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# Palliative care interventions in advanced dementia (Review)

Walsh SC, Murphy E, Devane D, Sampson EL, Connolly S, Carney P, O'Shea E

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[Intervention Review]

# Palliative care interventions in advanced dementia

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## ABSTRACT

### Background

Dementia is a chronic, progressive and ultimately fatal neurodegenerative disease. Advanced dementia is characterised by profound cognitive impairment, inability to communicate verbally and complete functional dependence. Usual care of people with advanced dementia is not underpinned universally by a palliative approach. Palliative care has focused traditionally on care of people with cancer, but for more than a decade, there have been calls worldwide to extend palliative care services to include all people with life-limiting illnesses in need of specialist care, including people with dementia.

This review is an updated version of a review first published in 2016.

### Objectives

To assess the effect of palliative care interventions in advanced dementia.

### Search methods

We searched ALOIS, the Cochrane Dementia and Cognitive Improvement Group's Specialised Register on 7 October 2020. ALOIS contains records of clinical trials identified from monthly searches of several major healthcare databases, trial registries and grey literature sources. We ran additional searches across MEDLINE (OvidSP), Embase (OvidSP), four other databases and two trial registries on 7 October 2020 to ensure that the searches were as comprehensive and as up-to-date as possible.

### Selection criteria

We searched for randomised (RCTs) and non-randomised controlled trials (nRCTs), controlled before-and-after studies and interrupted time series studies evaluating the impact of palliative care interventions for adults with advanced dementia of any type. Participants could be people with advanced dementia, their family members, clinicians or paid care staff. We included clinical interventions and non-clinical interventions. Comparators were usual care or another palliative care intervention. We did not exclude studies based on outcomes measured.

### Data collection and analysis

At least two review authors (SW, EM, PC) independently assessed all potential studies identified in the search against the review inclusion criteria. Two authors independently extracted data from eligible studies. Where appropriate, we estimated pooled treatment effects in a fixed-effect meta-analysis. We assessed the risk of bias of included studies using the Cochrane Risk of Bias tool and the overall certainty of the evidence for each outcome using GRADE.

**Main results**

Nine studies (2122 participants) met the review inclusion criteria. Two studies were individually-randomised RCTs, six were cluster-randomised RCTs and one was a controlled before-and-after study. We conducted two separate comparisons: organisation and delivery of care interventions versus usual care (six studies, 1162 participants) and advance care planning interventions versus usual care (three studies, 960 participants). Two studies were carried out in acute hospitals and seven in nursing homes or long-term care facilities. For both comparisons, we found the included studies to be sufficiently similar to conduct meta-analyses.

Changes to the organisation and delivery of care for people with advanced dementia may increase comfort in dying (MD 1.49, 95% CI 0.34 to 2.64; 5 studies, 335 participants; very low certainty evidence). However, the evidence is very uncertain and unlikely to be clinically significant. These changes may also increase the likelihood of having a palliative care plan in place (RR 5.84, 95% CI 1.37 to 25.02; 1 study, 99 participants; $I^2$ = 0%; very low certainty evidence), but again the evidence is very uncertain. Such interventions probably have little effect on the use of non-palliative interventions (RR 1.11, 95% CI 0.71 to 1.72; 2 studies, 292 participants; $I^2$ = 0%; moderate certainty evidence). They may also have little or no effect on documentation of advance directives (RR 1.46, 95% CI 0.50 to 4.25; 2 studies, 112 participants; $I^2$ = 52%; very low certainty evidence), or whether discussions take place about advance care planning (RR 1.08, 95% CI 1.00 to 1.18; 1 study, 193 participants; $I^2$ = 0%; very low certainty evidence) and goals of care (RR 2.36, 95% CI 1.00 to 5.54; 1 study, 13 participants; $I^2$ = 0%; low certainty evidence). No included studies assessed adverse effects.

Advance care planning interventions for people with advanced dementia probably increase the documentation of advance directives (RR 1.23, 95% CI 1.07 to 1.41; 2 studies, 384; moderate certainty evidence) and the number of discussions about goals of care (RR 1.33, 95% CI 1.11 to 1.59; 2 studies, 384 participants; moderate certainty evidence). They may also slightly increase concordance with goals of care (RR 1.39, 95% CI 1.08 to 1.79; 1 study, 63 participants; low certainty evidence). On the other hand, they may have little or no effect on perceived symptom management (MD -1.80, 95% CI -6.49 to 2.89; 1 study, 67 participants; very low certainty evidence) or whether advance care planning discussions occur (RR 1.04, 95% CI 0.87 to 1.24; 1 study, 67 participants; low certainty evidence).

**Authors' conclusions**

The evidence on palliative care interventions in advanced dementia is limited in quantity and certainty. When compared to usual care, changes to the organisation and delivery of care for people with advanced dementia may lead to improvements in comfort in dying, but the evidence for this was of very low certainty. Advance care planning interventions, compared to usual care, probably increase the documentation of advance directives and the occurrence of discussions about goals of care, and may also increase concordance with goals of care. We did not detect other effects. The uncertainty in the evidence across all outcomes in both comparisons is mainly driven by imprecision of effect estimates and risk of bias in the included studies.

## PLAIN LANGUAGE SUMMARY

### Palliative care for people with advanced dementia

**Review question**

In this research, we wanted to see if palliative care helps people with advanced dementia or helps their family or carers. We also wanted to describe how researchers tried to measure the effect of palliative care.

**Background**

People with dementia experience a gradual decline in their mental abilities and their ability to take care of themselves. The decline occurs over an extended period, so it is often difficult to identify the final, terminal phase of the disease. During the advanced stage of dementia, people are unable to communicate verbally, are completely dependent on others, have difficulty swallowing and often experience double incontinence. People with advanced dementia often become confined to a chair or bed and are at increased risk of infections, such as pneumonia.

Palliative care is a particular way of caring for people who have diseases that cannot be cured. The main aims of palliative care are to reduce pain and to maintain the best possible quality of life as death approaches. Palliative care is used a lot with people with cancer but is not used much for people with advanced dementia.

**Study characteristics**

We examined the research published up to October 2020. We found nine suitable studies that involved 2122 people. The studies came from the USA, Canada, the UK and Europe. Two studies were carried out in hospitals and seven in nursing homes or long-term care facilities.

**Key results**

Six studies tested changes to the way care for people with advanced dementia is organised and delivered. Five studies found that these changes may increase comfort in dying, but problems with study design and differences in outcome between studies make this result very uncertain, so it is possible that overall they may make little or no difference. Changes to care organisation and delivery may also mean

that people with advanced dementia are more likely to have a plan in place for their care, but this result came from only one study, and again we are very uncertain about it. Making changes to how care is organised and delivered probably has no effect on the use of non-palliative approaches to care and may have little or no effect on whether discussions take place between people with dementia, their family caregiver, and their doctors and nurses on the nature and type of palliative care they would like to receive.

Two studies found that helping the person with dementia and their family to plan ahead probably makes it more likely that the person with dementia has a written document giving instructions on the types of treatments they want to receive (an advance care plan), and that they have spoken to their doctors and nurses about what they would like from their care. One of these studies also found that advance planning may mean that there is slightly more agreement between what the doctors and nurses believe are the care goals and what the person with dementia believes. However, based on one study, planning may not impact on how well family caregivers feel the person with dementia's symptoms are managed.

**Conclusions**

Overall, the research done so far does not give a clear picture about how palliative care can best be used to help either the person with advanced dementia or their family. Little research has been done about people with advanced dementia, often because of ethical concerns. However, although it is hard to do research with people with dementia, more well-designed studies are required to work out how palliative care can be used best in this special population.

## Summary of findings 1. Organisation and delivery compared to usual care in advanced dementia

**Organisation and delivery compared to usual care in advanced dementia**

**Patient or population:** advanced dementia
**Setting:** long-term care facility or acute hospital
**Intervention:** organisation and delivery
**Comparison:** usual care

| Outcomes | № of participants (studies) | Certainty of the evidence (GRADE) | Relative effect (95% CI) | Anticipated absolute effects* (95% CI) | |
|---|---|---|---|---|---|
| | | | | Risk with usual care | Risk with organisation and delivery |
| Comfort in dying<br>assessed with: Comfort Assessment in Dying with Dementia (CAD-EOLD) Scale. Scores range from 14 to 42, with higher scores indicating more comfort. | 335<br>(5 RCTs) | ⊕⊖⊖⊖<br>Very low[a] | - | The mean comfort in dying score was 33.38 | MD 1.49 higher<br>(0.34 higher to 2.64 higher) |
| Symptom management<br>assessed with: Symptom Management at the End-of-Life in Dementia (SM-EOLD) Scale. Scores range from 0 to 45, with higher scores indicating better symptom management. | 226<br>(2 RCTs) | ⊕⊖⊖⊖<br>Very low[b] | - | Not pooled | Not pooled |
| Pain - not measured | - | - | - | - | - |
| Palliative care plan in place | 99<br>(1 RCT) | ⊕⊖⊖⊖<br>Very low[c] | RR 5.84<br>(1.37 to 25.02) | Study population | |
| | | | | 39 per 1000 | 190 more per 1000<br>(15 more to 942 more) |
| Quality of life<br>assessed with: Quality of Life in Late-Stage Dementia (QUALID) Scale. Ranges from 12 to 45, with higher scores indicating worse quality of life. | 15<br>(1 RCT) | ⊕⊖⊖⊖<br>Very low[c] | - | The mean quality of life score was 28.1 | MD 8.2 lower<br>(16.13 lower to 0.27 lower) |
| Advance care planning discussion occurred | 193<br>(1 RCT) | ⊕⊖⊖⊖<br>Very low[d] | RR 1.08<br>(1.00 to 1.18) | Study population | |
| | | | | 885 per 1000 | 71 more per 1000 |

| | | | | | |
|---|---|---|---|---|---|
| | | | | | (0 fewer to 159 more) |
| Concordance with goals of care - not measured | - | - | - | - | - |

*__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.

[a]Downgraded two levels due to concerns regarding risk of bias and one level due to inconsistency (large heterogeneity)
[b]Downgraded two levels due to concern regarding risk of bias, one level due to inconsistency (large unexplained heterogeneity) and one level due to imprecision (low-powered analysis and a wide confidence interval)
[c]Downgraded one level due to concern regarding risk of bias and two levels due to imprecision (data from a single study with a small number of participants and wide confidence interval)
[d]Downgraded two levels due to concerns regarding risk of bias and one level due to imprecision (data from a single study)

## Summary of findings 2. Advance care planning compared to usual care in advanced dementia

**Advance care planning compared to usual care in advanced dementia**

**Patient or population:** advanced dementia
**Setting:** long-term care facility or acute hospital
**Intervention:** advance care planning (ACP)
**Comparison:** usual care

| Outcomes | № of participants (studies) | Certainty of the evidence (GRADE) | Relative effect (95% CI) | Anticipated absolute effects* (95% CI) | |
|---|---|---|---|---|---|
| | | | | Risk with usual care | Risk with advance care planning |
| Comfort in dying - not measured | - | - | - | - | - |
| Symptom management assessed with: Symptom Management at the End-of-Life in Dementia (SM-EOLD) Scale. Scores range | 67 (1 RCT) | ⊕⊖⊖⊖ Very low[a] | - | The mean symptom management score was 35.5 | MD 1.8 lower (6.49 lower to 2.89 higher) |

| | | | | | |
|---|---|---|---|---|---|
| from 0 to 45, with higher scores indicating better symptom management. | | | | | |
| Pain - not measured | - | - | - | - | - |
| Palliative care plan in place - not measured | - | - | - | - | - |
| Quality of Life - not measured | - | - | - | - | - |
| Advance care planning discussion occurred | 67<br>(1 RCT) | ⊕⊕⊖⊖<br>Low[b] | RR 1.04<br>(0.87 to 1.24) | Study population<br>87 per 100 | <br>4 more per 100<br>(11 fewer to 21 more) |
| Concordance with goals of care | 63<br>(1 RCT) | ⊕⊕⊖⊖<br>Low[b] | RR 1.39<br>(1.08 to 1.79) | Study population<br>67 per 100 | <br>26 more per 100<br>(5 more to 53 more) |

*__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.

[a]Downgraded one level due to concerns regarding risk of bias and two levels due to imprecision (data from a single study with a small number of participants and wide confidence interval)
[b]Downgraded one level due to concerns regarding risk of bias and one level due to imprecision (data from a single study with a small number of participants)

# BACKGROUND

## Description of the condition

Dementia is a chronic, progressive and ultimately fatal neurodegenerative disease with several different causes. It currently affects 55 million people worldwide, with the incidence of dementia estimated to be nearly 10 million new cases per year (WHO 2021). In a ten-year longitudinal study of 18,248 people aged 65 years and over in the UK, the overall prevalence of dementia at death was 30%, and there was a marked increase in such deaths with age: from 6% of people aged 65 to 69 years up to 58% of people aged 95 years and older at time of death (Brayne 2006). Therefore, providing appropriate care to the growing number of older people living and dying with dementia is an issue of immense clinical and public health importance.

Although not a normal part of ageing, dementia affects mainly older people, eroding their cognitive and functional abilities and social skills, often leading to an increase in challenging behaviours and low mood. People with dementia experience a gradual decline in abilities over an extended period, but it is challenging to identify the final, terminal phase of the disease. Advanced or end-stage dementia is characterised by profound cognitive impairment, inability to communicate verbally, complete functional dependence, and often, dysphagia and double incontinence. People with advanced dementia are at increased risk of infections, such as urinary tract infections and pneumonia, typically becoming bed- or chair-bound, increasing the risk of developing pressure ulcers (Capon 2007).

