare Research and Quality 2 - question validated screening tool for depression,
5. burden via 2 non-validated questions.

Nutritional parameters:
1. problem swallowing,
2. took food supplements,
3. weight problems.

#### Notes
117 out of 156 family carers identified through the search were included in the study, the rest refused to participate, were living too far away, or had other reasons.

Study supported by the Minerva Foundation through a grant from the Minerva Center for Interdisciplinary Study of End of Life at Tel-Aviv University. Data collection was supported by the Helen Bader foundation. Declared no conflicts of interest.

### Chou 2020

#### Study characteristics

**Methods**

Observational study: the intervention was allocated to individuals, with outcome data available after the intervention/comparator only (different individuals).

The effect of the intervention was estimated by difference between groups (of individuals receiving either intervention or comparator).

The researchers used methods that controlled only for confounding by observed covariates.

Groups of individuals were allocated to the intervention as a result of clinical decision by a healthcare decision maker or practitioner.

Assessment of outcomes was carried out after the study was designed.
Neither characterisation of individuals before the intervention, nor actions and choices leading to an individual becoming a member of a group were carried out after the study was designed.

Neither potential confounders nor outcome variables were measured before the intervention.

The study was conducted over a 12-month period in home-care settings in Taiwan.

Participants
169 people with eating difficulties, advanced dementia using a score of ≥ 7A by the Functional Assessment Staging Test (FAST), fully dependent for functional status, eating difficulties, and age ≥ 60 years.

Participants were excluded if they were able to eat without any assistance, absence of outpatient or inpatient medical records in 2017, and missing information.

Interventions
Intervention: NG tube feeding
Comparison: advanced hand feeding

Outcomes
Mortality
Harm

Notes
The authors disclosed no receipt of any financial support for the study.

Cintra 2014

Study characteristics

Methods
Observational study: the intervention was allocated to individuals, with outcome data available after the intervention/comparator only (different individuals).

The effect of the intervention was estimated by difference between groups (of individuals receiving either intervention or comparator).

The researchers used methods that controlled only for confounding by observed covariates. However, they only considered some confounders which reached statistical significance in bivariate Cox analysis.

Groups of individuals were allocated to the intervention as a result of clinical decision by a healthcare decision maker or practitioner.

Assessment of outcomes was carried out after the study was designed.

Neither characterisation of individuals before the intervention, nor actions and choices leading to an individual becoming a member of a group were carried out after the study was designed.

Outcome variables were not measured before the intervention and not all important potential confounders were measured before the intervention.

Conducted in 5 health facilities, including a geriatric outpatient clinic, inpatient and acute wards of a general hospital, a community acute care unit and an emergency hospital in Belo Horizonte, Brazil.

Study period was from July 2011 to September 2012. Follow-up occurred every 3 months after recruitment, covering a minimum follow-up period of 6 months.

Participants
67 participants 60 years old or over with possible or probable Alzheimer’s dementia who:

1. scored from 7A to 7F on the FAST,
2. were fully dependent for daily living activities, as evaluated by the Katz Index,
3. had moderate to severe oropharyngeal dysphagia, as evaluated by a speech pathologist.
Participants were excluded when dysphagia was a consequence of stroke, amyotrophic lateral sclerosis, secondary Parkinsonism, Parkinson-plus, or Parkinson’s disease; or when participants had a tracheotomy or cancer when it was not in complete remission.

31 participants received alternative feeding such as gastrostomies or feeding tubes: 28 received NGT and for 3 participants, alternative feeding type was not specified. The other 36 received oral feeding.

Interventions

<table>
<thead>
<tr>
<th>Interventions</th>
<th>Reasons for the use of enteral nutrition were a reduced swallowing ability or aspiration pneumonia.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comparison</td>
<td>oral route</td>
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Outcomes

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<tr>
<th>Outcomes</th>
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<tbody>
<tr>
<td>Pressure ulcers</td>
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<tr>
<td>Mortality at 90 and 180 days follow up, after recruitment</td>
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<tr>
<td>Survival</td>
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<tr>
<td>Adverse events as pneumonia occurrence</td>
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Notes

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<th>Notes</th>
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<tbody>
<tr>
<td>Multiple analyses conducted</td>
</tr>
<tr>
<td>No reported sources of funding or conflicts of interest</td>
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</table>

Cintra 2014 (Continued)

Participants

6261 nursing home residents with advanced dementia.

Included residents scored 4 or 5 to a 6 CPS on a quarterly or annual Minimum Data Set assessment for the national repository.

Exclusion criteria were not specified.

1924 underwent PEG insertion, 4337 were not tube fed.

Interventions

<table>
<thead>
<tr>
<th>Interventions</th>
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<tbody>
<tr>
<td>Intervention: PEG tube.</td>
</tr>
</tbody>
</table>
### Hwang 2014 (Continued)

Reasons for the use of PEG were not reported, but occurred during hospitalisation.

**Comparison:** no enteral tube feeding.

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Mortality at 1 and 6 months after PEG insertion.</th>
</tr>
</thead>
</table>

**Notes**

Records reported adverse events like hospitalisations, hospital days and number of days in intensive care unit (ICU) but these are not identified on the study protocol so were not included.

Funding was received from grants 1RC1AG036418-01 and RO1 AG024265 from the National Institutes of Health, National Institute of Aging, and US Department of Health & Human Services. Authors declared no conflicts of interest.

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### Meier 2001

#### Study characteristics

**Methods**

Observational study: the intervention was allocated to individuals, with outcome data available after the intervention/comparator only (different individuals).

The effect of the intervention was estimated by difference between groups (of individuals receiving either intervention or comparator).

The researchers used methods that controlled only for confounding by observed covariates.

Groups of individuals were allocated to the intervention as a result of clinical decision by a healthcare decision maker or practitioner.

Actions or choices leading to an individual becoming a member of a group, and assessment of outcomes were carried out after the study was designed.

Characterisation of individuals before the intervention was not carried out after the study was designed.

Potential confounders were measured before the intervention, outcome variables were not measured before the intervention.

The study was conducted in a tertiary care hospital in New York City, USA over 3 years, between August 1994 and June 1997.

Follow-up was performed every 3 months until death.

**Participants**

99 hospitalised participants with advance dementia and an available surrogate decision maker.

Included participants had been hospitalised for an acute illness, staged FAST 6D or greater.

Participants were excluded if no surrogate was available, if surrogate was unable to understand the consent process or refused participation, or in cases where the participant was imminently dying or medically unstable, had been transferred, discharged or died, where language was a barrier or there was a family conflict precluding recruitment.

68 left hospital with a feeding tube, 51 had a new feeding tube placed during hospitalisation and 17 were admitted with a previous feeding tube in place, 31 left hospital without a feeding tube.

**Interventions**

Intervention: PEG tube insertion.

Reasons for feeding tube insertion were not provided.

Comparison: no new PEG inserted during hospitalisation.
Meier 2001 (Continued)

Outcomes
Mortality every 3 months until death, lost to follow-up, or last follow-up date 01 June 1999.

Notes
Study supported by grants from the Greenwall Foundation, and the Kornfeld Foundation, New York. No conflicts of interests stated.

Mitchell 1997

Study characteristics

Methods
Observational study: the intervention was allocated to individuals, with outcome data available after the intervention/comparator only (different individuals).

The effect of the intervention was estimated by difference between groups (of individuals receiving either intervention or comparator).

The researchers used methods that controlled only for confounding by observed covariates.

Groups of individuals were allocated to the intervention as a result of clinical decision by a healthcare decision maker or practitioner.

Assessment of outcomes was not carried out after the study was designed.

Neither characterisation of individuals before the intervention, nor actions and choices leading to an individual becoming a member of a group were carried out after the study was designed.

Potential confounders were measured before the intervention; outcome variables were not measured before the intervention.

The study used the Minimum Data Set assessments in the state of Washington, USA. Study period comprised data recorded from January 1991.

Participants
1386 nursing home residents 65 years or older who had recently progressed to advanced dementia.

Nursing home residents were included when they scored 5 or less in CPS at baseline and progressed to a score of 6 within the next 24 months.

Nursing home residents were excluded when there was an existing feeding tube in place at baseline, and when residents with CPS of 6 were in a coma.

135 underwent feeding tube placement, 1251 did not undergo placement of a feeding tube.

Interventions
Intervention: feeding tube insertion, tube type not specified.

Reasons for the use of tube feeding were not reported.

Comparison: no feeding tube inserted.

Outcomes
Survival was measured at follow-up.

Notes
Study supported by Hebrew Rehabilitation Center for Aged (HRCA) Research and Training Institute, the Marcus Applebaum Fund at the HRCA, Boston, Mass, National Institute on Aging, Men’s Associates Fellowship Award at the HRCA and the Fleet Bank of Massachusetts, Irving and Edyth S. Usen Chair in Geriatric Medicine. No conflicts of interest stated.
Murphy 2003

**Study characteristics**

**Methods**
Observational study: the intervention was allocated to individuals, with outcome data available after the intervention/comparator only (different individuals).

The effect of the intervention was estimated by difference between groups (of individuals receiving either intervention or comparator).

The researchers did not aim to control for confounding.

Groups of individuals were allocated to the intervention as a result of clinical decision by a healthcare decision maker or practitioner.

Assessment of outcomes was not carried out after the study was designed.

Neither characterisation of individuals before the intervention, nor actions and choices leading to an individual becoming a member of a group were carried out after the study was designed.

Neither potential confounders nor outcome variables were measured before the intervention.

The study was conducted over a 24-month period from 1997 in a Veterans Centre in Washington, USA.

**Participants**
41 veterans with dementia referred for PEG placement.

Included participants had advanced dementia, documented dysphagia, a life expectancy of at least 30 days, and were safe for conscious sedation.

Exclusion criteria were not specified.

23 underwent PEG placement, 18 did not undergo feeding tube placement.

**Interventions**
Intervention: PEG tube insertion.

Reason for the use of PEG tube was dysphagia.

Comparison: no feeding tube inserted.

**Outcomes**
Survival, follow-up was performed until death.

Adverse events derived from PEG insertion.

**Notes**
Characteristics of the cohort are not provided.

No funding source or conflicts of interest reported. Authors reported no financial interest.

Takayama 2017

**Study characteristics**

**Methods**
Observational study: the intervention was allocated to individuals, with outcome data available after the intervention/comparator only (different individuals).

The effect of the intervention was estimated by difference between groups (of individuals receiving either intervention or comparator).

The researchers used methods that controlled only for confounding by observed covariates.

Groups of individuals were allocated to the intervention as a result of clinical decision by a healthcare decision maker or practitioner.

Assessment of outcomes was carried out after the study was designed.
**Takayama 2017** (Continued)

Neither characterisation of individuals before the intervention, nor actions and choices leading to an individual becoming a member of a group were carried out after the study was designed.

Potential confounders were measured before the intervention; outcome variables were not measured before the intervention.