Advanced dementia is typically defined as having a formal diagnosis of dementia by a clinician, with dementia staged by a validated tool - for example, the Functional Assessment Staging Test (FAST) (Reisberg 1982). Reported six-month mortality rates for people with advanced dementia of 25% (Mitchell 2009), consistent with high mortality rates among people with advanced dementia from other studies (Mitchell 2004; Morrison 2000a), indicate a life expectancy similar to that in conditions generally recognised as terminal, for example, metastatic breast cancer (Mitchell 2009). Therefore, advanced dementia can be regarded as a terminal condition. The focus of much, though not necessarily all, of the care provided is palliative, maximising comfort and quality of life, rather than curative. However, studies have shown that people with advanced dementia are often subject to unnecessary investigations during the terminal phase of their illness (Mitchell 2009; Morrison 2000a), and have less analgesia prescribed in the last six months of life compared to people without cognitive impairment (Morrison 2000b). Failure to recognise and treat pain in dementia is widespread, and the risk increases with increased severity of the disease (Achterberg 2019). There is also evidence of a high prevalence of antimicrobial treatment in nursing home residents with advanced dementia (Di Giulio 2008; Givens 2010; Mitchell 2014), including evidence that antimicrobial treatment intensifies significantly as people approach death (D'Agata 2008). Thus, usual care of people with advanced dementia is not universally underpinned by a palliative approach.

There are important differences between dementia and other terminal diseases. In dementia, prognosis is less predictable, and the trajectory of the disease varies: without comorbidity, the median time from diagnosis to death depends strongly on age at diagnosis, varying from 6.7 years for people diagnosed aged 60 to 69 years to 1.9 years for people diagnosed at age 90 or over (Rait 2010). Shuster reported that advanced dementia can last two to three years (Shuster 2000), but even for people with advanced dementia, estimating prognosis is still difficult. Medical and nursing home staff overestimate prognosis in advanced dementia (Mitchell 2004), and proposed mortality risk models provide, at best, only modest accuracy in predicting six-month survival (Mitchell 2009; Mitchell 2012).

One systematic review concluded a need to identify reliable, sensitive and specific prognosticators of mortality in advanced dementia (Brown 2012). Unlike other leading causes of death, advanced dementia is characterised by persistently severe disability during the last year of life (Gill 2010). In addition, the diagnosis and evaluation of pain are more difficult due to challenges communicating with the person with advanced dementia. People with advanced dementia are not always able to express their wishes about their current and future care, due both to their very limited speech and to their lack of capacity to make decisions (Allen 2003). Thus, this adds to the complexity involved in meeting current care needs and developing an advance care plan, if a plan is not already in place. Further, clinicians or nurses are not always sensitive to non-verbal means of communicating pain and distress by people with dementia (Allan 2014; Hubbard 2002).

Palliative care has focused traditionally on care for people with cancer, but for more than a decade, there have been increased calls worldwide to extend palliative care services to include all people with life-limiting illnesses in need of specialist care, including people with dementia (Australian Government 2006; Cahill 2012; Davies 2004; National Council for Palliative Care 2006). In the US, there have been some specialist hospices for people with advanced dementia for some time (Volicer 1994), and there has been a significant increase in the provision of hospice care for people with dementia since the mid-2000s (Alzheimer's Association 2014; Torke 2010). But appropriate care is still not consistently available across the US for people with advanced dementia (Kim 2005; Mitchell 2007).

Globally, some examples of good practice in palliative care services for people with dementia have emerged, but overall, people with dementia tend to die in residential care, in acute hospitals or at home without palliative interventions (Houttekier 2010; Parker 2011; Ryan 2012). There is some evidence of good palliative care practice for people with dementia in low- and middle-income countries (Shaji 2009), but palliative care in general is underdeveloped in these regions (Lamas 2012).

The European Association of Palliative Care (EAPC) published a white paper providing a definition, for the first time, of optimal palliative care for people with dementia, based on a Delphi exercise involving experts from 23 countries (Van der Steen 2014). A Delphi exercise is an iterative process used to arrive at a group opinion or decision on a particular issue, with the goal of moving closer to expert consensus at each iteration. The EAPC defines palliative care as "the active, total care of the patients whose disease is not responsive to curative treatment. Control of pain, of other symptoms, and social, psychological and spiritual problems is paramount. Palliative care is interdisciplinary in its approach and encompasses the patient, the family and the community in its scope. In a sense, palliative care encapsulates the most basic concept of care - that of providing for the patient's needs wherever he or she is cared for, either at home or in the hospital. Palliative

care affirms life and regards dying as a normal process; it neither hastens nor postpones death. It sets out to preserve the best possible quality of life until death" (EAPC 2016).

### Description of the intervention

In this review, we included and appraised interventions to improve palliative care delivered to people with advanced dementia. An intervention can impact one or more of the following domains.

- The person with dementia, focusing on managing pain or on psychological, social or spiritual dimensions of the person with dementia.
- The family/carer, with an emphasis on carer well-being, carer burden and bereavement support.
- The quality of care, which may include interventions such as staff education programmes or the organisation and delivery of care.

The interventions may focus on individual components of care – for example, pain management – or be multi-component interventions aimed at changing the way care is delivered and at improving communication between clinicians, professional carers, the person with dementia and the family.

### How the intervention might work

There is some evidence of the benefits of palliative care teams, mainly for people with cancer (Gomes 2013; Higginson 2003), but evidence on the effects of other palliative care interventions is inconclusive (Candy 2012; Chan 2016). Given the complexity of managing people with advanced dementia in the terminal stages of their disease, we anticipated several different types of interventions could work to improve care in advanced dementia. It is likely that the mechanism by which the interventions may work will also vary significantly; for example:

- for the person with advanced dementia: by providing relief from pain, avoiding unnecessary investigations, medications and transitions, and by increasing comfort;
- for the family: by increasing their understanding of what to expect during the dying process, by maximising communication with healthcare professionals, by helping families cope with the illness and bereavement, and by reducing the care burden on family carers;
- on the system of care: by placing the person with advanced dementia at the centre of the care process, raising the level of awareness of the needs of the person with advanced dementia and enhancing the communication skills of professional carers.

### Why it is important to do this review

There is an increased focus worldwide on extending palliative care to all those in need of it, as evidenced by the 2014 white paper from the EAPC defining optimal palliative care for people with dementia (Van der Steen 2014). There is a need to synthesise the evidence available on interventions that improve care for people with advanced dementia for policy makers and clinicians. The chronic disease course of dementia gives families, carers, clinicians and – during the early stages of the disease, the person with dementia – the opportunity to look ahead and plan for the final stages of care. Such decisions should be underpinned by good-quality evidence.

There is potential for some overlap between this review and the Cochrane Review completed by Hall 2011 entitled 'Interventions for improving palliative care for older people living in nursing care homes'. However, our review differs from Hall 2011. It focuses on people with advanced dementia in need of palliative care, living in any setting, and includes both interventions that focus on individual components of palliative care (for example, pain management) and multi-component service interventions.

## OBJECTIVES

To assess the effect of palliative care interventions in advanced dementia.

## METHODS

### Criteria for considering studies for this review

#### Types of studies

Because of the complexity of conducting randomised controlled trials (RCTs) with people with advanced dementia, we anticipated few RCTs. Therefore, we considered it necessary to include a broader range of controlled comparison studies to help us to determine the effect of interventions to improve care in advanced dementia. Thus, we considered RCTs, trials where allocation was truly random (e.g. random number table); non-randomised controlled trials (nRCTs), where allocation was not truly random (e.g. alternation), controlled before-and-after studies (CBA) and interrupted time series (ITS) studies for inclusion in this review.

We used the criteria defined in the Cochrane Effective Practice and Organisation of Care (EPOC) Review Group guidelines (EPOC 2013) for the inclusion of CBA and ITS studies, as follows: CBA studies must have had at least two intervention sites and two control sites; ITS studies must have had a clearly defined point in time when the intervention occurred, and at least three data points before and three after the intervention.

#### Types of participants

Adults of either gender, with dementia of any type staged as advanced by a recognised and validated tool, such as stage 6d or above on the FAST (Reisberg 1988), CDR-3 (severe) on the Clinical Dementia Rating (CDR) Scale (Hughes 1982), stage 7 on the Global Deterioration Scale (GDS) (Reisberg 1982), or any other validated measure. We also included studies where the participants were informal or paid carers of people with advanced dementia.

We anticipated that there would be few studies where all participants had advanced dementia. Therefore, we decided a priori to include studies where separate results for people with advanced dementia were available or where more than 80% of the study population had advanced dementia, as defined above. Participants could be living in their own homes or with a family member, in supported housing, in any type of long-term care facility, in a hospice or hospital.

#### Types of interventions

We included clinical and non-clinical interventions including one or more of the following:

- assessment and management of physical, psychological and spiritual symptoms of the person;

- advance care planning, including decision-aid interventions for family carers/surrogates;
- management of transition(s) of the person with advanced dementia from one care setting to another;
- education and training on living and dying with advanced dementia for family members;
- education and training on advanced dementia for clinicians and professional care staff;
- changes in the organisation of care to incorporate a palliative approach to care for the person with advanced dementia.

These interventions are broadly grouped into two categories: (1) interventions relating to the organisation and delivery of care; and (2) advance care planning interventions.

#### *Comparison*

We prespecified these comparisons:

- organisation and delivery of palliative care interventions versus usual care;
- advance care planning intervention versus usual care;
- organisation and delivery of palliative care interventions versus advance care planning interventions.

### Types of outcome measures

We developed the outcomes for this review by drawing on the EAPC definition of palliative care (Van der Steen 2014), along with the "domains and dimensions of outcome measures in palliative care" (Bausewein 2011). We chose to measure patient comfort and symptom management as our primary outcomes. The selection of these outcomes was informed by the fact that a central aim of palliative care is to ensure the best possible quality of life, while also managing symptoms (Dixon 2015).

#### *Primary outcomes*

##### Patient- and family-centred outcomes

- Patient comfort in dying - patient- or proxy-reported by family or by nursing staff, using a validated scale (e.g. Comfort Assessment in Dying with Dementia (CAD-EOLD))
- Symptom management – overall symptom management or management of individual symptoms. Overall symptom management can be either patient- or proxy-reported by family or nursing staff, using a validated scale (e.g. Symptom Management at the End-of-Life in Dementia (SM-EOLD))

#### *Secondary outcomes*

##### Patient- and family-centred outcomes

- Quality of Life - patient- or proxy-reported, using a validated scale (e.g. Quality of Life in Late-Stage Dementia (QUALID))
- Pain - measured through observation or by a validated scale
- Palliative care plan in place/palliative domains in care plan

##### Prescribing practices

- Review of prescribing of antipsychotic medications
- Review of prescribing of analgesics

##### Non-palliative interventions (measured in any period before death)

- Use of non-palliative interventions. If more than one non-palliative intervention was measured, the order of selection was as follows: (1) hospital admissions/acute care episodes; (2) use of enteral (tube) feeding; (3) use of parenteral therapy (use of injections or intravenous (IV) fluids); (4) use of antibiotics

##### Advance care planning (ACP)

- Discussion with patient and/or family on ACP directives occurred
- Documentation of advance directives. If more than one advance directive was documented, we extracted data related to one advance directive only, based on the following order of selection: (1) documentation of 'do not tube-feed'; (2) documentation of 'do not resuscitate' (DNR); (3) documentation of 'do not use parenteral therapy'; (4) documentation of 'do not hospitalise' (DNH)
- Decisional conflict in carers
- Goals of care discussion occurred
- Care consistent with goals (concordance)

We analysed separately outcomes for the two intervention types: (1) organisation and delivery of care and (2) advance care planning. We did not exclude studies based on the outcomes measured.

## Search methods for identification of studies

### Electronic searches

We searched ALOIS (alois.medsci.ox.ac.uk/), the Cochrane Dementia and Cognitive Improvement Group Specialised Register on 7 October 2020. The search terms were: palliative OR "end of life" OR dying.

The Information Specialists of the Cochrane Dementia and Cognitive Improvement Group maintain ALOIS, which contains dementia and cognitive improvement studies identified from:

- monthly searches of several 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 several trial registers: metaRegister of Controlled Trials; Umin Japan Trial Register and World Health Organization (WHO) portal (which covers ClinicalTrials.gov, ISRCTN, Chinese Clinical Trials Register, German Clinical Trials Register, Iranian Registry of Clinical Trials, and the Netherlands National Trials Register, plus others);
- quarterly search of the Cochrane Library's Central Register of Controlled Trials (CENTRAL);
- monthly searches of grey literature sources via the Web of Science Core Collection and Embase (Ovid SP)

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

In addition, we performed separate searches in MEDLINE (Ovid SP), Embase (Ovid SP), PsycINFO (Ovid SP), CINAHL (EBSCOhost), Web of Science, LILACS (BIREME), NLM's ClinicalTrials.gov and the World Health Organization's International Clinical Trials Registry Portal to ensure we retrieved the most up-to-date results as well as capturing non-randomised studies. The search strategies run are in Appendix

1. We performed the most recent search for this review on 7 October 2020.

### Searching other resources

Not applicable.

## Data collection and analysis

We developed the methods used in this Cochrane Review in accordance with the recommendations described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011, hereafter referred to as the *Cochrane Handbook*).

### Selection of studies

After merging search results and discarding duplicates, two review authors (SW, EM) independently screened the titles and abstracts of all identified citations to identify potential studies. We classified the citations into three groups: 'exclude', 'potentially relevant' or 'unsure'. We excluded papers classified by both review authors as 'exclude'.

We retrieved the full-text versions of all 'potentially relevant' and 'unsure' citations for definitive assessment of eligibility. We obtained translations of non-English citations sufficient to judge whether to include or exclude the studies. For conference abstracts, we searched for related publications, and, when unable to find any, we contacted the study authors to see whether any further unpublished data were available. Two review authors (SW, EM) independently screened the full texts for a comprehensive assessment against the inclusion criteria. We resolved any disagreements through discussion, and when required, we consulted with the entire review team. We used EndNote software to manage citations (endnote.com/).

### Data extraction and management

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

- Data on the inclusion criteria for the original intervention (study design; setting, including the country; details on the place of residence of participants; types of participants; type of intervention; type of comparator; outcomes measured).
- Number of participants eligible, number randomised and reasons for not including eligible participants in the study, including both the person with dementia and carers.
- Length of follow-up, number of follow-up points.
- Participant characteristics, including details on diagnosis, how severity was staged and, where appropriate, details of comorbidity/comorbidities.
- Carer/family member characteristics, including involvement in delivering care to the person with advanced dementia.
- Details about the intervention (components, length, mode of delivery, materials given to participants, providers, level of contact with family, etc.) and the comparison (including definition of usual care).
- Data to assess the risk of bias of the original trial (randomisation; blinding of participants and personnel; description of dropouts, withdrawals and missing data; details on possible contamination between control and intervention groups; and selective outcome reporting).
- Baseline and end of intervention data on outcomes of interest for the review; scales used to measure outcomes.

At least two review authors (EM, SC, EoS and PC) extracted data using the agreed form and resolved discrepancies through discussion. We had planned to consult with another review author if required to reach agreement but this was unnecessary. When data were missing, unclear or incomplete, we attempted to contact authors of the original reports to request further details. We entered data in duplicate into Review Manager 5 (RevMan 5) (Review Manager 2014), and checked for accuracy.

### Assessment of risk of bias in included studies

At least two review authors (EM, SC and PC) independently assessed risk of bias for each included study. We used the *Cochrane Handbook* criteria for assessing risk of bias (Table 8.4.a, Higgins 2020c). We resolved any disagreements through discussion and did not need to consult a third review author.

We assessed the following domains as potential sources of bias for each included study.

#### *Selection bias: random sequence generation*

We assessed the risk that the random sequence generation method used did not produce comparable groups, scoring selection bias thus:

- low risk of bias: for RCTs, if the sequence generation process was clearly random (e.g. use of random number table);
- unclear risk of bias: for RCTs, if the sequence generation process was not specified in the paper and not available from the authors;
- high risk of bias: for nRCTs, CBA studies and ITS studies.

#### *Selection bias: allocation concealment*

We assessed the risk that the intervention allocation could have been foreseen (was not concealed adequately) in advance of or during recruitment or could have been changed after participants' assignment to intervention groups. We scored selection bias thus:

- low risk of bias: if sealed opaque envelopes were used, if randomisation and allocation was performed on all participants or units at the same time after recruitment was completed, if a person outside the study team was responsible for revealing the allocation or if some central allocation process was used (e.g. central telephone contact);
- unclear risk of bias: if the allocation concealment process was not specified in the paper and not available from the authors;
- high risk of bias: for RCTs, any inadequate concealment of allocation (e.g. allocation list available to researchers before recruitment of some participants); also, all nRCTs, CBA studies and ITS studies.

#### *Performance bias: blinding participants and personnel*

Given the nature of many palliative interventions, it is not possible to blind participants and study personnel to the interventions. However, we described the methods used, if any, to blind participants, including family members, and study personnel to the intervention and scored performance bias thus:

- low risk of bias: for all outcomes, if participants and study personnel were blinded or if we judged that the lack of blinding was unlikely to impact results;
- unclear risk of bias: when it was not clear whether lack of blinding of participants and study personnel impacted a particular outcome;
- high risk of bias: when we considered lack of blinding of participants and study personnel was likely to impact a given outcome.

#### *Detection bias: blinding of outcome assessors*

We attempted to ascertain whether outcome assessors were blinded to the intervention, and scored detection bias thus:

- low risk of bias: for all outcomes assessed blindly, as well as for objective outcomes (e.g. mortality), where outcome assessors were not blinded;
- unclear risk of bias: if it was not clear whether outcome assessors were blinded for an outcome that we considered would be impacted by a lack of blinding
- high risk of bias: for subjective outcomes (e.g. pain), where outcome assessors were not blinded.

#### *Attrition bias: incomplete outcome data*

We explored whether dropouts and withdrawals, and reasons why they occurred, were reported, with a particular focus on establishing if missing data were balanced across groups. We scored attrition bias thus:

- low risk of bias: if less than 20% of data were missing, and missing data were balanced across groups;
- unclear risk of bias: if the percentage of missing data were not clear or it was unclear whether the missing data were equally divided across groups;
- high risk of bias: if either more than 20% of data were missing or missing data were not balanced across groups.

#### *Reporting bias*

We compared the outcomes reported in the 'results' section of the study publications with the outcomes listed in the 'methods' section of the paper reporting the findings and the study protocol (where available) to identify any selective outcome reporting. We scored the risk of reporting bias thus:

- low risk of bias: if it was clear that all prespecified outcomes and all key expected outcomes were reported;
- unclear risk of bias: if there was doubt whether the outcomes reported included all outcomes measured;
- high risk of bias: if all the study's prespecified outcomes were not reported or if one or more of the reported primary outcomes were not prespecified. Also, if outcomes of interest were not reported completely or if a key outcome that one would expect to have been reported was not reported.

#### *Other potential sources of bias*

We examined the study reports for other potential sources of bias (e.g. the risk of contamination of controls).

For cluster-RCTs, we assessed specifically the risk of recruitment bias (i.e. were people recruited after clusters were randomised or were inclusion/exclusion criteria applied differently in different arms?).

We included one non-randomised study of an intervention (NRSI). In addition to the domains listed above, we drew on the ROBINS-I tool for assessment of risk of bias for NRSIs (Sterne 2021). In particular, we considered risk of bias in two pre-intervention domains; namely, confounding bias and selection bias (additional to that due to lack of randomisation or allocation concealment).

#### *Summary of risk of bias*

All outcomes reported in the summary of findings tables required a degree of subjective assessment. Therefore, we considered that all outcomes were subjective and assessed the overall risk of bias for all outcomes as a group, as follows (guided by Table 8.7.a in Higgins 2020c):

- if most information was from studies at low risk of bias: low risk;
- if the proportion of information from studies at high risk of bias was sufficient to affect the interpretation of the results: high risk;
- if most information was from studies at low or unclear risk of bias: unclear risk.

At an individual study level, we rated studies as high quality when they were at low risk of bias for allocation concealment and incomplete outcome data. We incorporated the results of the risk of bias assessment into our meta-analysis by displaying the risk of bias on each forest plot. We also examined the effect of the risk of bias by undertaking sensitivity analysis based on trial quality. In particular, we repeated our analyses including only those studies judged of 'high quality', defined, for the purposes of this review, as those judged low risk of bias for allocation concealment and incomplete outcome data.

### Measures of treatment effect

We undertook a meta-analysis of the outcomes using Review Manager 5.4.1 (Review Manager 2020). For dichotomous data, we present results as summary risk ratios (RR) with 95% confidence intervals (CIs). For continuous data, we use the mean difference (MD) with 95% CIs where outcomes were measured using the same scale or in the same way in the included studies. We use change-from-baseline data, or, if these were not available, final value scores. We planned to use the standardised mean difference (SMD) with 95% CIs if studies measured the same outcomes with different measurement scales (Higgins 2011).

### Unit of analysis issues

#### *Cluster-RCTs*

We included six cluster-randomised studies in our review. To address unit of analysis issues arising from the cluster-RCTs (e.g. trials in which assignment to the intervention or control group was made at the level of the nursing home) in our meta-analysis, we began by assessing whether an adjustment had been made in order to account for non-independence among the participants in a cluster. Where data were not already adjusted to take account of the clustering, we performed adjustment by multiplying the effect estimates' standard errors by the square root of the 'design effect'. The design effect is represented by the formula:

$1 + (M - 1) \times ICC$

Where M was the mean cluster size (number of participants per cluster); and ICC was the intra-cluster correlation coefficient.

We determined the mean cluster size (M) from each trial by dividing the total number of participants by the total number of clusters (Higgins 2020a). An estimate of the intra-cluster correlation coefficient (ICC) was not reported in the included studies, so we contacted the authors. Where authors did not respond, we estimated an ICC from a similar study or from a study of a similar population. We combined the adjusted final effect estimates in the meta-analysis using the generic inverse-variance method.

#### *Studies with more than two groups*

There were three relevant treatment groups in one included study (Boogaard 2018): one control (usual care) group and two groups receiving different versions of an organisation and delivery intervention. Following guidance from the *Cochrane Handbook*, we combined data from the two intervention groups to create a single pair-wise comparison (Higgins 2020b).

#### *More than one data point*

We also addressed unit of analysis issues stemming from studies with data from more than one data point. In this instance, we selected data from one clinically important time point (usually the intervention endpoint, or if there were multiple time points post-intervention, the last available time point) for inclusion in a meta-analysis. Additionally, when data were reported by both family and staff proxies, we selected data reported by family proxies for inclusion in the meta-analysis. If no family-reported data were available, we used staff-reported data.

### Dealing with missing data

Where data were missing from published reports, we contacted study authors to request data for included studies. We noted the level of attrition, per group, and per outcome or group of outcomes for included studies. If sufficient studies were available, we performed sensitivity analyses to assess how the overall results were affected by the inclusion of studies with a high risk of attrition bias from incomplete outcome data.

### Assessment of heterogeneity

We assessed heterogeneity between the studies through visual inspection of the forest plot, along with the $I^2$ statistic. $I^2$ calculates the percentage of variability due to heterogeneity rather than to chance, with values over 50% indicating substantial heterogeneity (Deeks 2017).

### Assessment of reporting biases

There was an insufficient number of included studies to make an overall quantitative assessment of reporting bias. Therefore, we assessed biases for individual studies.

### Data synthesis

If there were at least two studies with broadly similar population, intervention, comparison and outcome (PICO) measures, we performed meta-analysis in Review Manager 5 (Review Manager 2020). We carried out two separate meta-analyses, one for organisation and delivery of palliative care interventions, and one for advance care planning interventions.

We combined dichotomous data using risk ratios with 95% confidence intervals (CIs), with a fixed-effect model (due to the small number of included studies). For continuous data, we used the mean difference (MD) with 95% CIs, as outcomes were measured using the same scale in the included studies.

### Subgroup analysis and investigation of heterogeneity

If appropriate, we explored clinical heterogeneity using subgroup analyses. We assessed subgroup differences by interaction tests available in Review Manager 5 (RevMan 5) and used the $Chi^2$ statistic and P value, along with the $I^2$ value to report the results of subgroup analyses.

### Sensitivity analysis

If a sufficient number of studies was available, we performed sensitivity analyses for the primary and secondary outcomes to account for high risk of bias. We repeated our analyses including only those studies judged of 'high quality', defined, for the purposes of this review, as those judged low risk of bias for allocation concealment and incomplete outcome data.

### Summary of findings and assessment of the certainty of the evidence

We developed a summary of findings table using the GRADE system to assess each outcome's certainty of evidence (Guyatt 2008). In particular, we assessed study limitations, consistency between studies, imprecision of the effect estimates, indirectness of the evidence and possible publication bias (Schünemann 2020). For each comparison, we constructed a summary of findings table using the GRADE Development Tool software (GRADEpro GDT). We downgraded the evidence from the default of 'high quality' by one level when we considered the issue serious enough to influence the outcome estimate, and by two levels when we considered it very serious.

To identify the seven most important outcomes for inclusion in the summary of findings tables, we conducted a priority-setting exercise. An online survey listed the 11 outcomes, and each author on the review team independently ranked the outcomes from most to least important. From this process, we identified the top seven outcomes for inclusion in the summary of findings tables as:

- patient comfort in dying;
- symptom management;
- pain;
- palliative care plan in place;
- quality of life (QoL);
- discussion on advance care plan (ACP) directives occurred;
- care consistent with goals (concordance).

## RESULTS

### Description of studies

See the Characteristics of included studies table, Characteristics of excluded studies table and the Characteristics of ongoing studies table.

### Results of the search

We identified a total of 671 citations in this update (see Figure 1). After removing duplicates, we screened the titles and abstracts of 592 citations and excluded 553 citations. We reviewed the full texts of the remaining 39 citations for a more detailed evaluation. We contacted authors of 11 studies to clarify methodological queries. Nine authors responded, two of whom re-analysed data for the purposes of this review (Boogaard 2018; Hanson 2011; Hanson 2017; Hanson 2019). Of the full-text studies reviewed, seven studies (fourteen citations), met our inclusion criteria and were included for the first time in this review, in addition to the two studies from the original review (Ahronheim 2000; Hanson 2011). Two ongoing studies were also identified (Arendts 2019; Smaling 2018).