Study was conducted in 9 psychiatric hospitals in Okayama Prefecture, Japan, using data between January 2012 and December 2014.

**Participants**

185 inpatients living with dementia and psychiatric disorders, with oral intake difficulty and short life expectancy without enteral nutrition. Of them, 129 inpatients were living with dementia.

Participants were excluded if had terminal cancer.

150 participants underwent tube feeding, 35 participants did not undergo tube feeding.

**Interventions**

Intervention: NG or PEG tube feeding.

The reason for the use of enteral nutrition was the short life expectancy without enteral nutrition.

Comparison: peripheral venous nutrition (PVN) with oral intake.

**Outcomes**

Survival

**Notes**

Study partly supported by JSPS KAKENHI (grant numbers 15K09831 and 16K10251) (Tokyo, Japan) and by grants from the Zikei Institute of Psychiatry (Okayama, Japan). Authors declared no conflicts of interest.

**Takenoshita 2017**

**Study characteristics**

**Methods**

Observational study: the intervention was allocated to individuals, with outcome data available before (once) and after the intervention/comparator (different individuals).

The effect of the intervention was estimated by difference between groups (of individuals receiving either intervention or comparator).

The researchers only controlled for some confounders and not all important confounders.

Groups of individuals were allocated to the intervention as a result of clinical decision by a healthcare decision maker or practitioner.

Characterisation of individuals before the intervention and assessment of outcomes were carried out after the study was designed. Actions or choices leading to an individual becoming a member of a group were not carried out after the study was designed.

Only some potential confounders were measures before the intervention and no outcome variables were measured before the intervention.

Follow-up took place 12 weeks before and 12 weeks after tube feeding (NG or PEG) or peripheral venous nutrition (PVN) commenced.

**Participants**

58 participants living with advanced dementia, stage 6e or above on FAST scale.

Included participants were inpatients in psychiatric hospitals, had difficulties with oral intake, their attending physicians judged long-term artificial nutrition was necessary for survival, and the decision to use or not use artificial nutrition was made during 2014.

People were excluded if they had terminal cancer.
### Takenoshita 2017 (Continued)

46 participants underwent feeding tube insertion, 20 had PEG and 26 NG tube inserted, 12 did not undergo feeding tube insertion.

#### Interventions

**Intervention:** Long-term artificial nutrition via NG or PEG.

Reasons for the use of artificial nutrition were participants’ difficulty with oral intake during the 12 weeks prior to the decision made by the physician, who judged artificial nutrition was necessary for survival.

Comparison: peripheral venous nutrition (PVN) with oral intake.

#### Outcomes

Survival, unclear end of follow-up period.

Adverse events, including pneumonia and the need to use intravenous antibiotics.

#### Notes

Study funded by JSPS KAKENHI Grant Number 15 K09831 and 16 K10251 and the Zikei Institute of Psychiatry. Authors declared no competing interests and no influence by organisations funding the research.

### Teno 2012a

#### Study characteristics

**Methods**

Observational study: the intervention was allocated to individuals, with outcome data available after the intervention/comparator only (different individuals).

The effect of the intervention was estimated by difference between groups (of individuals receiving either intervention or comparator).

The researchers used methods that controlled only for confounding by observed covariates.

Groups of individuals were allocated to the intervention as a result of clinical decision by a healthcare decision maker or practitioner.

Assessment of outcomes was not carried out after the study was designed.

Neither characterisation of individuals before the intervention, nor actions and choices leading to an individual becoming a member of a group were carried out after the study was designed.

Potential confounders were measured before the intervention; outcome variables were not measured before the intervention.

Participants were identified through a match between a national repository of the Minimum Data Set and Medicare Part A and 20% of Medicare Part B claims between 1999 and 2007.

**Participants**

36,492 nursing home residents living with advanced dementia, and with new problems with eating.

Included residents staged 6 or over on CPS for the first time and had a diagnosis of dementia and developed a new eating problem.

Residents were excluded if they died within 2 weeks of the baseline assessment or who had any evidence of PEG feeding tubes in the prior 6 months.

1956 with feeding tube, 34,536 without feeding tube.

**Interventions**

**Intervention:** PEG tube insertion.

The reason for the use of enteral nutrition was the need of support with eating.
Comparison: no feeding tube.

Outcomes

Survival at 1, 2, 3, and 4 months after baseline when the resident converted to a CPS score of 6.

Notes

Study funded by National Institute of Aging Research Grants R01AG024265 and 1RC1AG036418–01, reported as a conflict of interest.

Study characteristics

Methods

Observational study: the intervention was allocated to individuals, with outcome data available after the intervention/comparator only (different individuals).

The effect of the intervention was estimated by difference between groups (of individuals receiving either intervention or comparator).

The researchers used methods that controlled only for confounding by observed covariates.

Groups of individuals were allocated to the intervention as a result of clinical decision by a healthcare decision maker or practitioner.

Assessment of outcomes was not carried out after the study was designed.

Neither characterisation of individuals before the intervention, nor actions and choices leading to an individual becoming a member of a group were carried out after the study was designed.

Potential confounders were measured before the intervention; outcome variables were not measured before the intervention.

Participants were identified through a match between Minimum Data Set and Medicare Part A and 20% of Medicare Part B claims between 1999 and 2007.

Participants

4421 nursing home residents with advanced cognitive impairment.

Included residents had been hospitalised at least once within the first year of entering the cohort, staged 6 or over on CPS, and needed for assistance in eating.

Residents were excluded if died within 2 weeks of the baseline assessment or who had any evidence of PEG feeding tubes in the prior 6 months. Residents with hospitalisations with diagnosis indicating a pressure ulcer were excluded from the analysis that examined PEG feeding tube and new pressure ulcers.

1585 residents with PEG, 2836 residents without PEG.

Interventions

Intervention: PEG tube insertion.

The reason for the use of enteral nutrition was difficulty eating.

Comparison: no feeding tube.

Outcomes

Pressure ulcers - whether residents without a pressure ulcer developed a stage 2 or higher pressure ulcer and improvement of pressure ulcers by their post-hospitalisation MDS assessment.

Mortality at 1, 2 and 6 months.

Notes

Study funded by National Institute of Aging grant ARRA 1RC1AG036418-01. Conflicts of interest not reported.
**Study characteristics**

**Methods**

Observational study: the intervention was allocated to individuals, with outcome data available after the intervention/comparator only (different individuals).

The effect of the intervention was estimated by difference between groups (of individuals receiving either intervention or comparator).

The researchers used methods that controlled only for confounding by observed covariates.

Groups of individuals were allocated to the intervention as a result of clinical decision by a healthcare decision maker or practitioner.

Assessment of outcomes was not carried out after the study was designed.

Neither characterisation of individuals before the intervention, nor actions and choices leading to an individual becoming a member of a group were carried out after the study was designed.

Potential confounders were measured before the intervention; outcome variables were not measured before the intervention.

Study period was between July 2013 and December 2013. 18-month follow-up.

**Participants**

184 consecutively malnourished people living with dementia and eating problems admitted to hospital.

Included participants were 65 years old or over, their life expectancy was over one month, had a diagnosis of dementia, staged FAST of 5 or over and CDR of 1 or over, had recently developed eating problems such as dysphagia or refusal to eat and had clinical signs of malnutrition or scored 2 on MUST.

People were excluded if they had advanced cancer, a terminal illness, dysphagia due to other causes like stroke, previous PEG placement or ongoing artificial nutrition by nasogastric tube and absence of caregivers or relatives.

56 people were not included as they refused to participate, died during hospital stay or the carer was not available or willing to respond to questions at follow-up.

54 were prescribed PEG, 130 were not prescribed PEG.

**Interventions**

Intervention: PEG tube insertion.

The reason for the use of enteral nutrition were eating problems of recent onset, such as dysphagia or refusal to eat with failure to target nutritional needs.

Comparison: oral nutrition.

**Outcomes**

Survival at 18 months follow-up.

Adverse events as hospital readmissions.

**Notes**

The study was carried out without any extra-institutional source of funding. Authors declared they did not have any personal or financial conflict of interest.

CDR: clinical dementia rating
CPS: cognitive performance scale
DSM-IV: diagnostic and statistical manual of mental disorders
FAST: functional assessment staging
GDS: global deterioration scale
MDS: minimum data set
MUST: malnutrition universal screening tool

**Enteral tube feeding for people with severe dementia (Review)**

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Characteristics of excluded studies [ordered by study ID]

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<thead>
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<th>Study</th>
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**Characteristics of studies awaiting classification [ordered by study ID]**

**Alvisi 2016**

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<td>Notes</td>
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</tr>
</tbody>
</table>

**Bell 2012**

<table>
<thead>
<tr>
<th>Method</th>
<th>Observational non-randomised, prospective cohort study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>238 nursing home residents in 180-bed hospital-affiliated nursing home; 175 (74%) had dementia</td>
</tr>
<tr>
<td>Interventions</td>
<td>Intervention: tube feeding (not specified)</td>
</tr>
<tr>
<td></td>
<td>Comparison: not reported</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Survival</td>
</tr>
<tr>
<td></td>
<td>Mortality</td>
</tr>
<tr>
<td></td>
<td>Pneumonia episodes</td>
</tr>
<tr>
<td>Notes</td>
<td>Conference abstract with insufficient detail to determine eligibility, unable to identify full text and no response from authors</td>
</tr>
</tbody>
</table>

**Burke 2001**

<table>
<thead>
<tr>
<th>Method</th>
<th>No information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>No information</td>
</tr>
<tr>
<td>Interventions</td>
<td>No information</td>
</tr>
<tr>
<td>Study</td>
<td>Methods</td>
</tr>
<tr>
<td>---------------</td>
<td>----------------------------------------</td>
</tr>
<tr>
<td><strong>Burke 2001</strong></td>
<td>Retrospective cohort study of medical notes</td>
</tr>
<tr>
<td><strong>Colby 2015</strong></td>
<td>Retrospective chart review</td>
</tr>
<tr>
<td><strong>Eghbalieh 2010</strong></td>
<td>Retrospective study (lack of information to specify further)</td>
</tr>
</tbody>
</table>

**Enteral tube feeding for people with severe dementia (Review)**

Copyright © 2021 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.
### Kimyagarov 2008

**Methods**
Retrospective study (lack of information to specify further)

**Participants**
90 nursing home residents who underwent PEG placement

**Interventions**
Intervention: PEG  
Comparison: no comparison

**Outcomes**
Survival  
Mortality (within 30 days)  
Nutritional parameters

**Notes**
Insufficient detail to determine eligibility, unable to identify full text and no response from authors

### Kurien 2014

**Methods**
Prospective cohort study

**Participants**
1733 participants from two hospitals over 9-year period who received gastrostomy insertions

**Interventions**
Intervention: gastrostomy insertions  
Comparison: compared disease groups but no control

**Outcomes**
Mortality (30 day and 1 year)  
Nutritional parameters

**Notes**
Conference abstract with insufficient detail to determine eligibility, unable to identify full text and no response from authors