**Figure 1. Study flow diagram**

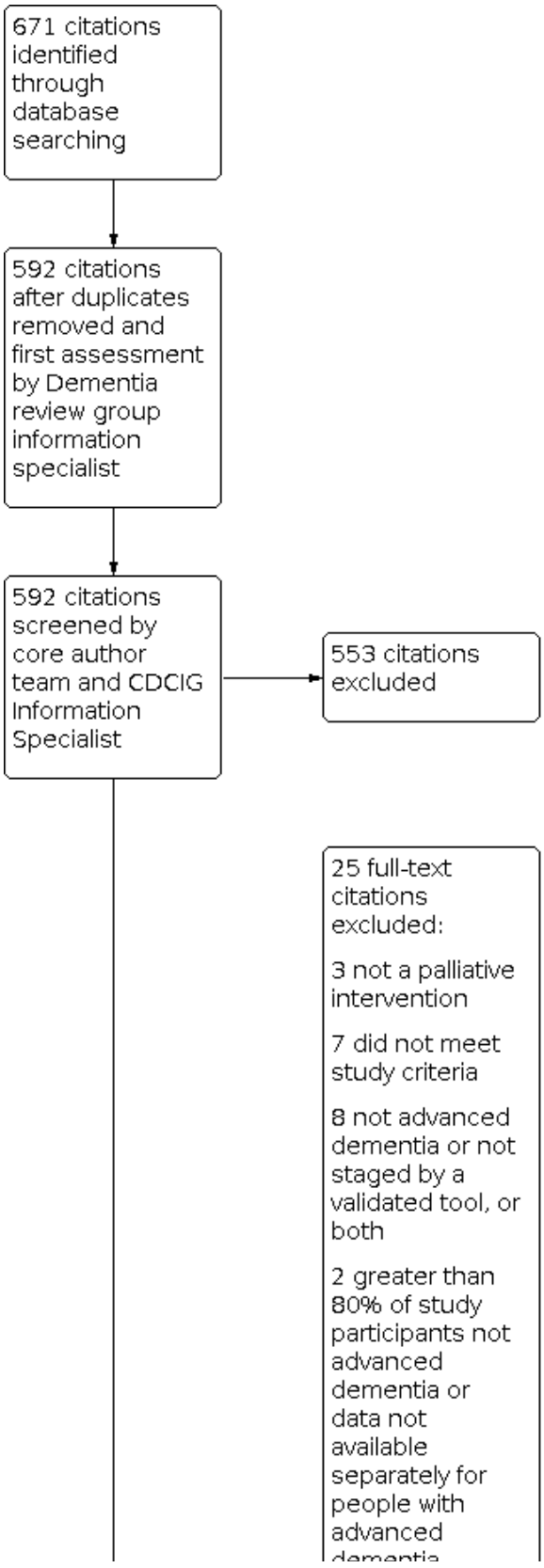
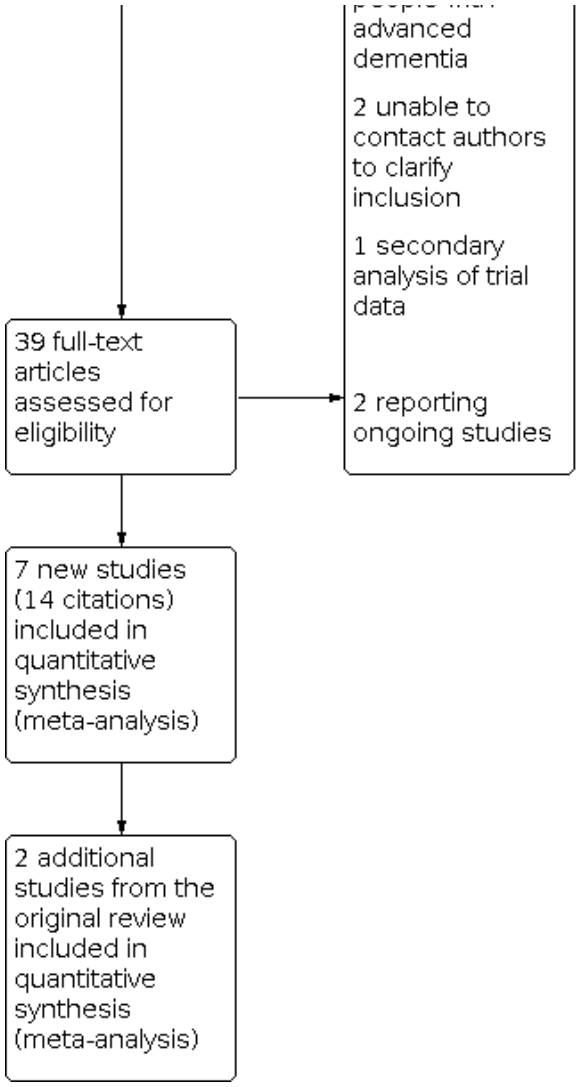


**Figure 1. (Continued)**




### Included studies

All studies are described in detail in the Characteristics of included studies tables. We included nine eligible studies: two individually-randomised RCTs, six cluster-RCTs and one controlled before-and-after study. We grouped the studies into two comparisons. Six studies compared organisation and delivery to usual care (Agar 2017; Ahronheim 2000; Boogaard 2018; Froggatt 2020; Hanson 2019; Verreault 2018). Three studies compared advance care planning to usual care (Hanson 2011; Hanson 2017; Mitchell 2018).

#### *Comparison 1: organisation and delivery of care versus usual care*

In total, 1162 participants were randomised across six studies (Agar 2017; Ahronheim 2000; Boogaard 2018; Froggatt 2020; Hanson 2019; Verreault 2018).

Agar 2017 was a cluster-RCT comparing the efficacy of a facilitated approach to family case conferencing with usual care. The 286 participants were residents with advanced dementia (FAST stage > 6a) in nursing homes in Australia. Nursing homes were randomly assigned to receive facilitated case conferencing, whereby a registered nurse was trained as a Palliative Care Planning Coordinator. In nursing homes randomised to usual care, no staff education, training or support was provided. The primary outcome was family-rated quality of end of life care, while secondary outcomes included symptoms and care in the last month of life.

Ahronheim 2000 was a RCT measuring the effectiveness of a palliative care team established at an acute hospital. The 99 participants were people with advanced dementia (FAST stage 6d to 7f) who were hospitalised with acute illness in the USA. The palliative care team visited each person and discussed their management with the primary healthcare team in the hospital daily during admission. They also discussed participant care with surrogates when possible. The primary care team treated the control group without the input of the palliative care team. Outcomes measured were number of non-palliative procedures and interventions; decisions to forgo life-sustaining treatments; and decision to adopt a palliative care plan, during hospitalisation and on discharge.

Boogaard 2018 was a cluster-RCT assessing the effect of two feedback strategies on perceived quality of end of life care and

comfort in dying for nursing home residents with dementia. The 490 participants were family caregivers of nursing home residents who died in a psychogeriatric ward in the Netherlands. Of these, 120 were caregivers of people with dementia staged as 6 on the Cognitive Performance Scale (CPS) scale, thus meeting our inclusion criteria, and the authors re-analysed the data for this subset of participants. In nursing homes assigned to an intervention group, feedback (generic and specific) was provided to staff showing bereaved family caregivers' ratings on the end of life in dementia scales. The aim of the feedback was to improve quality of end of life care and quality of dying in nursing home residents with dementia. Suggestions for improvement were also provided, and nursing homes were instructed to discuss the feedback and identify improvement actions. In nursing homes randomised to the control condition, a feedback report was issued only after data collection concluded. The outcome of relevance to this review was patient comfort in dying,

Froggatt 2020 was a cluster-RCT comparing the effect of Namaste Care – which is a complex group intervention that provides structured, personalised care in a dedicated space – to usual care as part of a feasibility study. The 32 participants were people with advanced dementia (FAST stage 6 to 7), informal carers and nursing home staff in the UK. Nursing homes were randomly assigned to receive Namaste Care. At least two care staff in each home were trained in Namaste Care. Nursing homes randomised to the control condition received only the education, training and support in care typically provided in each home. Outcomes included patient comfort in dying and quality of life.

Hanson 2019 was a RCT designed to test dementia-specific specialty palliative care triggered by hospitalisation. The 62 dyads (pairs of participants treated as one) were people with late-stage dementia (GDS 5 to 7) and family decision-makers in an acute hospital in the USA. Thirteen patients were staged as GDS 7, thus meeting the criteria for inclusion in this systematic review, and the authors re-analysed the data for this subset of participants. Dyads randomised to the intervention received a specialty palliative care consultation while hospitalised and an information booklet. Consultants provided individualised recommendations, while transitional care was also provided. Dyads allocated to the control condition received information on care-giving for late-stage dementia from the Alzheimer's Association, and participants received usual hospital care. Relevant outcomes included patient comfort in dying, documentation of advance directives and goals of care discussion.

Verreault 2018 was a non-randomised controlled before-and-after-study evaluating the impact of a multidimensional intervention to improve quality of care and quality of dying in people with advanced dementia in long-term care facilities. The 193 participants were people with advanced dementia (FAST stage 7e,f) living in nursing homes in Canada. The intervention included five components: training of physicians, nurses and nurses' aides; clinical monitoring of pain; regular mouth care routine; communication with families; and use of nurse facilitator on site to implement and monitor the intervention. Relevant outcomes included patient comfort in dying, symptom management, non-palliative interventions, and advance care planning discussion.

**Comparison 2: advance care planning versus usual care**

In total, 960 participants were randomised across three studies (Hanson 2011; Hanson 2017; Mitchell 2018).

Hanson 2011 was a cluster-RCT designed to test whether a decision aid for surrogates of nursing home residents with advanced dementia improved the quality of decision-making about feeding options. The 256 dyads were people with advanced dementia (GDS 6 to 7) and their surrogates in nursing homes in the USA. Of the 256 dyads in the study, 90 residents were staged as GDS 7, thus meeting the inclusion criteria for this systematic review. The authors re-analysed the data for this subset of participants. In nursing homes randomised to the intervention, surrogates received a structured decision aid providing information about dementia. The decision aid also discussed the surrogate's role in decision-making, and they were encouraged to discuss the decision aid with healthcare providers. Control surrogates received usual care, including any information typically provided by healthcare providers. The outcome relevant to this review was decisional conflict.

Hanson 2017 was a cluster-RCT designed to test a goals of care (GOC) decision aid intervention to improve quality of communication and palliative care for nursing home residents with advanced dementia. The 302 dyads were people with advanced dementia (GDS 5 to 7) and their surrogates in nursing homes in the USA. Of the 302 dyads in the study, 76 residents were staged as GDS 7, and the authors re-analysed the data for this subset of participants. In nursing homes randomised to the intervention, family decision-makers received an 18-minute goals of care video decision aid and a structured discussion with the nursing home care team. Family decision-makers in control sites experienced an informational video on interaction with someone with dementia and a usual care plan meeting with staff. Outcomes included symptom management, advance care planning discussion, documentation of advance directives, goals of care discussion and concordance with care goals.

Mitchell 2018 was a cluster-RCT designed to test whether an advance care planning (ACP) video impacted documented advance directives, level of care preferences, goals of care discussions, and burdensome treatments among nursing home residents with advanced dementia. The 402 participants were nursing home residents with advanced dementia and their proxies in the USA. In nursing homes randomised to the intervention, an ACP video was shown to proxies and a form was provided to the residents' primary care team, indicating the proxy's preferred level of care after viewing the video. Proxies in control facilities were read descriptions of the levels of care and asked their preferences. Their choice was not communicated to providers. Outcomes included documentation of advance directives and goals of care discussion.

### Excluded studies

We excluded 23 citations at full-text stage: eight did not stage dementia using a validated functional assessment tool; seven did not meet the study design criteria; three did not describe a palliative intervention; two had less than 80% of the study participants with advanced dementia or separate data were not available for people with advanced dementia; two were excluded because we were unable to contact the study authors to clarify inclusion; and one was a secondary analysis of trial data. The

Characteristics of excluded studies table lists details of studies excluded at full-text stage.

### Risk of bias in included studies

The risk of bias assessments for each study is detailed in the Characteristics of included studies table. The risk of bias across all included studies is summarised in Figure 2 and Figure 3. While the risk of bias was low for some domains, there were many studies with a high risk of bias for blinding of participants, personnel and outcome assessment. Due to the large number of cluster-RCTs in the review, there was also a high level of recruitment bias. However, we judged the risk of random sequence generation, allocation concealment, incomplete outcome data and selective reporting as low in most cases.

**Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies**

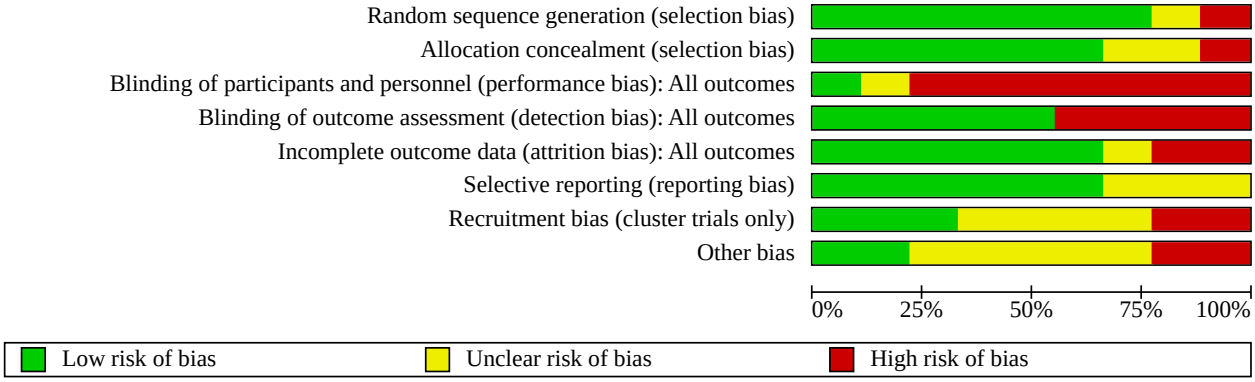
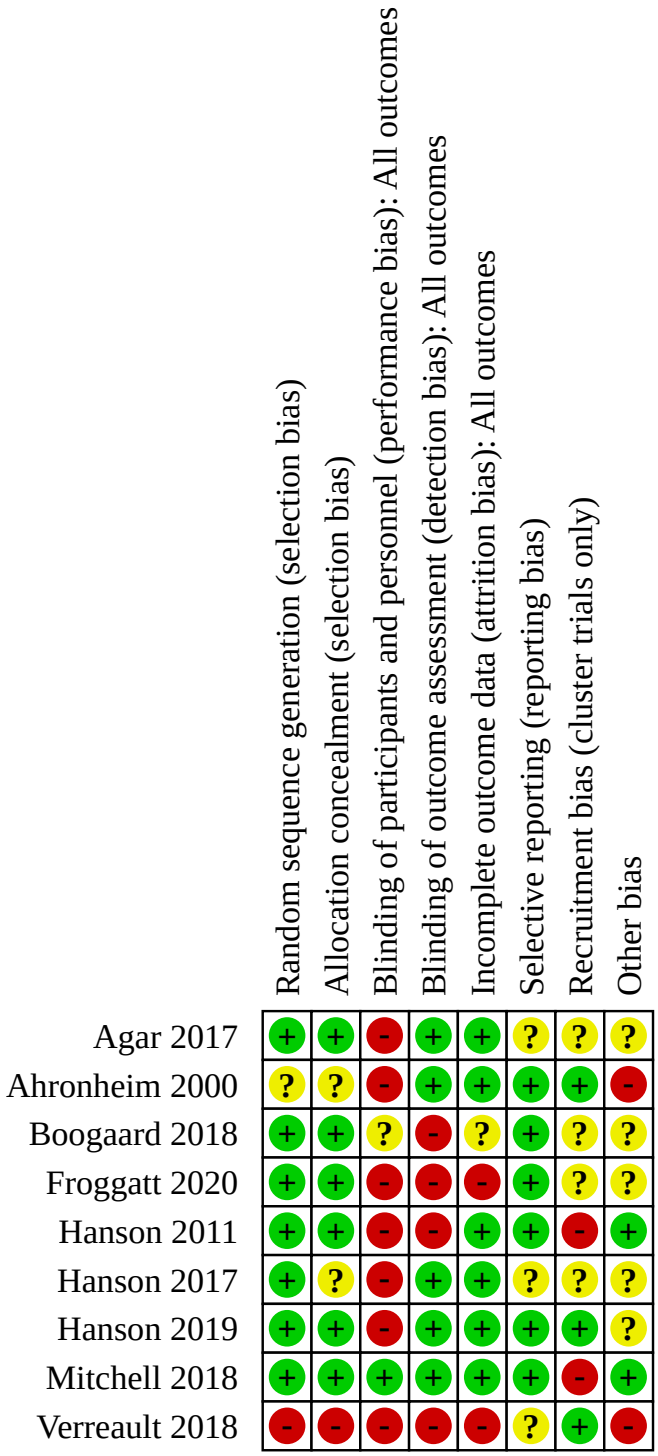


**Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study**



### Allocation

One study was at high risk of selection bias (Verreault 2018), as allocation to intervention or control arms was not randomised. Details on the methods of sequence generation and allocation concealment were insufficient in Ahronheim 2000, while Hanson 2017 did not provide information on the method of allocation concealment. The other studies were at low risk of selection bias.

### Blinding

We judged one study at low risk of performance bias (blinding of participants and personnel) (Mitchell 2018), while one study had unclear risk regarding performance bias due to insufficient information (Boogaard 2018). The remaining seven studies were at high risk of performance bias.

Three studies were at high risk of detection bias (blinding of outcome assessors)(Boogaard 2018; Froggatt 2020; Hanson 2011), while Verreault 2018 had unclear risk due to insufficient information. The remaining five studies were at low risk of detection bias.

### Incomplete outcome data

Two studies were at high risk of attrition bias, with more than 20% of missing data (Froggatt 2020; Verreault 2018), while one study had unclear risk regarding performance bias due to insufficient information (Boogaard 2018). The remaining studies were at low risk of bias.

### Selective reporting

We judged six studies at low risk of selective reporting because they reported all the outcome measures detailed in the methods sections of the papers. Where possible, we also compared the study protocol to the published papers. We judged the three remaining studies as having an unclear risk of selective reporting. Agar 2017 collected data on quality of life, but only reported in full at baseline. Also, some outcomes listed in the protocol paper are not reported to date. Hanson 2017 reported some outcomes at three- and nine-months follow-up, and others at six- and nine-months follow-up. In Verreault 2018, it is unclear whether data presented are family- or nurse-rated.

### Other potential sources of bias

One other source of bias is recruitment bias. Six of the studies are cluster-RCTs. In two of these, the care facilities were randomised before participants were recruited, indicating a high risk of bias (Hanson 2011; Mitchell 2018). For the remaining four cluster-RCTs, the risk of recruitment bias is unclear (Agar 2017; Boogaard 2018; Froggatt 2020; Hanson 2017).

We included one non-randomised study of an intervention (NRSI) in the review (Verreault 2018). In addition to the domains outlined above, we drew on the ROBINS-I tool for assessment of risk of bias for NRSIs (Sterne 2021). In particular, we considered risk of bias in two pre-intervention domains; namely, confounding bias and selection bias (additional to that due to lack of randomisation or allocation concealment). We judged the risk of confounding bias to be low, while the risk of selection bias was high.

## Effects of interventions

See: **Summary of findings 1** Organisation and delivery compared to usual care in advanced dementia; **Summary of findings 2** Advance care planning compared to usual care in advanced dementia

See Summary of findings 1 and Summary of findings 2.

### Comparison 1: organisation and delivery of care versus usual care

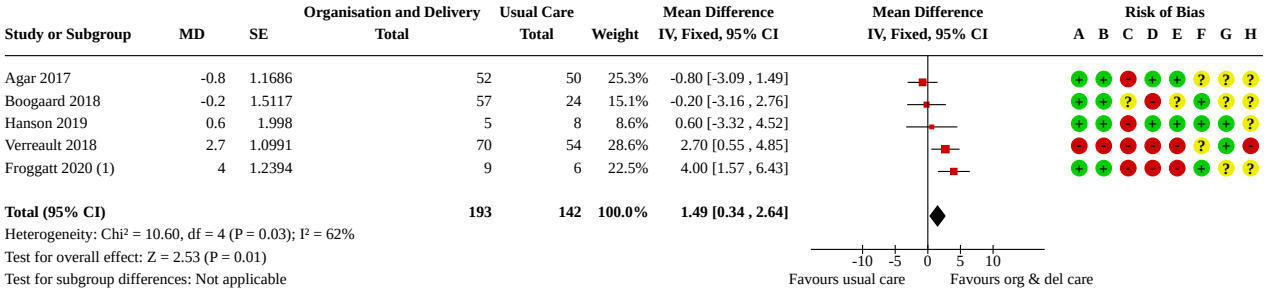
Six studies contributed data to this comparison (Agar 2017; Ahronheim 2000; Boogaard 2018; Froggatt 2020; Hanson 2019; Verreault 2018). We judged the studies to be sufficiently similar to justify synthesising the data.

#### *Primary outcomes*

##### 1.1 Comfort in dying

We performed a meta-analysis for comfort in dying, including five studies (Agar 2017; Boogaard 2018; Froggatt 2020; Hanson 2019; Verreault 2018). We calculated mean difference since all five studies used the CAD-EOLD scale to assess comfort in dying. As Agar 2017, Boogaard 2018 and Froggatt 2020 were cluster-RCTs, we used the generic inverse-variance method. Interventions aimed at the organisation and delivery of care may increase comfort in dying at post-intervention compared with usual care, but the evidence is very uncertain and unlikely to be of any clinical significance (MD 1.49, 95% CI 0.34 to 2.64; 5 studies, 335 participants; Analysis 1.1; Figure 4). The time period in which comfort in dying was assessed ranged from the last 48 hours to the last seven days before death. We judged the certainty of evidence as very low, downgrading two levels for risk of bias and one level for inconsistency arising from large heterogeneity ($I^2$ = 62%). To explore the source of this heterogeneity, we ran sensitivity analysis. In particular, we removed studies with high risk of bias for allocation concealment or incomplete outcome data, or both, as these were prespecified as key risk of bias domains. When these studies are removed, heterogeneity is eliminated and there is no evidence of an effect.

**Figure 4. Forest plot of comparison: 1 Organisation and Delivery versus Usual Care, outcome: 1.1 Comfort in dying (CAD-EOLD).**




**Footnotes**
(1) Staff-rated CAD-EOLD

**Risk of bias legend**
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Recruitment bias (cluster trials only)
(H) Other bias

### 1.2 Symptom management

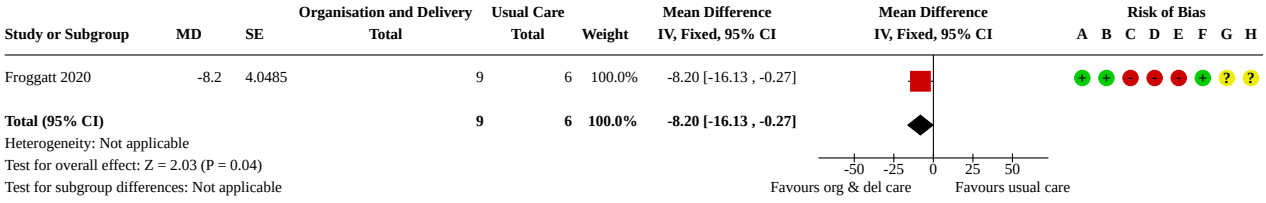
Two studies investigated the effects of organisation and delivery interventions on symptom management (Agar 2017; Verreault 2018). However, given the inconsistency in the direction of the effect, meta-analysis was not appropriate. Both studies employed the SM-EOLD scale, which ranges from 0 to 45, to assess symptom management. Agar 2017 found that the mean SM-EOLD score for those receiving usual care was 31.7, while those in receipt of the facilitated case conferencing intervention had a mean SM-EOLD score of 29.0 (MD -2.7, 95% CI -6.0 to 0.6, a non-significant difference favouring usual care). In the Verreault 2018 study, the mean SM-EOLD score for the usual care group was 29.8, while those receiving the multidimensional intervention had a mean SM-EOLD score of 34.7 (MD 4.9, 95% CI 1.15 to 8.65, a significant difference in favour of the multidimensional intervention).

## *Secondary outcomes*

### 1.3 Quality of life

Based on one study (Froggatt 2020), the evidence is very uncertain about the effect of organisation and delivery interventions on quality of life (MD -8.20, 95% CI -16.13 to -0.27; 1 study, 15 participants; Analysis 1.3; Figure 5). As the data were from a single small study, event rates were very low. We judged the certainty of evidence as very low, downgrading one level due to risk of bias and two levels for imprecision (low-powered analysis from one study and a wide confidence interval).

**Figure 5. Forest plot of comparison: 1 Organisation and Delivery versus Usual Care, outcome: 1.3 Quality of Life.**




**Risk of bias legend**
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Recruitment bias (cluster trials only)
(H) Other bias

### 1.4 Pain

No studies reported on pain measured through observation or by a validated scale.

### 1.5 Palliative care plan in place

Based on one study (Ahronheim 2000), changes to the organisation and delivery of care may increase the likelihood of having a

palliative care plan in place, but the evidence is very uncertain (RR 5.84, 95% CI 1.37 to 25.02; 1 study, 99 participants; Analysis 1.5). We downgraded the evidence one level due to concerns regarding risk of bias (unclear risk of allocation concealment, which is one of our key risk of bias domains), and two levels due to imprecision (very low-powered analysis with data from one study, and a wide confidence interval).

#### 1.6 Review of prescribing of antipsychotic medications

No studies reported on review of prescribing of antipsychotic medications.

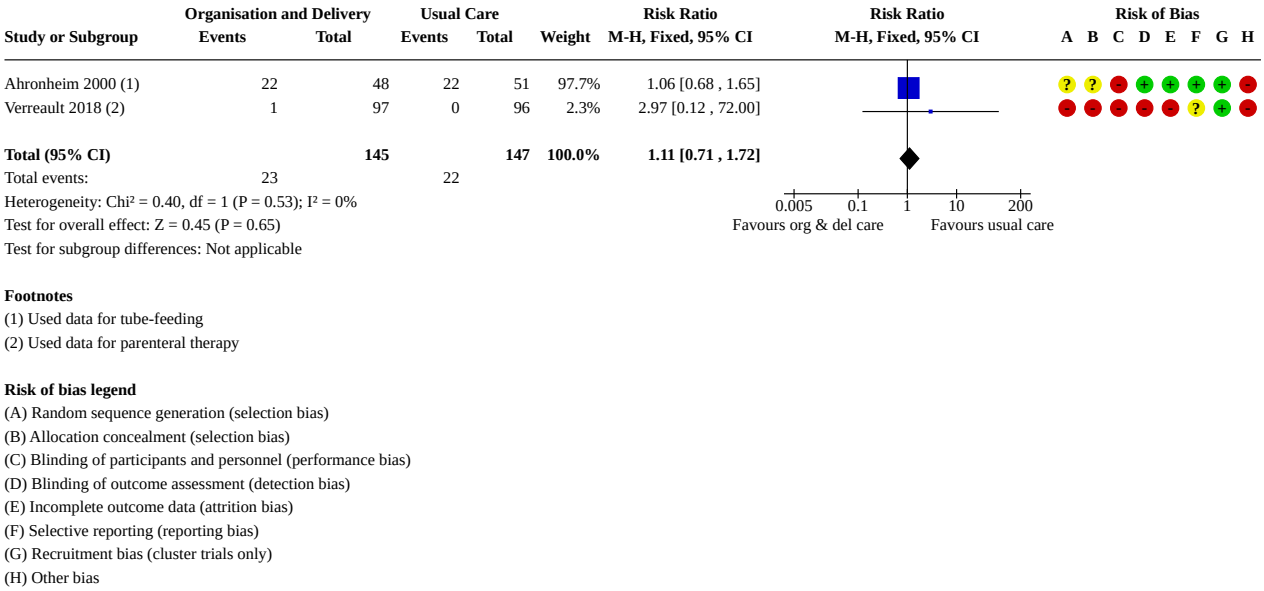
#### 1.7 Review of prescribing of analgesics

No studies reported on review of prescribing of analgesics.

#### 1.8 Use of non-palliative interventions

Two studies tested the effect of an organisation and delivery intervention on the use of non-palliative interventions (Ahronheim 2000; Verreault 2018). For the Ahronheim 2000 study, we used data on use of tube-feeding, while for the Verreault 2018 study, we used data on the use of parenteral therapy (IV). We found that the interventions probably have little effect on the use of non-palliative interventions (RR 1.11, 95% CI 0.71 to 1.72; 2 studies, 292 participants; Analysis 1.8; Figure 6). Overall, the certainty of the evidence was considered moderate, downgrading one level due to risk of bias.

**Figure 6. Forest plot of comparison: 1 Organisation and Delivery versus Usual Care, outcome: 1.8 Use of non-palliative interventions.**




**Footnotes**
(1) Used data for tube-feeding
(2) Used data for parenteral therapy

**Risk of bias legend**
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Recruitment bias (cluster trials only)
(H) Other bias

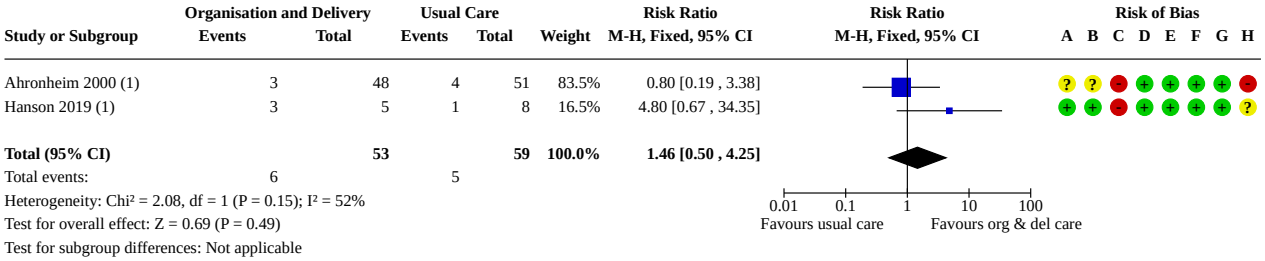
#### 1.9 Advance care planning discussion

Based on one study (Verreault 2018), we found that organisation and delivery interventions may have little to no effect on advance care planning discussions, and the evidence is very uncertain (RR 1.08, 95% CI 1.00 to 1.18; 1 study, 193 participants; Analysis 1.9). We judged the certainty of evidence as very low, downgrading two levels due to risk of bias and one level for imprecision (low-powered analysis from one study).

#### 1.10 Documentation of advance directives

Two studies examined the effect of organisation and delivery interventions on the documentation of advance directives (Ahronheim 2000; Hanson 2019). For both studies, we used data on documentation of 'do not tube-feed'. The pooled analysis indicates that the interventions may have little or no effect on the documentation of advance directives and the evidence is very uncertain (RR 1.46, 95% CI 0.50 to 4.25; 2 studies, 112 participants; Analysis 1.10; Figure 7). There was high heterogeneity in this analysis ($I^2$ = 52%), which we were unable to explain. We considered the evidence behind this result to be very low quality. We downgraded one level due to inconsistency and two levels for imprecision (low-powered analysis and a wide confidence interval).

**Figure 7. Forest plot of comparison: 1 Organisation and Delivery versus Usual Care, outcome: 1.10 Documentation of advance directives.**




**Footnotes**
(1) Used data on do not tube-feed

**Risk of bias legend**
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Recruitment bias (cluster trials only)
(H) Other bias

#### 1.11 Decisional conflict in carers

No studies reported on decisional conflict in carers.

#### 1.12 Goals of care discussion occurred

Based on one study (Hanson 2019), the evidence suggests that organisation and delivery interventions may have little or no effect on whether discussion took place about goals of care (RR 2.36, 95% CI 1.00 to 5.54; 1 study, 13 participants; Analysis 1.12). For the purposes of this review, the authors re-analysed the data for 13 study dyads with advanced dementia staged as GDS 7 (21% of total study population). We judged the certainty of the evidence as low, downgrading two levels due to imprecision (low-powered analysis from one study and a wide confidence interval).

#### 1.13 Concordance with goals of care

No studies reported on concordance with goals of care.

### Comparison 2: advance care planning versus usual care

Three studies contributed data to this comparison (Hanson 2011; Hanson 2017; Mitchell 2018). We judged the studies to be sufficiently similar to justify synthesising the data.

#### *Primary outcomes*

#### 2.1 Comfort in dying

No studies reported on comfort in dying.

#### 2.2 Symptom management

One study tested the effect of a goals of care decision aid on symptom management (Hanson 2017). For the purposes of this review, the authors re-analysed the data for 76 study dyads with advanced dementia staged as GDS 7 (25% of total study population). The analysis indicates that the intervention may have little or no effect on family rating of symptom management, and the evidence is very uncertain (MD -1.80, 95% CI -6.49 to 2.89; 1 study, 67 participants; Analysis 2.2). The certainty of evidence was found to be very low. We downgraded one level due to risk of bias and two levels for imprecision (low-powered analysis from one study and a wide confidence interval).

#### *Secondary outcomes*

#### 2.3 Quality of life

No studies reported on the quality of life.

#### 2.4 Pain

No studies reported on pain measured through observation or by a validated scale.

#### 2.5 Palliative care plan in place

No studies reported on palliative care plan in place.

#### 2.6 Review of prescribing antipsychotics

No studies reported on review of antipsychotics.

#### 2.7 Review of analgesics

No studies reported on review of analgesics.

#### 2.8 Use of non-palliative interventions

No studies reported on the use of non-palliative interventions.

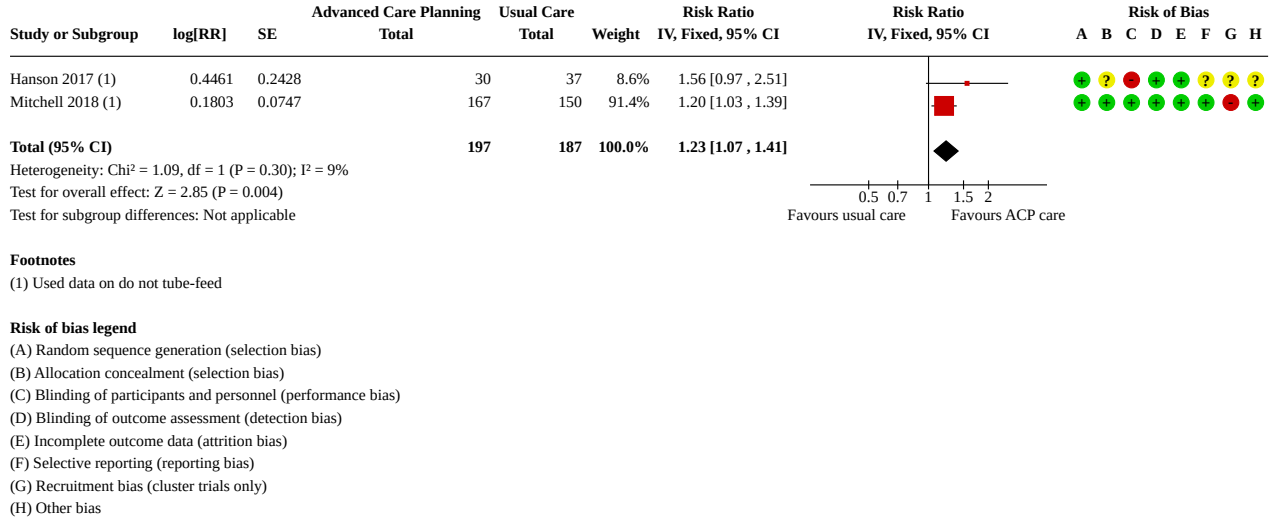
#### 2.9 Advance care planning discussion

Based on one study (Hanson 2017), advance care planning interventions may have little or no effect on whether an advance care planning discussion occurs (RR 1.04, 95% CI 0.87 to 1.24; 1 study, 67 participants; Analysis 2.9). For the purposes of this review, the authors re-analysed the data for 76 study dyads with advanced dementia staged as GDS 7 (25% of total study population). We judged the certainty of the evidence as low, downgrading one level for risk of bias and one level due to imprecision (low-powered analysis from one study).

### 2.10 Documentation of advance directives

Two studies examined the effect of advance care planning on the documentation of advance directives (Hanson 2017; Mitchell 2018). For both studies, we used data on documentation of 'do not tube-feed'. The analysis suggests that an advance care planning intervention probably increases the documentation of advance directives (RR 1.23, 95% CI 1.07 to 1.41; 2 studies, 384 participants; Analysis 2.10; Figure 8). Heterogeneity is shown to be low in this analysis ($I^2$ = 9%). We considered the certainty of the evidence to be moderate due to concerns regarding risk of bias.

**Figure 8. Forest plot of comparison: 2 Advance Care Planning versus Usual Care, outcome: 2.10 Documentation of advance directives.**




**Footnotes**
(1) Used data on do not tube-feed

**Risk of bias legend**
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Recruitment bias (cluster trials only)
(H) Other bias

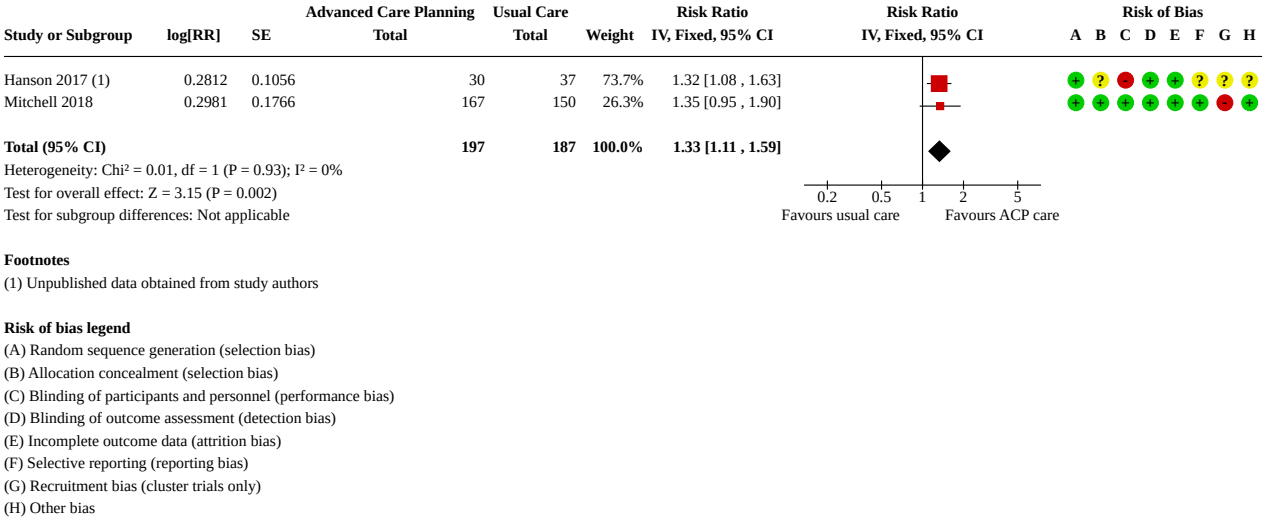
### 2.11 Decisional conflict

Based on one study (Hanson 2011), we found that receiving a structured decision aid may result in little or no difference in decisional conflict (MD -0.30, 95% CI -0.63 to 0.03; 1 study, 79 participants; Analysis 2.11). For the purposes of this review, the authors re-analysed the data for 90 study dyads with advanced dementia staged as GDS 7 (35% of total study population). We judged the certainty of the evidence as low, downgrading one level for risk of bias and one level for imprecision (low-powered analysis from one study).

### 2.12 Goals of care discussion

Two studies investigated the effect of advance care planning interventions on whether a goals of care discussion had occurred (Hanson 2017; Mitchell 2018). As mentioned above, Hanson 2017 re-analysed data for 76 study dyads with advanced dementia. The analysis suggests that participants in receipt of an advance care planning intervention are probably more likely to have a goals of care discussion compared to those in the control group (RR 1.33, 95% CI 1.11 to 1.59; 2 studies, 384 participants; Analysis 2.12; Figure 9). Heterogeneity is shown to be low in this analysis ($I^2$ = 0%). We judged the certainty of evidence as moderate due to concerns regarding risk of bias.

**Figure 9. Forest plot of comparison: 2 Advance Care Planning versus Usual Care, outcome: 2.12 Goals of care discussion.**




**Footnotes**
(1) Unpublished data obtained from study authors

**Risk of bias legend**
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Recruitment bias (cluster trials only)
(H) Other bias

#### 2.13 Concordance with goals of care

Based on one study (Hanson 2017), we found that dyads who receive an advance care planning intervention may be slightly more likely to have concordance than dyads in the control group (RR 1.39, 95% CI 1.08 to 1.79; 1 study, 63 participants; Analysis 2.13). As mentioned, these data represent a subset of participants who met our criteria for advanced dementia. We judged the certainty of evidence as low, downgrading one level due to risk of bias and one level for imprecision (low-powered analysis from one study).

## DISCUSSION

### Summary of main results

The primary aim of this review was to assess the effect of palliative care interventions in advanced dementia. This is the first update of the original review (Murphy 2016). Nine trials met our inclusion criteria. We carried out separate comparisons for organisation and delivery of care interventions versus control, and advance care planning interventions versus control. Six studies with 1162 participants investigated the effect of interventions targeting the organisation and delivery of palliative care, while three studies with 960 participants examined the effect of advance care planning interventions. For each comparison, we found the studies to be sufficiently similar to conduct a meta-analysis. However, it is important to acknowledge the heterogeneity in interventions, particularly with respect to comparison one (organisation and delivery interventions versus usual care). For this comparison, two studies were based in a hospital setting, and the interventions were focused on the involvement of specialist palliative care teams, while the remaining four studies were based in long-term care settings, with interventions aimed at different elements of how care was organised and delivered. Despite this, we considered that the studies were sufficiently similar for pooled estimates of effects to be meaningful, as they are all centred on changes to the organisation and delivery of care.