### Maeda 2013

**Methods**
Unable to determine

**Participants**
304 older participants with PEG placement

**Interventions**
Intervention: PEG placement  
Comparison: no comparison

**Outcomes**
Harm  
Survival
### Maeda 2013 (Continued)

| Notes | Conference abstract with insufficient detail to determine eligibility, unable to identify full text and no response from authors |

### Nohara 2017

<table>
<thead>
<tr>
<th>Methods</th>
<th>Survey</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>19 neurodegenerative participants who underwent PEG insertion</td>
</tr>
<tr>
<td>Interventions</td>
<td>Intervention: PEG, Comparison: no comparison</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Survival</td>
</tr>
<tr>
<td>Notes</td>
<td>Conference abstract with insufficient detail to determine eligibility, unable to identify full text and no response from authors</td>
</tr>
</tbody>
</table>

### Pannick 2019

<table>
<thead>
<tr>
<th>Methods</th>
<th>Retrospective cohort study of case medical notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>155 participants who underwent PEG or RIG placement over 12 months in one hospital</td>
</tr>
<tr>
<td>Interventions</td>
<td>Intervention: PEG or RIG</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Harm</td>
</tr>
<tr>
<td>Notes</td>
<td>Conference abstract with insufficient detail to determine eligibility, unable to identify full text and no response from authors</td>
</tr>
</tbody>
</table>

### Sakakibara 2019

<table>
<thead>
<tr>
<th>Methods</th>
<th>Retrospective cohort study of case medical notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>314 participants who had undergone PEG at 1 hospital</td>
</tr>
<tr>
<td>Interventions</td>
<td>Intervention: PEG, Comparison: no comparison</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Mortality, Nutritional parameters</td>
</tr>
<tr>
<td>Notes</td>
<td>Conference abstract with insufficient detail to determine eligibility, unable to identify full text and no response from authors</td>
</tr>
<tr>
<td>Study</td>
<td>Methods</td>
</tr>
<tr>
<td>---------------</td>
<td>--------------------------</td>
</tr>
<tr>
<td>Slawson 2000</td>
<td>No information</td>
</tr>
<tr>
<td>Vanis 2016</td>
<td>Retrospective cohort study of case medical notes</td>
</tr>
<tr>
<td>Vazquez-Lopez 2013</td>
<td>Prospective cohort study</td>
</tr>
<tr>
<td>Wakita 2014</td>
<td>No information</td>
</tr>
</tbody>
</table>
### Wakita 2014 (Continued)

<table>
<thead>
<tr>
<th>Comparison: no comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcome</td>
</tr>
<tr>
<td>Harm</td>
</tr>
<tr>
<td>Survival</td>
</tr>
<tr>
<td>Notes</td>
</tr>
<tr>
<td>Conference abstract with insufficient detail to determine eligibility, unable to identify full text and no response from authors</td>
</tr>
</tbody>
</table>

### Widjaja 2010

<table>
<thead>
<tr>
<th>Methods</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retrospective study (no further information)</td>
</tr>
<tr>
<td>Participants</td>
</tr>
<tr>
<td>274 older adults with dementia who underwent PEG placement</td>
</tr>
<tr>
<td>Interventions</td>
</tr>
<tr>
<td>Intervention: PEG</td>
</tr>
<tr>
<td>Comparison: no comparison</td>
</tr>
<tr>
<td>Outcome</td>
</tr>
<tr>
<td>Harm</td>
</tr>
<tr>
<td>Notes</td>
</tr>
<tr>
<td>Conference abstract with insufficient detail to determine eligibility, unable to identify full text and no response from authors</td>
</tr>
</tbody>
</table>

### Zelante 2015

<table>
<thead>
<tr>
<th>Methods</th>
</tr>
</thead>
<tbody>
<tr>
<td>No information</td>
</tr>
<tr>
<td>Participants</td>
</tr>
<tr>
<td>205 participants receiving PEG</td>
</tr>
<tr>
<td>Interventions</td>
</tr>
<tr>
<td>Intervention: PEG</td>
</tr>
<tr>
<td>Comparison: no comparison</td>
</tr>
<tr>
<td>Outcome</td>
</tr>
<tr>
<td>Mortality</td>
</tr>
<tr>
<td>Harm</td>
</tr>
<tr>
<td>Notes</td>
</tr>
<tr>
<td>Conference abstract with insufficient detail to determine eligibility, unable to identify full text and no response from authors</td>
</tr>
</tbody>
</table>

RIG: radiologically-inserted percutaneous gastrostomy
### ADDITIONAL TABLES

#### Table 1. Study designs

<table>
<thead>
<tr>
<th>1. Was the intervention/comparator (answer ‘yes’ to more than one item, if applicable):</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocated to (provided for/administered to/chosen by) individuals?</td>
</tr>
<tr>
<td>Allocated to (provided for/administered to/chosen by) clusters of individuals?</td>
</tr>
<tr>
<td>Clustered in the way it was provided (by practitioner or organisational unit)?</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2. Were outcome data available (answer ‘yes’ to only one item):</th>
</tr>
</thead>
<tbody>
<tr>
<td>After intervention/comparator only (same individuals)?</td>
</tr>
<tr>
<td>After intervention/comparator only (not all same individuals)?</td>
</tr>
<tr>
<td>Before (once) AND after intervention/comparator (same individuals)?</td>
</tr>
<tr>
<td>Before (once) AND after intervention/comparator (not all same individuals)?</td>
</tr>
<tr>
<td>Multiple times before AND multiple times after intervention/comparator (same individuals)?</td>
</tr>
<tr>
<td>Multiple times before AND multiple times after intervention/comparator (not all same individuals)?</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>3. Was the intervention effect estimated by (answer ‘yes’ to only one item):</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change over time (same individuals at different time-points)?</td>
</tr>
<tr>
<td>Change over time (not all same individuals at different time-points)?</td>
</tr>
<tr>
<td>Difference between groups (of individuals or clusters receiving either intervention or comparator)?</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>4. Did the researchers aim to control for confounding (design or analysis) (answer ‘yes’ to more than one item, if applicable):</th>
</tr>
</thead>
<tbody>
<tr>
<td>using methods that control in principle for any confounding?</td>
</tr>
<tr>
<td>using methods that control in principle for time invariant unobserved confounding?</td>
</tr>
<tr>
<td>Using methods that control for confounding by observed covariates?</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>5. Were groups of individuals or clusters formed by (answer ‘yes’ to more than one item, if applicable):</th>
</tr>
</thead>
<tbody>
<tr>
<td>Randomisation?</td>
</tr>
<tr>
<td>Quasi-randomisation?</td>
</tr>
<tr>
<td>Explicit rule for allocation based on a threshold for a variable measured on a continuous or ordinal scale or boundary (in conjunction with identifying the variable dimension, below)?</td>
</tr>
<tr>
<td>Using methods that control only for confounding by observed covariates?</td>
</tr>
<tr>
<td>Some other action of researchers?</td>
</tr>
<tr>
<td>Assessment of outcomes?</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>6. Were the following features of the study carried out after the study was designed (answer ‘yes’ to more than one item, if applicable):</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characterisation of individuals/clusters before intervention?</td>
</tr>
<tr>
<td>Potential confounders?</td>
</tr>
<tr>
<td>Outcome variable(s)?</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>7. Were the following variables measured before intervention (answer ‘yes’ to more than one item, if applicable):</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actions/choices leading to an individual/cluster becoming a member of a group?</td>
</tr>
<tr>
<td>Location differences?</td>
</tr>
<tr>
<td>Time differences?</td>
</tr>
<tr>
<td>Study</td>
</tr>
<tr>
<td>-------</td>
</tr>
<tr>
<td>Bentur 2015</td>
</tr>
<tr>
<td>Arvizu Fernandez 2005</td>
</tr>
<tr>
<td>Alvarez-Fernandez 2005</td>
</tr>
</tbody>
</table>

Table 1. Study Designs (Continued)
<table>
<thead>
<tr>
<th>Study</th>
<th>Allocated to intervention/comparator</th>
<th>After intervention/comparator only (all same individuals)</th>
<th>Difference between groups (of individuals or clusters receiving either intervention or comparator)</th>
<th>Using methods that control only for confounding by observed covariates</th>
<th>Healthcare decision makers/practitioners</th>
<th>Assessment of outcomes</th>
<th>Confounders:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chou 2020</td>
<td>Allocated to (provided for/administered to/chosen by) individuals</td>
<td>After intervention/comparator only (not all same individuals)</td>
<td>Difference between groups (of individuals or clusters receiving either intervention or comparator)</td>
<td>Using methods that control only for confounding by observed covariates</td>
<td>Healthcare decision makers/practitioners</td>
<td>Assessment of outcomes</td>
<td>Confounders: No, Outcomes: No</td>
</tr>
<tr>
<td>Cintra 2014</td>
<td>Allocated to (provided for/administered to/chosen by) individuals</td>
<td>After intervention/comparator only (not all same individuals)</td>
<td>Difference between groups (of individuals or clusters receiving either intervention or comparator)</td>
<td>Using methods that control only for confounding by observed covariates, however only considered some confounders which reach statistical significance in bivariate cox analysis.</td>
<td>Healthcare decision makers/practitioners</td>
<td>Assessment of outcomes</td>
<td>Confounders: No, not all important confounders were measured. Outcomes: No</td>
</tr>
<tr>
<td>Hwang 2014</td>
<td>Allocated to (provided for/administered to/chosen by) individuals</td>
<td>After intervention/comparator only (same individuals)</td>
<td>Difference between groups (of individuals or clusters receiving either intervention or comparator)</td>
<td>Using methods that control only for confounding by observed covariates</td>
<td>Healthcare decision makers/practitioners</td>
<td>No</td>
<td>Confounders: Yes (however unclear which confounders), Outcomes: No</td>
</tr>
<tr>
<td>Meier 2001</td>
<td>Allocated to (provided for/administered to/chosen by) individuals</td>
<td>After intervention/comparator only (not all same individuals)</td>
<td>Difference between groups (of individuals or clusters receiving either intervention or comparator)</td>
<td>Using methods that control only for confounding by observed covariates</td>
<td>Healthcare decision makers/practitioners</td>
<td>Actions/choices leading to an individual/cluster becoming a member of a group</td>
<td>Confounders: Yes, Outcomes: No</td>
</tr>
</tbody>
</table>

AND

Assessment of outcomes
Table 1. Study designs (Continued)