Implementing changes to the organisation and delivery of care for people with advanced dementia may increase comfort in dying, though the evidence is very uncertain and unlikely to be clinically significant. These interventions may also increase the likelihood of having a palliative care plan in place, but again the evidence is very uncertain. Such interventions probably have little effect on the use of non-palliative interventions. They may also have little or no effect on documentation of advance directives, or whether discussions take place about advance care planning and goals of care. However, given the relatively small number of included studies for each outcome, as well as imprecision in the estimates, these results should be interpreted with caution.

Advance care planning interventions for people with advanced dementia probably increase the documentation of advance directives and the number of discussions about goals of care. They may also slightly increase concordance with goals of care. On the other hand, they may have little or no effect on perceived symptom management or whether advance care planning discussions occur. Again, the overall certainty of this evidence is low due to imprecision.

### Overall completeness and applicability of evidence

The number of included studies and the variety of the interventions have improved since the first review, making it feasible to conduct a meta-analysis of data for the majority of potential outcomes needed to assess the effect of palliative care interventions in advanced dementia. The growing convergence in the outcomes makes it possible to have a meaningful discussion on effectiveness based on the available trials. That said, the number of published trials remains low, and there are none available for people with advanced dementia living at home or in housing with care accommodation (Miranda 2019). Nor are there any trials available that include pain as a primary or secondary outcome. One of the difficulties in relation to the latter is the multitude of assessment tools available for use with the elderly cognitively-impaired population. Unfortunately, there is limited evidence about the reliability, validity and clinical utlity of existing pain assessment tools for people with dementia (Lichtner 2014). Based on Lichtner and colleagues' systematic review, no one tool can be recommended, given the existing evidence (Lichtner 2014).

There is also an absence of any treatment of costs or economic evaluation of the interventions in the studies included in this review. This includes an absence of contingent valuation studies and discrete choice experiments on preferences for palliative care. Palliative care interventions in advanced dementia should be subject to economic analysis and comparison given the range of potential interventions available and the importance of the efficient use of scarce resources. The lack of data on optimal palliative care interventions to meet the needs of people with advanced dementia highlights the importance of future research being focused on this population, despite the many ethical challenges. Costs and outcomes need to be considered in any future work to ensure that resources for people with advanced dementia can be directed to those most in need and those who can benefit most from new forms of support.

Of particular concern when considering the ethical issues involved in the research process, is the lack of coherence and consistency in existing guidelines and protocols in relation to vulnerability, consent and ongoing assent, as well as variability between countries (Kim 2011). Different approaches may be needed to facilitate the inclusion of people with advanced dementia in research, including advance directives that may allow people with dementia to specify their willingness to be involved in research before they lose capacity to consent, or can specify ahead of time a research proxy to act on their behalf (West 2017). While outside the scope of this review, ethics committees may have a role to play in facilitating more research in this area through a more proactive insistence on the inclusion of people with more advanced dementia, based on the principles of equity and inclusion (Alzheimer Europe 2011).

## Quality of the evidence

We employed the GRADE approach to evaluate degree of certainty in study findings, taking account of the risk of bias of included studies, inconsistency and imprecision in the results, directness of the evidence, and publication bias (GRADEpro GDT). Based on this, we found that there is very limited, mostly low- or very low-certainty evidence relating to the effect of palliative care interventions in advanced dementia.

## Potential biases in the review process

This review was conducted as outlined in the *Cochrane Handbook* (Higgins 2011); therefore, the introduction of bias during the review process was minimised. We are confident that the search strategy identified all relevant studies. Some bias may have been introduced by limiting the re-analysis of data in the Boogaard 2018, Hanson 2011, Hanson 2017 and Hanson 2019 studies to a subset of the original study outcomes, but the re-analyses were conducted long after study end, specifically for this review.

### Limitations of this review

The limitations of this work are related to the relatively small number of studies that met the criteria for inclusion in the review. While the number of studies has increased since the last version of the review, the evidence base remains limited. The definition of advanced dementia for this review led to the exclusion of some quality studies conducted on a more general population of people with dementia, but our definition does retain a focus on the most vulnerable people with dementia. Retrospective cohort studies such as Ennis 2015 are also not included as part of this review. However, such studies offer important insights into the provision of palliative care. Another factor impacting on the number of included studies is the relatively low priority given to palliative care for people with advanced dementia in most countries, making it difficult for different types and forms of interventions to emerge, let alone be implemented or evaluated. Methodological issues in respect of randomisation and outcome measures may also be inhibiting work in this important area. However, the increase in the number of studies since the last review provides an indication that the number of studies will likely continue to grow in the future.

## Agreements and disagreements with other studies or reviews

Hines 2011 conducted a systematic review on the effectiveness and appropriateness of a palliative approach to care for people with advanced dementia. Hines and colleagues included quantitative, qualitative and discursive text articles in the review. However, no quantitative meta-analysis was possible due to clinical and statistical heterogeneity. The quantitative studies supported the use of 'do not resuscitate' and other forms of advance directives to prevent interventions unwanted by the individual or their family, or both. Feeding tubes and the use of intravenous antibiotics were not found to be an effective intervention. Interventions designed to treat the burdensome symptoms of advanced dementia (such as pain and agitation) were found to be of most benefit to patients. The qualitative data highlighted the difficulties for families in discussing or engaging in planning conversations on palliative care for the person with dementia. These conversations were hindered by knowledge deficiencies and differences, lack of understanding of the disease trajectory of dementia, the unpredictable nature of dementia itself, and religious and socioeconomic issues. Textual analysis suggested that a palliative approach to end of life care in advanced dementia is both appropriate and effective in terms of benefit to people with dementia and their significant others.

Moon 2018 conducted a systematic review on the quality of end of life care for people with dementia in a hospital setting. The presence of advanced dementia was indicated in three of the studies included in the review, defined as scoring above 7 on the FAST measurement tool. The results suggest a general awareness of the importance of a palliative approach to end of life care for all people with dementia in hospital. While the review found that people with dementia were less likely to receive aggressive care at the end of life, the provision of palliative care interventions was inconsistently provided at all stages of dementia. The findings indicate that there may be particularly inadequate palliative care intervention for symptom control, linked to the failure to conceptualise dementia as a terminal condition, even at an advanced stage. The authors point to the role and potential of qualitative research in enhancing our understanding of healthcare professionals' and families' experiences of end of life care.

Durepos 2017 carried out a systematic review of palliative care content in dementia care guidelines within and across eleven jurisdictions worldwide, including Canada, USA, Europe, UK and Malaysia. The review assessed and quantified palliative care content integrated within current international clinical practice guidelines (CPGs). Seven CPGs had minimal content or did not address palliative care directly at end of life. There was, however, strong support within the international guidelines for clinicians to assess the need for palliative care services. But, criteria or triggers for referral to specialists or hospice care was conspicuously

lacking. What did emerge strongly was the view that clinicians discuss with individuals and families the limitations of treatment for dementia and the need for continual evaluation of perceived functional benefits compared to risks. Another strong theme was that treatment scope and duration should correlate with existing advance care plans and directives. Most guidelines discussed the discontinuation of pharmacologic therapy at end of life, without offering much guidance for specific timing of withdrawal. Apart from discussion of overall advance care planning, only one CPG specifically recommended determining individuals' preferred place of death.

Mataqi 2020 produced a systematic review on factors influencing palliative care in advanced dementia. The review included 34 studies: 25 providing qualitative data; 6 providing quantitative data; and 3 mixed-methods studies. The authors focused on barriers and facilitators in relation to the provision of palliative care for people with advanced dementia from the perspective of stakeholders across different care settings. The findings identified different types of barriers and facilitators that the authors grouped into three categories: organisational; healthcare professionals; and patient-related. The most commonly reported barriers were: lack of skills and training opportunities of the staff specific to palliative care in dementia; lack of awareness that dementia is a terminal illness and a palliative condition; pain and symptoms assessment/management difficulties; discontinuity of care for people with dementia and lack of coordination across care settings; difficulty communicating with the person with dementia; and the lack of advance care planning. The findings indicated that seven studies rejected palliative care as a management step in caring for people with advanced dementia. While many of these issues reflect practice and policy issues, they also show the importance of undertaking high quality new research on palliative care interventions that might shed light on improving multifaceted outcomes in people with advanced dementia.

## AUTHORS' CONCLUSIONS

### Implications for practice

Despite the increased number of included studies, there is still no clear message from the literature about how palliative care is best organised and delivered for people with advanced dementia, or how provision of care in line with a patient's wishes is best achieved.

### Implications for research

It is evident that high-quality studies of many different palliative care interventions in all settings are required to improve palliative care delivered to people with advanced dementia. Because insufficient evidence is currently available, research is required to identify the nature of these interventions. However, palliative care researchers face many challenges, including the vulnerability of the population from which study participants are recruited; the difficulty in assessing the risks and benefits of participating in the research; and issues around consent, emotional distress and randomisation (Krouse 2004). These challenges are exacerbated when the focus is on people with advanced dementia, particularly related to communication, capacity and appropriate outcome measures. Therefore, there is a need to conduct methodological research to develop best practice guidelines for research in this area.

The foregoing discussion brings into focus the potential of public patient involvement (PPI) to improve our understanding of both need and capabilities in relation to palliative care for people with advanced dementia. Studies included in this review show no evidence of the voice of the person with dementia, or their carers, influencing the research design, choice of outcomes or interpretation of data. Indeed, interventions are likely designed around the priorities of researchers and clinicians rather than being driven by identified needs of patients and families. Thus, there is potential going forward for researchers to work with people living with early-stage dementia, as well as carers of people with advanced dementia, during the design phase of research to help define outcomes of importance. This PPI approach would also help to address some of the ethical challenges that arise when conducting research in a vulnerable population such as this one.

There is also a clear need for the development of a core outcome set for palliative care for people with advanced dementia, which should be underpinned by a PPI approach. Developing a core outcome set will need to take account of the personhood of people with dementia, including holistic measures that incorporate standard measures such as pain and quality of life alongside functioning and capabilities assessment. This will, in turn, require increased collaboration and interdisciplinary work, bringing together not just clinicians from psychiatry, geriatrics and palliative care, but also expertise in pain management, communication (verbal and non-verbal), psychology, social gerontology, health economics and, indeed, people with dementia.

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* Indicates the major publication for the study

# CHARACTERISTICS OF STUDIES

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

### Agar 2017

| ***Study characteristics*** | |
|---|---|
| Methods | **Design:** cluster-randomised controlled trial<br><br>**Unit of randomisation:** nursing home<br><br>**Setting and timeframe:** 20 nursing homes in two major Australian cities, conducted over an 18-month period (February 2013 to December 2014) |
| Participants | **Participants:** people with advanced dementia (staged FAST 6a or above), a family member involved in making decisions about the resident's care and nursing/care staff<br><br>**Recruitment:** potentially eligible residents were identified by nursing home managers and screened by the study team.<br><br>**Number of participants:** 286 (156 intervention, 130 control). Of these, 131 died during the study period (67 intervention, 64 control) |
| Interventions | **Intervention condition:** a registered nurse was trained as a Palliative Care Planning Coordinator (PCPC) in each nursing home, working for two days per week or equivalent, in order to:<br><br>• identify residents with advanced dementia likely to benefit from a case conference;<br>• organise, set an agenda, chair and document case conferences with optimal participation by family, multidisciplinary nursing home staff and external health professionals (e.g. General Practitioners);<br>• develop and oversee implementation of palliative care plans;<br>• train nursing and direct care staff in person-centred palliative care |

**Agar 2017** *(Continued)*

| | |
|---|---|
| | The key features of the facilitated case conference model were:<br>• use of pre-defined specific clinical triggers for a case conference;<br>• use of a shared agenda-setting model where the resident, their family and all multidisciplinary staff could specify a priori areas for discussion;<br>• required attendance of the resident and/or their substitute decision-maker or family member(s);<br>• was facilitated by the PCPC to ensure optimal participation of attendees, and was followed by a communication strategy to summarise actions and plan arising from the case conference;<br>• discussion topics were not limited and were individualised to what was seen as important for the resident, and could include care planning, current and future treatment decision-making, information sharing, meeting resident preferences or needs, and advance care planning<br><br>**Control condition:** no staff education, training or support was provided. No restrictions were placed on nursing homes' education programme, or approach to care planning and decision-making. |
| Outcomes | **Outcomes:**<br>• family-rated quality of end of life care - End of Life Dementia (EOLD) scales<br>• nurse-rated EOLD scales<br>• resident quality of life (QUALID)<br>• quality of care over last month of life<br><br>**Data collection:** family-rated quality of end of life care was optimally assessed 4 to 6 weeks following the patient's death. Nurse-rated EOLD scales were completed as soon as possible following the resident's death, and symptoms and care in the last month of life extracted from nursing home and medical records. |
| Notes | 127/131 (97%) participants who died had advanced dementia as defined for this systematic review (staged FAST 6d or above). Funding source: Australian Department of Health |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | Block randomisation of nursing homes was carried out. Randomisation was stratified by organisational affiliation to control for influence of organisational culture, policy and procedures on quality of care. A computer-generated allocation sequence was used to allocate nursing homes to each arm based on institutional-level baseline data. |
| Allocation concealment (selection bias) | Low risk | Randomisation was done at nursing home level after baseline data were collected. |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | There was no blinding of nursing home staff or of family carer participants but they were not aware of the evaluative aim of the study. However, they were aware of the changes in practice (family case conferencing (FCC)). |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Low risk | Blinded to nursing home identity for randomisation and analysis |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | Everyone who died during the time period is included in the trial. There are missing data for 24% of family carers – presumably not returned by family carers. |