<table>
<thead>
<tr>
<th>Study</th>
<th>Allocated to (provided for/administered to/chosen by) individuals</th>
<th>After intervention / comparator only (not all same individuals)</th>
<th>Difference between groups (of individuals or clusters receiving either intervention or comparator)</th>
<th>Using methods that control only for confounding by observed covariates</th>
<th>Healthcare decision makers/practitioners</th>
<th>Confounders:</th>
<th>Outcomes:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mitchell 1997</td>
<td>Allocated to (provided for/administered to/chosen by) individuals</td>
<td>After intervention / comparator only (not all same individuals)</td>
<td>Difference between groups (of individuals or clusters receiving either intervention or comparator)</td>
<td>Using methods that control only for confounding by observed covariates</td>
<td>Healthcare decision makers/practitioners</td>
<td>No</td>
<td>Outcomes:</td>
</tr>
<tr>
<td>Murphy 2003</td>
<td>Allocated to (provided for/administered to/chosen by) individuals</td>
<td>After intervention / comparator only (not all same individuals)</td>
<td>Difference between groups (of individuals or clusters receiving either intervention or comparator)</td>
<td>No</td>
<td>Healthcare decision makers/practitioners</td>
<td>No</td>
<td>Confounders: No, Outcomes: No</td>
</tr>
<tr>
<td>Takayama 2017</td>
<td>Allocated to (provided for/administered to/chosen by) individuals</td>
<td>Before (once) AND after intervention/comparator (not all same individuals)</td>
<td>Difference between groups (of individuals or clusters receiving either intervention or comparator)</td>
<td>Using methods that control only for confounding by observed covariates</td>
<td>Healthcare decision makers/practitioners</td>
<td>Assessment of outcomes</td>
<td>Confounders: yes, Outcomes: No</td>
</tr>
<tr>
<td>Takenoshita 2017</td>
<td>Allocated to (provided for/administered to/chosen by) individuals</td>
<td>Before (once) AND after intervention/comparator (not all same individuals)</td>
<td>Difference between groups (of individuals or clusters receiving either intervention or comparator)</td>
<td>No, they only considered some confounders not all important confounders</td>
<td>Healthcare decision makers/practitioners</td>
<td>Characterization of individuals/clusters before intervention</td>
<td>Confounders: No, not all important confounders were measured Outcomes: Yes AND Assessment of outcomes</td>
</tr>
<tr>
<td>Teno 2012a</td>
<td>Allocated to (provided for/administered to/chosen by) individuals</td>
<td>After intervention / comparator only (not all same individuals)</td>
<td>Difference between groups (of individuals or clusters receiving either intervention or comparator)</td>
<td>Using methods that control only for confounding by observed covariates</td>
<td>Healthcare decision makers/practitioners</td>
<td>No</td>
<td>Confounders: Yes, Outcomes: No</td>
</tr>
<tr>
<td>Teno 2012b</td>
<td>Allocated to (provided for/administered to/chosen by) individuals</td>
<td>After intervention / comparator only (not all same individuals)</td>
<td>Difference between groups (of individuals or clusters receiving either intervention or comparator)</td>
<td>Using methods that control only for confounding by observed covariates</td>
<td>Healthcare decision makers/practitioners</td>
<td>No</td>
<td>Confounders: Yes, Outcomes: No</td>
</tr>
</tbody>
</table>
Table 1. Study designs (Continued)

<table>
<thead>
<tr>
<th>Study</th>
<th>Bias due to confounding</th>
<th>Bias in selection of participants into the study</th>
<th>Bias in classification of interventions</th>
<th>Bias due to deviations from the intended intervention</th>
<th>Bias due to missing data</th>
<th>Bias in measurement of outcomes</th>
<th>Bias in selection of the reported result</th>
<th>Overall risk of bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ticinesi 2016</td>
<td></td>
<td>Allocated to (provided for/administered to/chosen by) individuals</td>
<td>After intervention / comparator only (not all same individuals)</td>
<td>Difference between groups (of individuals or clusters receiving either intervention or comparator)</td>
<td>Using methods that control only for confounding by observed covariates</td>
<td>Healthcare decision makers/practitioners</td>
<td>Characterization of individuals/clusters before intervention</td>
<td>Confounders: yes, Outcomes: No</td>
</tr>
</tbody>
</table>

This row describes ‘explicit’ clustering. In randomised controlled trials, participants can be allocated individually or by virtue of ‘belonging’ to a cluster such as a primary care practice or a village.

bThis row describes ‘implicit’ clustering. In randomised controlled trials, participants can be allocated individually but with the intervention being delivered in clusters (e.g. group cognitive therapy). Similarly, in a cluster-randomised trial (by general practice), the provision of an intervention could also be clustered by therapist, with several therapists providing ‘group’ therapy.

A study should be classified as ‘yes’ for this feature, even if it involves comparing the extent of change over time between groups.

dFor (nested) case control studies, ‘group’ refers to the case/control status of an individual.

eThe distinction between these options is to do with the exogeneity of the allocation.

Table 2. ROBINS-I assessments for: PEG versus no enteral tube feeding: survival time

<table>
<thead>
<tr>
<th>Study</th>
<th>Bias due to confounding</th>
<th>Bias in selection of participants into the study</th>
<th>Bias in classification of interventions</th>
<th>Bias due to deviations from the intended intervention</th>
<th>Bias due to missing data</th>
<th>Bias in measurement of outcomes</th>
<th>Bias in selection of the reported result</th>
<th>Overall risk of bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Teno 2012a</td>
<td>Moderate</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>Moderate</td>
</tr>
</tbody>
</table>

Participants not randomly assigned to “intervention” and “no intervention” groups so not possible to control for all confounders. However, they did control for important confounders.

People were excluded if there was evidence of PEG prior to review of medicare claims.

All participants had PEG and groups are clear.

“No residents with feeding tubes accounted for 5.4% of the cohort.”

No reported deviations from intended intervention.

No missing data reported.

Assessors were not blinded and would have been aware of the intervention received by study participants. It may not be different measurements including timing of the intervention, but this does not influence con.

Based on the highest rating across the categories.
"Sociodemographic variables; evidence of advance care planning including advance directives, do-not-resuscitate (DNR) orders, do not-hospitalize (DNH) orders, and any feeding restrictions; pertinent medical diagnoses from the MDS; clinical conditions including dehydration, inability to consume food or fluids, fever, wound infection, weight loss, swallowing problems, chewing problems, syringe feeding, mechanically altered diet, dietary supplementation, the amount of body fat as measured according to body mass index (BMI), and presence of a pressure ulcer; measures of functional status and disease severity including activity of daily living (ADL) score; and two models that predict mortality (Advanced Dementia Prognostic Tool score and Changes in Health, End-stage disease and Symptoms and Signs score).

"Multivariate survival model using the Weibull distribution with all the covariates mentioned above and inverse probability of treatment weights to account for the potential selection bias of which NH residents underwent PEG feeding tube insertion treatment was used."

This is appropriate for this design.

"[Cases where there was] any evidence of PEG feeding tubes in the prior 6 months based on review of Medicare claims and MDS assessments were excluded."

However, survival time is an objective measure so will not be affected by knowledge of the intervention.

| Table 2. ROBINS-I assessments for: PEG versus no enteral tube feeding: survival time (Continued) |
|-----------------------------------------------|--|--|--|--|--|--|--|
| Murphy 2003 | Serious | Low | Low | Low | NI | Low | Low | Serious |
| Participants not randomly assigned to “intervention” and “no intervention groups” so not possible to control for all confounders. | No participants had PEG before starting baseline and being included in the study. | All participants had PEG and groups are clear. | No reported deviations from intended intervention. | Missing data were not discussed and unclear if data available for | Assessors were not blinded and would have been aware of the intervention. | They do not conduct multiple measurements and analyses. | Based on the highest rating across the categories. |
They did not control for confounders and did not record many baseline characteristics. They only reported: “evaluation includes the attainment of a brief medical history, a physical examination, and a review of comorbid conditions, nutrition-associated laboratory variables and bleeding risk.”

“a 2-year retrospective medical record review of the survival of veteran patients with dementia referred to us for PEG”

“Percutaneous endoscopic tubes were placed in only 23 patients with dementia. The other 18 similar patients with dementia did not undergo PEG.”

All participants.

Based on the highest rating across the categories.

<table>
<thead>
<tr>
<th>Ticinesi 2016</th>
<th>Moderate</th>
<th>Low</th>
<th>Low</th>
<th>Low</th>
<th>Serious</th>
<th>Low</th>
<th>Low</th>
<th>Serious</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants not randomly assigned to “intervention” and “no intervention” groups so not possible to control for all confounders. However, they controlled for important confounders.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All people with dementia were eligible.</td>
<td>All participants had PEG and groups are clear.</td>
<td>No reported deviations from intended intervention.</td>
<td>Do not report if all data available but unlikely they were able to get information for all consecutive participants admitted.</td>
<td>Assessors were not blinded and would have been aware of the intervention received by study participants. It may not be feasible to blind assessors with this type of intervention.</td>
<td>They do discuss all findings within the discussion.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>“All patients with dementia consecutively admitted to Internal Medicine and Critical Subacute Care Unit of Parma University Hospital, Italy, from July to December 2013”</td>
<td>“Enteral nutrition by PEG was initiated during hospital stay in 29.6% of cases (58 patients, 17 M, 41 F). Since 4 (2 M, 2 F) of them were withdrawn at follow-up, the final PEG group was composed of 54 subjects. Oral nutrition (ON) was instead continued by study participants. It may not be feasible to blind assessors with this type of intervention.”</td>
<td>However, survival time is an objective measure so will not be affected by knowledge of the intervention.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
A subgroup analysis was also performed, according to different stages of dementia. The whole cohort was split in three subgroups (subgroup A: CDR score 1 or 2; subgroup B: CDR score 3; subgroup C: CDR score 4 or 5) and multivariate Cox proportional regression models, accounting for age, Charlson Index and setting of living as possible confounders, were built to test the predictive value of PEG feeding over mortality.

Some participants had tube feeding (intervention of interest) before the start of the study. The characteristics were observed after the start of tube feeding.

Therefore, the group with PEG tube feeding (intervention of interest) may have been more ill than the control; this will influence the outcome.

“A feeding tube was present on admission in 17 subjects (17%). Of the 99 study subjects, 80 (80%) did not have a feeding tube on admission and were not admitted to the hospital specifically for this purpose. Two subjects (2%) were brought into the hospital specifically for the purpose of placing a feeding tube. Of the 82 subjects not randomized to "intervention" and "no intervention" groups so not possible to control for all confounders. However, they performed a series of Cox proportional hazard regression models to control for important confounders.

Variables of borderline significance (p<.15), and variables that have been previously shown to be related to survival in advanced dementia (dementia stage, sex, age, prior hospitalizations, prior pneumonia, degree of involvement of surrogate decision maker, long-term primary care physician, presence of pressure ulcer, presence of a feeding tube, and residence at home vs nursing home) randomization status, and presence of feeding tube were entered into the final survival model.

Groups were clearly defined.

No reported deviations from intended intervention.

“Absence of caregivers or relatives were considered as exclusion criteria.”

Participants not randomly assigned to “intervention” and “no intervention” groups so not possible to control for all confounders. They do not conduct multiple measurements and analyses. They do discuss all findings within the discussion.

Meier 2001

<table>
<thead>
<tr>
<th>Meier 2001</th>
<th>Moderate</th>
<th>Critical</th>
<th>Low</th>
<th>Low</th>
<th>Low</th>
<th>Low</th>
<th>Low</th>
<th>Critical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants not randomly assigned to “intervention” and “no intervention” groups so not possible to control for all confounders. However, they performed a series of Cox proportional hazard regression models to control for important confounders.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
There was a lag between start of intervention and follow-up.

“A feeding tube was present on admission in 17 subjects (17%).”

“Of these persons, 1124 had a PEG feeding tube inserted”

Table 2. ROBINS-I assessments for: PEG versus no enteral tube feeding: survival time (Continued)

<table>
<thead>
<tr>
<th>Study</th>
<th>Bias due to confounding</th>
<th>Bias in selection of participants into the study</th>
<th>Bias in classification of interventions</th>
<th>Bias due to deviations from the intended intervention</th>
<th>Bias due to missing data</th>
<th>Bias in measurement of outcomes</th>
<th>Bias in selection of the reported result</th>
<th>Overall risk of bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Teno 2012b</td>
<td>Moderate</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>Serious</td>
<td>Low</td>
<td>Serious</td>
</tr>
</tbody>
</table>
|         | Participants not randomly assigned to “intervention” and “no intervention” groups so not possible to control for all confounders. However, they used propensity score matching to control for important confounders.  

“Propensity-score matching was used to address issues of selection bias due to differences in risk factors between those who received a PEG tube and those who did not.”  

People were excluded if there was evidence of PEG prior to review of medicare claims. This is appropriate for this design.

All participants had PEG and groups are clear.  

There are no deviations from intended intervention.  

No missing information reported.  

Outcome assessors were not blinded, collected by nurses measuring pressure ulcers and the knowledge of the intervention may have influenced the outcome measure.  

They do not conduct multiple measurements and analyses. They do discuss all findings within the discussion.  

Based on the highest rating across the categories.

MDS: minimum data set  
NH: nursing home

Table 3. ROBINS-I assessments for: PEG versus no enteral tube feeding: pressure ulcers
Variables included in the model were (1) socio-demographic variables (age, sex, race, marital status, education); (2) evidence of advance-care planning including advance directives, do-not-resuscitate order, do-not-hospitalize order, and any feeding restrictions; (3) 19 medical diagnoses (e.g., cancer, clostridium difficile diarrhoea, stroke, hip fracture, diabetes); (4) clinical conditions including dehydration, inability to consume food or fluids, fever, wound infection, weight loss, swallowing problems, chewing problems, syringe feeding, mechanically altered diet, and dietary supplementation; (5) body mass index (BMI); (6) measures of functional status and disease severity, including activities of daily living score; and (7) 2 models that predict mortality (the ADEPT [advanced dementia prognostic tool] score and CHESS [changes in health, end-stage disease, and symptoms and signs] score).”

However, they did account for selection bias using propensity score matching.

“We used a propensity-matched cohort design that addressed the issue of selection bias”

It may not be feasible to blind assessors with this type of intervention.

All data collected were the same for all participants from the minimum data set.

<table>
<thead>
<tr>
<th>Study</th>
<th>Bias due to confounding</th>
<th>Bias in selection of participants into the study</th>
<th>Bias in classification of interventions</th>
<th>Bias due to deviations from the intended intervention</th>
<th>Bias due to missing data</th>
<th>Bias in measurement of outcomes</th>
<th>Bias in selection of the reported result</th>
<th>Overall risk of bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ticinesi 2018</td>
<td>Moderate</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>Serious</td>
<td>Low</td>
<td>Low</td>
<td>Serious</td>
</tr>
</tbody>
</table>

Participants not randomly assigned to “intervention” and “no intervention” groups so not possible to control for all confounders. All people with dementia were eligible. All participants had PEG and No reported deviations from intended intervention. Do not report if all data available but un-blinded. Assessors were not blinded and would have. They do not conduct multiple measures. Based on the highest rating.
“multivariate Cox proportional regression model testing the effects of PEG feeding on mortality was then built. Age, dementia staging (assessed by CDR and FAST), type of dementia (Alzheimer disease vs others), Charlson Comorbidity Index and setting of living at follow-up (community vs nursing home) were considered as possible confounders and thus included in the multivariate analysis.”

“A subgroup analysis was also performed, according to different stages of dementia. The whole cohort was split in three subgroups (subgroup A: CDR score 1 or 2; subgroup B: CDR score 3; subgroup C: CDR score 4 or 5) and multivariate Cox proportional regression models, accounting for age, Charlson Index and setting of living as possible confounders, were built to test the predictive value of PEG feeding over mortality.”

“Enteral nutrition by PEG was initiated during hospital stay in 29.6% of cases (58 patients, 17 M, 41 F). Since 4 (2 M, 2 F) of them were withdrawn at follow-up, the final PEG group was composed of 54 subjects. Oral nutrition (ON) was instead continued despite eating problems in 136 patients (46 M, 90 F). Among them, 6 (3 M, 3 F) withdrew at follow-up, so that the final ON group included 130 subjects.”

“Of these, 1924 persons underwent intervention. Therefore, the group likely they were able to get information for all consecutive participants admitted. Participants were excluded if died or family carer was not contactable.

“absence of caregivers or relatives were considered as exclusion criteria”

“all patients with dementia consecutively admitted to Internal Medicine and Critical Subacute Care Unit of Parma University Hospital, Italy, from July to December 2013 were considered for enrolment in this prospective observational non-randomized unblinded study”

“all patients with dementia subsequently admitted to Internal Medicine and Critical Subacute Care Unit of Parma University Hospital, Italy, from July to December 2013 were considered for enrolment in this prospective observational non-randomized unblinded study.”

Participants not randomly assigned to “intervention” and “no intervention” groups so not possible to control for all confounders. However they do control for important confounders.

Hwang 2014

<table>
<thead>
<tr>
<th>ROBINS-I assessments for: PEG versus no enteral tube feeding: mortality (Continued)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hwang 2014</td>
</tr>
<tr>
<td>Serious</td>
</tr>
<tr>
<td>Participants not randomly assigned to “intervention” and “no intervention” groups so not possible to control for all confounders. However they do control for important confounders.</td>
</tr>
<tr>
<td>Based on the highest rating</td>
</tr>
</tbody>
</table>
However, they used 3:1 propensity score matched participants to help address the potential selection bias, but limited details regarding which variables were used in the propensity.

"For each hospitalization following conversion to CPS of six (baseline), propensity scores were calculated with logistic regression models. Regression covariates were chosen based on former studies' findings on factors that predict likelihood of receiving PEG feeding tubes." PEG feeding (intervention of interest) may have been more ill than the control; this will influence the outcome.

We included those NH residents who received and did not receive PEG feeding tube insertion during the hospitalization. However, we used a 3:1 propensity score match with replacement to help address the potential selection bias of those who chose to insert or forgo PEG feeding tubes.

"We used a 3:1 propensity score match with replacement to help address the potential selection bias of those who chose to insert or forgo PEG feeding tubes." PEG feeding (intervention of interest) may have been more ill than the control; this will influence the outcome.

However, mortality is an objective measure so will not be affected by knowledge of the intervention. It may not be feasible to blind assessors with this type of intervention. They may not be included within the discussions and analyses of the intervention across the categories.
CPS: cognitive performance scale
NH: nursing home

Table 5. ROBINS-I assessments for: nasogastric tube versus no enteral tube feeding: mortality

<table>
<thead>
<tr>
<th>Study</th>
<th>Bias due to confounding</th>
<th>Bias in selection of participants into the study</th>
<th>Bias in classification of interventions</th>
<th>Bias due to deviations from the intended intervention</th>
<th>Bias due to missing data</th>
<th>Bias in measurement of outcomes</th>
<th>Bias in selection of the reported result</th>
<th>Overall risk of bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alvarez-Fernandez 2005</td>
<td>Serious</td>
<td>Critical</td>
<td>Low</td>
<td>Low</td>
<td>NI</td>
<td>Low</td>
<td>Low</td>
<td>Critical</td>
</tr>
</tbody>
</table>

Participants not randomly assigned to “intervention” and “no intervention” groups so not possible to control for all confounders.

There is limited controlling for confounding with not all important confounders controlled for.

“Those variables related with survival time were then included in a Cox proportional hazards model. The final model included the following factors (Table 4): pneumonia during the previous year (RR: 3.7; p<0.001), the presence of

Clear from table 1 in the paper that 14 had nasogastric tube feeding. However, they classify diet as normal, soft, blended and do not detail this in the results.

No deviation from intended intervention.

No information presented on missing data.

Assessors were not blinded and would have been aware of the intervention received by study participants. It may not be feasible to blind assessors with this type of intervention.

They do not conduct multiple measurements and analyses. They do discuss all findings within the discussion.

However, mortality is an objective measure so will not be affected by knowledge of the intervention.

Based on the highest rating across the categories.
Participants not randomly assigned to “intervention” and “no intervention” groups so not possible to control for all confounders.

There is limited controlling for confounding with not all important confounders controlled for.

"After adjusting for sex, age, feeding status, Barthel index, pressure sores, and Norton scale, the mortality rate was not significantly different between the NGF and AHF".

Table 5. ROBINS-I assessments for: nasogastric tube versus no enteral tube feeding: mortality (Continued)

<table>
<thead>
<tr>
<th>Study</th>
<th>Bias</th>
<th>Confounding</th>
<th>Performance</th>
<th>Detection</th>
<th>Baseline</th>
<th>Induction</th>
<th>Bias Due to Outcome</th>
<th>Coherence</th>
<th>Overall</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chou 2020</td>
<td>Serious</td>
<td>Critical</td>
<td>Low</td>
<td>Low</td>
<td>Serious</td>
<td>Low</td>
<td>Low</td>
<td>Critical</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Some participants already had nasogastric (NG) tube at the start of the study.

Clear from table 1 in the paper that 39 had advanced hand feeding and 130 had nasogastric tube feeding.

Exclusion criteria included those with missing information. It is not clear how many this excluded or what data were missing.

Assessors were not blinded and would have been aware of the intervention received by study participants. It may not be feasible to blind assessors with this type of intervention.

"Exclusion criteria were as follows: self-oral intake without any assistance; absence of outpatient or inpatient medical records in 2017; and missing information (i.e., MNA-SF, BMI, serum albumin, Hb, or WBC)."

However, mortality is an objective measure so will not be affected by knowledge of the intervention.

AHF: assisted hand feeding
BMI: body mass index
HB: hemoglobin

Based on the highest rating across the categories.
MNA-SF: mini nutritional assessment-short form
NGF: nasogastric tube feeding
WBC: white blood cell

Table 6. ROBINS-I assessments for: nasogastric tube versus no enteral tube feeding: nutritional parameters

<table>
<thead>
<tr>
<th>Study</th>
<th>Bias due to confounding</th>
<th>Bias in selection of participants into the study</th>
<th>Bias in classification of interventions</th>
<th>Bias due to deviations from the intended intervention</th>
<th>Bias due to missing data</th>
<th>Bias in measurement of outcomes</th>
<th>Bias in selection of the reported result</th>
<th>Overall risk of bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alvarez-Fernandez 2005</td>
<td>Serious</td>
<td>Critical</td>
<td>Low</td>
<td>Low</td>
<td>NI</td>
<td>Low</td>
<td>Low</td>
<td>Critical</td>
</tr>
</tbody>
</table>

Participants not randomly assigned to “intervention” and “no intervention” groups so not possible to control for all confounders.

There is limited controlling for confounding with not all important confounders controlled for.

“Those variables related with survival were then included in a Cox proportional hazards model. The final model included the following factors (Table 4): pneumonia during the previous year (RR: 3.7; *p*<0.001), the presence of a permanent NGT (RR: 3.5; *p*<0.003) and a serum albumin level lower than 3.5 g/dL (RR: 2.9; *p*<0.028).”

There is a lag between start of intervention and measuring nutritional outcomes.

Clear from table 1 in the paper that 14 had nasogastric tube feeding. However, they classify diet as normal, soft, blended and do not detail this in the results.

No deviation from intended intervention

No information presented on missing data.

Assessors were not blinded and would have been aware of the intervention received by study participants. It may not be feasible to blind assessors with this type of intervention.

They do not conduct multiple measurements and analyses. They do discuss all findings within the discussion.

Based on the highest rating across the categories.

However, the main measures used were laboratory data for nutritional outcomes which are objective measures and would not be influenced by knowledge of the intervention.
## Table 7. ROBINS-I assessments for: mixed (nasogastric or PEG) or unspecified enteral tube feeding: survival time

<table>
<thead>
<tr>
<th>Study</th>
<th>Bias due to confounding</th>
<th>Bias in selection of participants into the study</th>
<th>Bias in classification of interventions</th>
<th>Bias due to deviations from the intended intervention</th>
<th>Bias due to missing data</th>
<th>Bias in measurement of outcomes</th>
<th>Bias in selection of the reported result</th>
<th>Overall risk of bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cintra 2014</td>
<td>Serious</td>
<td>Critical</td>
<td>Moderate</td>
<td>Low</td>
<td>NI</td>
<td>Low</td>
<td>Low</td>
<td>Critical</td>
</tr>
<tr>
<td></td>
<td>Participants not randomly assigned to “intervention” and “no intervention” groups so not possible to control for all confounders. They conducted a regression; however, they did not consider all important confounders. They considered: “variables that reached a significance level of 0.25 or below in the bivariate analysis were included in the stepwise regression. They were: sex, feeding route, duration of diagnosis, duration of dysphagia, FAST classification (numeric variables from 1 to 6 corresponding to FAST 7A to 7F), calf perimeter, presence or not of pressure ulcers equal or above grade 2, number of pressure ulcers, arterial hypertension, diabetes, place of recruitment and story of hospital admission”. Feeding tubes were in place prior to baseline. Therefore, the group with enteral tube feeding (intervention of interest) may have been more ill than the control; this will influence the outcome. “Patients with gastrostomies or feeding tubes were included in the alternative feeding group”. It is not clear which type of tube feeding is used for all participants. There are no deviations from intended intervention. “Patients with gastrostomies or feeding tubes were included in the alternative feeding group”. Missing data are not discussed in the paper. Paper does not state if assessors were not blinded and would have been aware of the intervention received by study participants. It may not be feasible to blind assessors with this type of intervention. However, survival time is an objective measure so will not be affected by knowledge of the intervention. They calculate results for multiple time points; however, they reported results for each time point in the abstract, so not trying to focus on one set of results. No evidence of bias in the reported results. Based on the highest rating across the categories.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mitchell 1997</td>
<td>Moderate</td>
<td>Low</td>
<td>Moderate</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td>Participants not randomly assigned to “intervention” and participants with a feeding tube at baseline. Unclear what intervention. There are no deviations. Only 4% missing data. Assessors were not blinded and they do not conduct. Based on the high-</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
"no intervention" groups so not possible to control for all confounders. However, they performed a Cox hazards model and adjusted for confounders.

"Using Cox proportional hazards linear regression, we examined the association between feeding tube status and mortality while adjusting for the independent risk factors for feeding tube placement (age <87 years, aspiration, chewing or swallowing problems, stroke, functional impairment, no dementia, pressure ulcers, and DNR status)." These were all measured using validated measures were applicable.

"We defined our study population to include residents who had a CPS score of 5 or less at their baseline assessment, but who progressed, at some point during the next 24 months, to a CPS score of 6. We also required our study sample to be free of feeding tubes at their baseline assessments."

Some participants received tube feeding before the start of the study and were placed into the intervention group. Therefore, the group with enteral tube feeding (intervention of interest) may have been more ill than the control; this will influence the outcome.

It is clear whether participants receive tube feeding or not and what type.

"There were 60 patients who received PEG tube feeding from intended intervention."

There are no deviations from intended intervention. No evidence of missing data. However, missing data are not discussed.

Assessors were not blinded and would have been aware of the intervention received by study participants. It may not be feasible to blind assessors with this type of intervention.

135 (9.7%) underwent placement of a feeding tube."

"Data were missing in less than 4% of cases for all variables analyzed." However, survival time is an objective measure so will not be affected by knowledge of the intervention.

Based on the highest rating across the categories.

<table>
<thead>
<tr>
<th>Takayama 2017</th>
<th>Serious</th>
<th>Critical</th>
<th>Low</th>
<th>Low</th>
<th>NI</th>
<th>Low</th>
<th>Low</th>
<th>Critical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants not randomly assigned to “intervention” and “no intervention&quot; groups so not possible to control for all confounders. However, they used a Cox proportional hazards regression accounting for age, gender, diagnosis and method of artificial nutrition.</td>
<td>Some participants received tube feeding before the start of the study and were placed into the intervention group. Therefore, the group with enteral tube feeding (intervention of interest) may have been more ill than the control; this will influence the outcome.</td>
<td>It is clear whether participants receive tube feeding or not and what type.</td>
<td>There are no deviations from intended intervention.</td>
<td>No evidence of missing data. However, missing data are not discussed.</td>
<td>Assessors were not blinded and would have been aware of the intervention received by study participants. It may not be feasible to blind assessors with this type of intervention.</td>
<td>They do not conduct multiple measurements and analyses. They do discuss all findings within the discussion. Based on the highest rating across the categories.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Regression) using survival time as the dependent variable. Independent variables were age, gender, diagnosis (dementia = 0, others = 1), and method of artificial nutrition”. They were all measured using validated measures.

However, some important confounders were not measured: ethnicity, frailty, co-morbidities, pressure ulcers, function in ADL, BMI, presence of advance directive or DNACPR.

“Detailed clinical status and laboratory findings at the start of artificial nutrition were not evaluated in this study. Therefore, it seems quite probable that clinicians selected peripheral venous nutrition for patients in more severe general condition and chose PEG or NG for those in better general condition.”

Participants not randomly assigned to “intervention” and “no intervention” groups so not possible to control for all confounders. They did perform a Cox proportional hazard regression analysis, controlling for some confounders; however this does not cover many of the important covariates detailed in the methods of this review.

“The effects of several variables (TF or PVN, age, sex, CCI scores) on survival time were investi-

<table>
<thead>
<tr>
<th>Takenoshita 2017</th>
<th>Serious</th>
<th>Low</th>
<th>Low</th>
<th>Low</th>
<th>NI</th>
<th>Low</th>
<th>Low</th>
<th>Serious</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants not randomly assigned to “intervention” and “no intervention” groups so not possible to control for all confounders. They did perform a Cox proportional hazard regression analysis, controlling for some confounders; however this does not cover many of the important covariates detailed in the methods of this review.</td>
<td>Baseline happened before intervention. “This study retrospectively compared pre- and postintervention incidences of pneumonia”. Data collected 12 weeks before and 12 weeks after tube feeding (nasogastric or PEG) or peripheral venous nutrition (PVN) commenced.</td>
<td>It is clear whether participants receive PEG, NG or not. “The patients undergoing TF comprised those with a PEG tube (n = 20) and those with a NG tube (n = 26).”</td>
<td>There are no deviations from intended intervention.</td>
<td>Assessors were not blinded and would have been aware of the intervention received by study participants. It may not be feasible to blind assessors with this type of intervention.</td>
<td>They do not conduct multiple measurements and analyses. They do discuss all findings within the discussion.</td>
<td>Based on the highest rating across the categories.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
"In patients receiving TF, records for a maximum 12 weeks before and 12 weeks after the start of TF were considered."

Objective measure so will not be affected by knowledge of the intervention.

Table 7. ROBINS-I assessments for: mixed (nasogastric or PEG) or unspecified enteral tube feeding: survival time (Continued)

<table>
<thead>
<tr>
<th>Study</th>
<th>Bias due to confounding</th>
<th>Bias in selection of participants into the study</th>
<th>Bias in classification of interventions</th>
<th>Bias due to deviations from the intended intervention</th>
<th>Bias due to missing data</th>
<th>Bias in measurement of outcomes</th>
<th>Bias in selection of the reported result</th>
<th>Overall risk of bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arinzon 2008</td>
<td>Serious</td>
<td>Critical</td>
<td>Low</td>
<td>Low</td>
<td>NI</td>
<td>Moderate</td>
<td>Low</td>
<td>Critical</td>
</tr>
<tr>
<td></td>
<td>Participants not randomly assigned to “intervention” and “no intervention” groups so not possible to control for all confounders.</td>
<td>Participants were selected based on having tube feeding or not. All enteral nutrition group participants had several potential indications for initiation of the enteral nutrition. Therefore, the group with enteral tube feeding (intervention of interest) may have been more ill than the control; this will influence the outcome.</td>
<td>Intervention groups were clearly defined.</td>
<td>There are no deviations from intended intervention.</td>
<td>Missing data are not discussed in the paper.</td>
<td>It is not clear if assessors were blinded and would have been aware of the intervention received by study participants. It may not be feasible to blind assessors with this type of intervention.</td>
<td>They do not conduct multiple measurements and analyses. They do discuss all findings within the discussion.</td>
<td>Based on the highest rating across the categories.</td>
</tr>
</tbody>
</table>

Data collection processes from

Table 8. ROBINS-I assessments for: mixed (nasogastric or PEG) or unspecified enteral tube feeding: pressure ulcers

<table>
<thead>
<tr>
<th>Study</th>
<th>Bias due to confounding</th>
<th>Bias in selection of participants into the study</th>
<th>Bias in classification of interventions</th>
<th>Bias due to deviations from the intended intervention</th>
<th>Bias due to missing data</th>
<th>Bias in measurement of outcomes</th>
<th>Bias in selection of the reported result</th>
<th>Overall risk of bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arinzon 2008</td>
<td>Serious</td>
<td>Critical</td>
<td>Low</td>
<td>Low</td>
<td>NI</td>
<td>Moderate</td>
<td>Low</td>
<td>Critical</td>
</tr>
<tr>
<td></td>
<td>Participants not randomly assigned to “intervention” and “no intervention” groups so not possible to control for all confounders.</td>
<td>Participants were selected based on having tube feeding or not. All enteral nutrition group participants had several potential indications for initiation of the enteral nutrition. Therefore, the group with enteral tube feeding (intervention of interest) may have been more ill than the control; this will influence the outcome.</td>
<td>Intervention groups were clearly defined.</td>
<td>There are no deviations from intended intervention.</td>
<td>Missing data are not discussed in the paper.</td>
<td>It is not clear if assessors were blinded and would have been aware of the intervention received by study participants. It may not be feasible to blind assessors with this type of intervention.</td>
<td>They do not conduct multiple measurements and analyses. They do discuss all findings within the discussion.</td>
<td>Based on the highest rating across the categories.</td>
</tr>
</tbody>
</table>

Data collection processes from

ADL: activities of daily living
BMI: body mass index
CCI: charlson comorbidity index
CPS: cognitive performance scale
DNACPR: do not attempt cardiopulmonary resuscitation
FAST: functional assessment staging
TF: tube feeding
PVN: peripheral venous nutrition
The patients in both groups had similar medical backgrounds and diseases, except for a higher prevalence of patients with underweight and presence of pressure sores in ENG than in CG (30% versus 16%, $P = .043, \chi^2 = 4.11$, and 26% versus 12%, $P = .017, \chi^2 = 5.65$; respectively).

**Table 8. ROBINS-I assessments for: mixed (nasogastric or PEG) or unspecified enteral tube feeding: pressure ulcers (Continued)**

<table>
<thead>
<tr>
<th>Bentur 2015</th>
<th>Serious</th>
<th>Critical</th>
<th>Low</th>
<th>Low</th>
<th>Low</th>
<th>Serious</th>
<th>Low</th>
<th>Critical</th>
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<tbody>
<tr>
<td>Participants not randomly assigned to “intervention” and “no intervention” groups so not possible to control for all confounders.</td>
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<td>Participants were interviewed after their relative had received a feeding tube or not.</td>
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<td>Therefore, the group with enteral tube feeding (intervention of interest) may have been more ill than the control; this will influence the outcome.</td>
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<td>“cross-sectional survey of 117 caregivers of OPAD living in the community. Of 117 patients, 26% had feeding tubes”.</td>
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<tr>
<td>Bentur 2015</td>
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<td>Intervention group was clearly defined.</td>
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<td>“Of 117 patients, 26% had feeding tubes”, and they specify what type – “Of the 117 OPAD, 30 (26%) had feeding tubes — 15 (13%) with PEG and 15 (13%) with</td>
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<tr>
<td>Answers were self-report from carers; therefore, there was no blinding of outcome assessors. It may not be feasible to blind assessors with this type of intervention.</td>
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<tr>
<td>They do not conduct multiple measurements and analyses. They do discuss all findings within the discussion.</td>
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<td>“Interviews were conducted with 117 family caregivers of OPAD living in the community.”</td>
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</table>
Table 8. ROBINS-I assessments for: mixed (nasogastric or PEG) or unspecified enteral tube feeding: pressure ulcers (Continued)

<table>
<thead>
<tr>
<th></th>
<th>Cintra 2014</th>
<th>Serious</th>
<th>Critical</th>
<th>Moderate</th>
<th>Low</th>
<th>NI</th>
<th>Serious</th>
<th>Low</th>
<th>Critical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants not randomly assigned to “intervention” and “no intervention” groups so not possible to control for all confounders.</td>
<td>Participants already had enteral tube feeding in place at the start of the study. Therefore, the group with enteral tube feeding (intervention of interest) may have been more ill than the control; this will influence the outcome.</td>
<td>It is not clear which type of tube feeding is used for all participants.</td>
<td>There are no deviations from intended intervention.</td>
<td>Missing data are not discussed in the paper.</td>
<td>Information was collected from patient notes so there is a potential for bias, and data were also collected from questionnaires with carers.</td>
<td>They calculate results for multiple time points; however, they reported results for each time point in the abstract, so not trying to focus on one set of results. No evidence of bias in the reported results.</td>
<td>Based on the highest rating across the categories.</td>
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<tr>
<td>They did not take into account confounders when estimating pressure ulcer risk, only when analysing survival.</td>
<td>“Patients with gastrostomies or feeding tubes were included in the alternative feeding group”.</td>
<td>“Patients with gastrostomies or feeding tubes were included in the alternative feeding group”.</td>
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</table>

OPAD: older people with advanced dementia
### Table 9. ROBINS-I assessments for: mixed (nasogastric or PEG) or unspecified enteral tube feeding: pain and comfort

<table>
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<tr>
<th>Study</th>
<th>Bias due to confounding</th>
<th>Bias in selection of participants into the study</th>
<th>Bias in classification of interventions</th>
<th>Bias due to deviations from the intended intervention</th>
<th>Bias due to missing data</th>
<th>Bias in measurement of outcomes</th>
<th>Bias in selection of the reported result</th>
<th>Overall risk of bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bentur 2015</td>
<td>Serious</td>
<td>Critical</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>Serious</td>
<td>Low</td>
<td>Critical</td>
</tr>
</tbody>
</table>

Participants not randomly assigned to “intervention” and “no intervention” groups so not possible to control for all confounders.

Participants were interviewed after their relative had received a feeding tube or not.

Intervention group was clearly defined.

There are no deviations from intended intervention.

All outcomes report results for 117 patients.

Answers were self-report from carers, therefore there was no blinding of outcome assessors.

They do not conduct multiple measurements and analyses.

They do discuss all findings within the discussion.

Based on the highest rating across the categories.

Therefore, the group with enteral tube feeding (intervention of interest) may have been more ill than the control; this will influence the outcome.

“Of 117 patients, 26% had feeding tubes”, and they specify what type – “Of the 117 OPAD, 30 (26%) had feeding tubes—15 (13%) with PEG and 15 (13%) with nasogastric tubes.”

“Interviews were conducted with 117 family caregivers of OPAD living in the community”.

Data collection processes from both groups were the same.

A validated measure for comfort which includes questions on pain was used (CAD-EOLD) scale but this is not a standardised measure of pain.

“cross-sectional survey of 117 caregivers of OPAD living in the community.

Of 117 patients, 26% had feeding tubes”.

OPAD: older people with advanced dementia
Table 10. ROBINS-I assessments for: mixed (nasogastric or PEG) or unspecified enteral tube feeding: mortality

<table>
<thead>
<tr>
<th>Study</th>
<th>Bias due to confounding</th>
<th>Bias in selection of participants into the study</th>
<th>Bias in classification of interventions</th>
<th>Bias due to deviations from the intended intervention</th>
<th>Bias due to missing data</th>
<th>Bias in measurement of outcomes</th>
<th>Bias in selection of the reported result</th>
<th>Overall risk of bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arinzon 2008</td>
<td>Serious</td>
<td>Critical</td>
<td>Low</td>
<td>Low</td>
<td>NI</td>
<td>Low</td>
<td>Low</td>
<td>Critical</td>
</tr>
<tr>
<td>Participants not randomly assigned to “intervention” and “no intervention” groups so not possible to control for all confounders.</td>
<td>Participants were selected based on having enteral tube feeding or not.</td>
<td>It is clear which participants had the intervention and what intervention.</td>
<td>There are no deviations from intended intervention.</td>
<td>Missing data are not discussed in the paper.</td>
<td>It is not clear if assessors were blinded and would have been aware of the intervention received by study participants. It may not be feasible to blind assessors with this type of intervention.</td>
<td>They do not use multiple outcomes. They do not conduct multiple analyses.</td>
<td>Based on the highest rating across the categories.</td>
<td></td>
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<tr>
<td></td>
<td>There is no controlling for confounding.</td>
<td>All enteral nutrition group patients had had several potential indications for initiation of the enteral nutrition. Therefore, the group with nasogastric (NG) tube feeding (intervention of interest) may have been more ill than the control; this will influence the outcome.</td>
<td>“ENG included 57 severely demented and dependent patients; 74% (42/57) of ENG patients received nutrition through NGT and the remainder by PEG.”</td>
<td>“All enteral nutrition group (ENG) patients had severe cognitive impairment and had several potential indications for initiation of the enteral nutrition.”</td>
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<tr>
<td>Cintra 2014</td>
<td>Serious</td>
<td>Critical</td>
<td>Moderate</td>
<td>Low</td>
<td>NI</td>
<td>Low</td>
<td>Low</td>
<td>Critical</td>
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<tr>
<td>Participants not randomly assigned to “intervention” and “no intervention”</td>
<td>Feeding tubes were in place prior to baseline.</td>
<td>It is not clear which type of tube feeding</td>
<td>There are no deviations from intended intervention.</td>
<td>Missing data are not</td>
<td>Paper does not state if assessors were not blinded</td>
<td>They calculate results for multi-</td>
<td>Based on the highest rating</td>
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</table>
groups so not possible to control for all confounders. They conducted a regression; however, they did not consider all important confounders.

Therefore, the group with enteral tube feeding (intervention of interest) may have been more ill than the control; this will influence the outcome.

They considered: “variables that reached a significance level of.25 or below in the bivariate analysis were included in the stepwise regression. They were: sex, feeding route, duration of diagnosis, duration of dysphagia, FAST classification (numeric variables from 1 to 6, corresponding to FAST 7A to 7F), calf perimeter, presence or not of pressure ulcers equal or above grade 2, number of pressure ulcers, arterial hypertension, diabetes, place of recruitment and story of hospital admission”.

“Patients with gastrostomies or feeding tubes were included in the alternative feeding group”.

"Patients with gastrostomies or feeding tubes were included in the alternative feeding group".

However, survival time is an objective measure so will not be affected by knowledge of the intervention.

Therefore, the group with enteral tube feeding (intervention of interest) may have been more ill than the control; this will influence the outcome.

**Table 10. ROBINS-I assessments for: mixed (nasogastric or PEG) or unspecified enteral tube feeding: mortality** (Continued)

<table>
<thead>
<tr>
<th>Study</th>
<th>Bias due to confounding</th>
<th>Bias in selection of participants into the study</th>
<th>Bias in classification of interventions</th>
<th>Bias due to deviations from the intended intervention</th>
<th>Bias due to missing data</th>
<th>Bias in measurement of outcomes</th>
<th>Bias in selection of the reported result</th>
<th>Overall risk of bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arinzon 2008</td>
<td>Serious</td>
<td>Critical</td>
<td>Low</td>
<td>Low</td>
<td>NI</td>
<td>Low</td>
<td>Low</td>
<td>Critical</td>
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</tbody>
</table>
Participants not randomly assigned to “intervention” and “no intervention” groups so not possible to control for all confounders.

Authors use Pearson’s correlation; consequently, the analysis does not account for confounders.

Participants were selected based on having tube feeding or not. All enteral nutrition group patients had several potential indications for initiation of the enteral nutrition. Therefore, the group with enteral tube feeding (intervention of interest) may have been more ill than the control; this will influence the outcome.

“All enteral nutrition group (ENG) patients had severe cognitive impairment and several potential indications for initiation of the enteral nutrition.”

Intervention groups were clearly defined. “ENG included 57 severely demented and dependent patients; 74% (42/57) of ENG patients received nutrition through NGT and the remainder by PEG.”

There are no deviations from intended intervention.

Missing data are not discussed in the paper.

It is not clear if assessors were blinded and would have been aware of the intervention received by study participants. It may not be feasible to blind assessors with this type of intervention.

However, they used laboratory data which is objective measure and will not be influenced by knowledge of the intervention.

They do not use multiple outcomes. They do not conduct multiple analyses.

Based on the highest rating across the categories.

### Table 11. ROBINS-I assessments for: mixed (nasogastric or PEG) or unspecified enteral tube feeding: nutritional parameters (Continued)

<table>
<thead>
<tr>
<th>Category</th>
<th>Assessments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mixed (nasogastric or PEG) or unspecified enteral tube feeding:</strong> Nutritional parameters</td>
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<td><strong>1. Bias in outcome measurement:</strong></td>
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<td><strong>2. Bias in selection of participants:</strong></td>
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<td><strong>3. Bias in measurement of interventions:</strong></td>
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<td><strong>5. Bias in selection of participants:</strong></td>
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<td><strong>6. Bias in measurement of interventions:</strong></td>
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<td><strong>7. Bias in outcome measurement:</strong></td>
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<td><strong>100. Bias in outcome measurement:</strong></td>
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</tbody>
</table>
APPENDICES

Appendix 1. Sources searched and search strategies

<table>
<thead>
<tr>
<th>Source</th>
<th>Search strategy</th>
<th>Hits retrieved</th>
</tr>
</thead>
</table>
| CENTRAL (The Cochrane Library) http://cr-so.cochrane.org/SearchSimple.php | #1 dement*<br>#2 MeSH descriptor: [Dementia] explode all trees<br>#3 alzheimer*<br>#4 MeSH descriptor: [Alzheimer Disease] explode all trees<br>#5 #1 or #2 or #3 or #4<br>#6 "enteral nutrition"<br>#7 "nutritional support"<br>#8 "percutaneous feeding"<br>#9 "artificial feeding"<br>#10 "artificial hydration"<br>#11 "endoscopic gastrostomy"<br>#12 "tube feeding"<br>#13 peg<br>#14 "enteral feeding"<br>#15 "stomach tub"
#16 "forced feed"
#17 "artificial nutrition"
#18 "nutritional support"
#19 "feeding methods"
#20 #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
#21 #5 and #20                                                                 | Dec 2019: 87<br>April 2021: 33 |
| ALOIS: Cochrane Dementia and Cognitive Improvement Group Specialized Register (CRS web) | enteric OR enteral OR endoscopic OR gastrostomy OR stomach OR feeding AND INREGISTER                                                                                                                        | Dec 2019: 140<br>April 2021: 32 |
MEDLINE In-process and other non-indexed citations and MEDLINE 1950-present (Ovid SP)

1. dement$.mp.
2. alzheimer$.mp.
3. "lewy bod*$".mp.
4. FTLD.mp.
5. PDD.mp.
6. "major neurocognitive disorder"*.mp.
7. exp Dementia/
9. or/1-8
10. exp Enteral Nutrition/
11. nutritional support/
12. percutaneous feed*.ti,ab.
13. artificial feeding.ti,ab.
14. artificial hydration.ti,ab.
15. endoscopic gastrostomy.ti,ab.
16. peg.ti,ab.
17. enteral feed*.ti,ab.
18. stomach tube$.ti,ab.
19. forced feeding.ti,ab.
20. forced fed.ti,ab.
21. force fed.ti,ab.
22. force feeding.ti,ab.
23. artificial nutrition.ti,ab.
24. nutritional support.ti,ab.
25. enteral nutrition.ti,ab.
26. feeding methods.ti,ab.
27. (tube adj2 (nasogastric or naso-jejunal or jejunostomy post-pyloric feeding*)).ti,ab.
28. tube feeding*.ti,ab.
29. eating disturbance*.ti,ab.
30. eating problem*.ti,ab.
31. gastrostom*.ti,ab.

Enteral tube feeding for people with severe dementia (Review)

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Enteral tube feeding for people with severe dementia (Review)

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32. percutaneous feed*.mp.
33. peg.mp.
34. stomach tube*.mp.
35. tube feed*.mp.
36. (tube adj2 (nasogastric or naso-jejunal or jejunostomy post-pyloric feeding*)).mp.
37. or/14-36
38. 13 and 37

---

PsycINFO (Ovid SP)
1. alzheimer*.mp.
2. dement*.mp.
3. FTLD.mp.
4. "lewy bod**.mp.
5. "major neurocognitive disorder**.mp.
6. neurocognitive dysfunction.mp.
7. PDD.mp.
8. vascular cognitive impair*.mp.
9. VCI.mp.
10. VAD.mp.
11. exp dementia/
12. (severe adj2 cognit* impair*).mp.
13. or/1-12
14. exp Food Intake/
15. Eating Behavior/
16. Dysphagia/
17. Nutrition/
18. artificial feeding.mp.
19. artificial* hydration.mp.
20. enteral feed*.mp.
21. enteric feed*.mp.
22. eating disturbance*.mp.
23. eating problem*.mp.
24. endoscopic gastrostomy.mp.
25. enteral nutrition.mp.

[Date of most recent search: 14 April 2021]
(Continued)

26. feeding option*.mp.
27. forced feeding.mp.
28. forced fed.mp.
29. force fed.mp.
30. force feeding.mp.
31. feeding methods.mp.
32. gastrostom*.mp.
33. nutritional support.mp.
34. percutaneous feed*.mp.
35. peg.mp.
36. stomach tube*.mp.
37. tube feed*.mp.
38. (tube adj2 (nasogastric or naso-jejunal or jejunostomy post-pyloric feeding*)).mp.
39. or/14-38
40. 13 and 39

<table>
<thead>
<tr>
<th>CINAHL (EBSCOhost)</th>
<th>Dec 2019: 892</th>
</tr>
</thead>
<tbody>
<tr>
<td>S1 TX alzheimer*</td>
<td>April 2021: 118</td>
</tr>
<tr>
<td>S2 TX dement*</td>
<td></td>
</tr>
</tbody>
</table>

[Date of most recent search: 14 April 2021]

S3 TX FTLD
S4 TX "lewy bod**
S5 TX "major neurocognitive disorder**
S6 TX neurocognitive dysfunction
S7 TX PDD
S8 TX vascular cognitive impair*
S9 TX VCI
S10 TX VAD
S11 (MH "Dementia") OR (MH "Delirium, Dementia, Amnestic, Cognitive Disorders")
S12 (MH "Cognition Disorders")
S13 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12
S14 (MH "Enteral Nutrition")
S15 (MH "Enteral Feeding Pumps") OR (MH "Feeding Tubes")
S16 TX artificial feeding
S17 TX artificial* hydration
(Continued)

S18 TX enteral feed*
S19 TX enteric feed*
S20 TX eating disturbance*
S21 TX eating problem*
S22 TX endoscopic gastrostomy
S23 TX enteral nutrition
S24 TX feeding option*
S25 TX forced feeding
S26 TX forced fed
S27 TX force fed
S28 TX force feeding
S29 TX feeding methods
S30 TX gastrostom*
S31 TX nutritional support
S32 TX percutaneous feed*
S33 TX peg
S34 TX stomach tube*
S35 TX jejunostomy post-pyloric feeding*
S36 S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35
S37 S13 AND S36

ISI Web of Science – core collection

[Date of most recent search: 14 April 2021]

TOPIC: (enteral nutrition OR percutaneous feed* 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 enteric) AND TOPIC: (dement* OR alzheimer* OR "lew* bod*" OR frontotemporal OR FTD OR FTLD OR "severe* cognit* impair")


LILACS (BIREME)

[Date of most recent search: 14 April 2021]

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 [Words] and demência OR dementia OR demencia OR alzheimer$ [Words]

Dec 2019: 12
April 2021: 1

ClinicalTrials.gov

(www.clinicaltrials.gov)

Intervention: Enteral OR enteric OR feeding OR gastrostomy OR stomach tube OR artificial nutrition
Condition: dementia OR alzheimer OR alzheimers OR lewy body OR frontotemporal OR FTD OR FTLD

Dec 2019: 16
April 2021: 1
Recruitment status: All

ICTRP (http://apps.who.int/trialsearch.aspx)  
Intervention: Enteral OR enteric OR feeding OR gastrostomy OR stomach tube OR artificial nutrition
Condition: dementia OR alzheimer OR alzhiemers OR lewy body OR frontotemporal OR FTD OR FTLD

[Date of most recent search: 14 April 2021]

TOTAL before de-duplication  
Dec 2019: 6846  
April 2021: 1163

TOTAL after de-duplication  
Dec 2019: 4970  
April 2021: 892  
TOTAL: 5862

TOTAL after first assessment by CDCIG information specialist  
651

HISTORY

Protocol first published: Issue 12, 2019

CONTRIBUTIONS OF AUTHORS

All authors contributed to the conception and design of this review.

All authors contributed to drafting the review, commented on it critically for intellectual content, and approved the final version for publication.

DECLARATIONS OF INTEREST

Nathan Davies: none known.
Yolanda Barrado-Martin: none known.
Greta Rait: none known.
Akiko Fukui: none known.
Bridget Candy: none known.
Christina H Smith: none known.
Jill Manthorpe: none known.
Kirsten J Moore: none known.
Elizabeth L Sampson: none known.
Victoria Vickerstaff: none known.

SOURCES OF SUPPORT

Internal sources

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Alzheimer’s Society, UK

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External sources

- NIHR, UK

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We planned to include participants with poor nutritional intake at baseline, assessed using objective (scale-based) clinical tools (e.g. Malnutrition Universal Screening Tool (MUST) (Elia 2003). However, no studies reported use of such a measure and so we accepted studies which simply reported the use of enteral tube feeding.

We planned to include participants with severe dementia according to validated diagnostic criteria. However, many of the studies did not refer to validated criteria, but relied on a clinical diagnosis. We chose to include these studies as, had we not, this review would have included only two studies. We considered that this would exclude important, clinically-informative evidence.

We included studies with a mixed population where a separate analysis was conducted on those with severe dementia, or where the mixed population included 50% or more with severe dementia. This was not previously specified in the protocol.

Finally, we originally planned to include a range of controlled comparison studies: randomised controlled trials (RCTs), controlled trials, controlled before-and-after studies, and interrupted time-series studies. We also planned to include observational studies with no control group. However, following further consultation with Cochrane, we did not include studies without a control group and we included any controlled, non-randomised studies.