**Agar 2017** *(Continued)*

| | | |
|---|---|---|
| Selective reporting (reporting bias) | Unclear risk | QUALID is collected but only reported in full at baseline, reported as "associated with" certain factors at the end of the intervention. Other outcomes listed in protocol paper are not reported. |
| Recruitment bias (cluster trials only) | Unclear risk | Unclear whether individuals were recruited before or after randomisation. |
| Other bias | Unclear risk | It is reported in the paper that the usual care group also received family case conferencing but no data were collected on this so as to not highlight the evaluative criteria. 44% of participants in the usual care arm received case conferencing versus 69% in the FCC arm. Also, the FCC arm reported that nurses had greater knowledge of and confidence in providing palliative care for advanced dementia. |

**Ahronheim 2000**

| ***Study characteristics*** | |
|---|---|
| Methods | **Design:** randomised controlled trial<br><br>**Unit of randomisation:** individual<br><br>**Setting and timeframe:** one acute hospital in New York, USA over a 3-year period (study dates not reported) |
| Participants | **Participants:** people with advanced dementia (staged as FAST 6d or greater) who had been hospitalised for an acute illness<br><br>**Recruitment:** eligible people admitted to Mount Sinai Hospital over a 3-year period were identified through daily rounds by the palliative care team nurse. Individuals were assessed by the palliative care nurse as to appropriateness for inclusion.<br><br>**Number of participants:** 99 (48 in intervention group, 51 in control group) |
| Interventions | **Intervention condition**: a palliative care team was established in the hospital, consisting of an experienced clinical nurse specialist and one or more attending geriatrician(s), who also held academic appointments. The palliative care team conducted a palliative consultation for each participant, visited the participant and discussed participant management with the primary healthcare team in the hospital on a daily basis. The palliative care team also met with family carers or other surrogates when they were available, and attempted to arrange meetings after hours or by telephone.<br><br>The goal of the intervention was to enhance participant comfort. During consultation, options discussed included:<br><br>• avoidance of non-palliative procedures;<br>• avoidance of mechanical constraints;<br>• administration of pain medication for painful manoeuvres (e.g. ulcer debridement);<br>• rehabilitation methods (e.g. repositioning, massage);<br>• counselling of surrogates and care providers about participant's rights and surrogates' responsibilities as decision-makers;<br>• alternate planning (e.g. forgoing life-sustaining treatments, discharge to hospice, discharge with palliative care plans and avoidance of re-hospitalisation).<br><br>**Control condition**: treatment by primary care team without the input of the palliative care team |
| Outcomes | **Outcomes**<br><br>• Number of admissions |

**Ahronheim 2000** *(Continued)*

- Length of stay in hospital
- Number of deaths in hospital
- Number of non-palliative procedures and interventions
- Decisions to forgo life-sustaining treatments
- Decision to adopt a palliative care plan, during hospitalisation and on discharge

**Data collection:** after informed consent, complete history was obtained and physician examination performed. After this baseline evaluation, participants were randomised and outcomes assessed until final discharge or in-hospital death. Date of death for participants who survived the hospitalisation was ascertained by telephone follow-up.

| | |
|---|---|
| Notes | One additional participant was randomised but lost to the study (discharged from the hospital within 24 hours of randomisation) and not included in the analysis.<br><br>Funding source: grants from the Greenwall Foundation and the Kornfeld Foundation |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | "After this baseline evaluation, patients were randomly assigned to either the intervention or to the control group."<br><br>No details given on method of randomisation used |
| Allocation concealment (selection bias) | Unclear risk | "After this baseline evaluation, patients were randomly assigned to either the intervention or to the control group."<br><br>No details given on method of allocation concealment |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Given the nature of the intervention, there was no blinding of participants or personnel. We judged the risk of bias due to this lack of blinding to be high for all subjective outcomes, as the primary care team may have made different decisions knowing whether a participant was in the intervention or control group. |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Low risk | "A research assistant blinded to randomisation status gathered information from the charts of patients in both arms of the study." |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | "One patient was discharged in the first 24 hrs [hours] after randomisation and was not readmitted, and was excluded from analysis." |
| Selective reporting (reporting bias) | Low risk | All outcomes listed in the Methods section, with the exception of one (do not resuscitate), were reported in the Results. |
| Recruitment bias (cluster trials only) | Low risk | Not applicable |
| Other bias | High risk | Potential contamination of control participants, who were being treated by the same primary care team that were receiving input from the palliative care team for the intervention participants. |

**Boogaard 2018**

| ***Study characteristics*** | |
|---|---|
| Methods | **Design:** three-armed cluster-randomised controlled trial<br><br>**Unit of randomisation:** nursing home<br><br>**Setting and timeframe:** 18 Dutch nursing homes over a 2.5-year period (pre-intervention phase started in January 2012 with the first nursing home triplets, and the intervention phase started in November 2012. In July 2014, all nursing homes concluded data collection). |
| Participants | **Participants:** family caregivers of nursing home residents with dementia who died on a psychogeriatric ward<br><br>**Recruitment:** all participating nursing homes sent questionnaires, along with a letter explaining the study goals and procedures, to the family member who was most involved, according to the nursing home representative. The questionnaires were sent 6 to 8 weeks after the death of a nursing home resident with dementia.<br><br>**Number of participants:** 490 (291 in two interventions, 199 in control). Of these, 103 met the review criteria for advanced dementia (73 in two interventions, 30 in control). |
| Interventions | **Intervention condition:** during a pre-intervention phase, all participating nursing homes collected data on bereaved family caregivers' ratings on the Satisfaction With Care at the End-of-Life in Dementia (SWC-EOLD) and the Comfort Assessment in Dying with Dementia (CAD-EOLD) scales. In the intervention phase, feedback was provided to staff based on the accumulated data, showing bereaved family caregivers' ratings on the SWC-EOLD and CAD-EOLD scales. Two different feedback strategies were tested:<br><br>• *generic feedback strategy:* in each nursing home, a mean score for EOLD total and item-specific was generated based on a minimum of ten responses. These mean scores were compared to a norm based on combined data from 372 nursing homes, collected previously in three nationwide Dutch studies. Feedback reports flagged scores that were significantly ($P < 0.05$) higher or lower than the norm, and for those lower, provided suggested quality improvements.The nursing homes were instructed to discuss the feedback reports and choose improvement actions at multidisciplinary team meetings, not attended by researchers.<br>• *patient-specific feedback strategy:* nursing homes discussed in multidisciplinary team meetings all questionnaires with family caregivers' feedback (using the EOLD instruments at the patient level). At the start of the intervention phase, they received the document with all improvement suggestions to inspire initiation of care improvement actions based on the feedback.<br><br>**Control condition:** only after data collection in the intervention phase concluded, the nursing homes of the control condition received a feedback report that included the mean EOLD item and total scores along with a document that included all the improvement suggestions similar to the patient-specific intervention group. The research team was available to all nursing homes upon their request, to provide additional support with the implementation of the intervention and the improvement actions. |
| Outcomes | **Outcomes:**<br><br>• Comfort in dying (CAD-EOLD)<br>• Satisfaction with care at end of life (SWC-EOLD)<br><br>**Data collection:** in the pre-intervention and intervention phases, questionnaires were sent 6 to 8 weeks after the death of a nursing home resident with dementia. |
| Notes | Funding source: Fonds NutsOhra, the Netherlands (project number 0904-020) and the Netherlands Organisation for Health Research and Development (ZonMw, project number 11150.0003.1) |

| ***Risk of bias*** | | |
|---|---|---|
| **Bias** | **Authors' judgement** | **Support for judgement** |

**Boogaard 2018** *(Continued)*

| | | |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | Randomisation by blinded bag |
| Allocation concealment (selection bias) | Low risk | Assigned immediately after randomisation so no allocation concealment required |
| Blinding of participants and personnel (performance bias)<br>All outcomes | Unclear risk | Not stated whether family members were blinded and not possible to blind staff |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Not stated if family members were blinded (low risk); not stated if statisticians were blinded (high risk) |
| Incomplete outcome data (attrition bias)<br>All outcomes | Unclear risk | Levels of incomplete outcome data not clear |
| Selective reporting (reporting bias) | Low risk | Appears to have reported all variables identified in protocol |
| Recruitment bias (cluster trials only) | Unclear risk | Unclear whether individuals were recruited before or after randomisation. |
| Other bias | Unclear risk | A potential source of bias is the fact that nursing homes could opt out. According to the study protocol, the most common reasons not to participate were lack of time, organisational changes or staff shortage, and nursing homes not having end of life care quality improvement as their current priority. |

**Froggatt 2020**

| ***Study characteristics*** | |
|---|---|
| Methods | **Design:** feasibility cluster-randomised controlled trial<br><br>**Unit of randomisation:** nursing home<br><br>**Setting and timeframe:** 8 nursing homes in the north-west of England, conducted over a 15-month period (August 2017 to November 2018). |
| Participants | **Participants:** residents with advanced dementia (staged as FAST 6–7) living in a nursing home, informal carers and nursing home staff<br><br>**Recruitment:** senior staff in the nursing home were asked to identify residents who met the inclusion criteria. As all participants lacked mental capacity, the process of recruitment and consent involved personal or nominated consultees. Eligible informal carers of residents participating in the trial were identified by the nursing home manager or a senior staff member.<br><br>**Number of participants:** 32 (18 in intervention, 14 in control) |
| Interventions | **Intervention condition:** Namaste Care, which is a complex group intervention that provides structured, personalised care in a dedicated space, focusing on enhancements to the physical environment, comfort management and sensory engagement. At least 2 care staff in each home were trained on Namaste Care at a 1-day workshop, with a follow-up training session to train additional staff. Nursing homes were given a copy of the Namaste Care guide. Timing, regularity and duration of sessions were different across all 4 intervention sites. |

**Froggatt 2020** *(Continued)*

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|---|---|
| | **Control condition:** usual care provided in a nursing home for people with dementia that addressed the key components of good palliative care practice. The study team provided no further education, training or support on care to the nursing homes in the control arm of the trial. |
| Outcomes | **Outcomes:**<br>• Comfort in dying (CAD-EOLD)<br>• Quality of life in late-stage dementia (QUALID)<br>• Psychiatric state (NPI-Q)<br>• Pain (PAIN-AD)<br>• Quality of life (EQ-5D-5L)<br>• Capability at end of life (ICECAP-SCM)<br>• Well-being (ICECAP-O)<br>• Agitation (CMAI)<br>• Sleep/activity ActiGraph<br>• Resource use<br>**Data collection:** data collection was undertaken at baseline and at 2 weeks, 4 weeks and monthly until 24 weeks (and post-bereavement, if appropriate) using 5 methods: questionnaires, observation, interviews (individual and group), completion of a session activity log and use of an ActiGraph device. |
| Notes | Funding source: National Institute for Health Research (NIHR) Health Technology Assessment programme |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | Nursing homes were randomised to either the intervention arm or the control arm by assigning an ID to each nursing home and then randomly selecting each ID. A one-off computer-generated randomisation procedure was used. |
| Allocation concealment (selection bias) | Low risk | Randomisation took place after all 8 nursing homes were recruited. |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Neither the researchers nor the staff completing the proxy measures were blinded. |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Neither the researchers nor the staff completing the proxy measures were blinded; statisticians were blinded. |
| Incomplete outcome data (attrition bias)<br>All outcomes | High risk | Outcomes at 24 weeks missing from 15 of 32 participants |
| Selective reporting (reporting bias) | Low risk | All pre-specified outcomes were reported. |
| Recruitment bias (cluster trials only) | Unclear risk | Unclear whether individuals were recruited before or after randomisation |
| Other bias | Unclear risk | None |

### Hanson 2011

| *Study characteristics* | |
|---|---|
| Methods | **Design:** cluster-randomised controlled trial<br><br>**Unit of randomisation:** nursing home<br><br>**Setting and timeframe:** 24 nursing homes in North Carolina in the USA, with enrolment over a 2-year period (August 2007 to July 2009) |
| Participants | **Participants:** dyads consisting of a resident with advanced dementia (staged as GDS 6 or 7) and feeding problems, and their surrogate, were enrolled<br><br>**Recruitment:** nursing home residents with advanced dementia and feeding problems were enrolled with their surrogate decision-makers. Eligible surrogates were identified as the resident's guardian, Health Care Power of Attorney, or the primary family contact and most likely to be involved in clinical decision-making. Surrogates who responded to an informational letter gave informed consent for themselves and the resident.<br><br>**Number of participants:** 256 (127 in intervention, 129 in control). Of these, 90 dyads included a resident with advanced dementia staged as GDS 7 (46 in intervention, 44 in control). |
| Interventions | **Intervention condition**: surrogates received a structured decision aid (printed or audio version) providing information about dementia and feeding options, including feeding for comfort near the end of life, and the outcomes, advantages and disadvantages of feeding tubes or assisted oral feeding. The decision aid also discussed the surrogate's role in decision-making. Surrogates reviewed the decision aid during their enrolment interview and received the printed decision aid to take home. Research assistants prompted the surrogates to discuss the decision aid with healthcare providers.<br><br>**Control condition**: surrogates received usual care, including any information typically provided by healthcare providers. |
| Outcomes | **Outcomes:**<br><br>• Decisional conflict at 3 months (Decisional Conflict Scale)<br>• Surrogate knowledge about dementia and feeding options<br>• Surrogate-reported frequency of feeding discussions between surrogate and care provider<br>• Feeding treatment use<br>• Use of new feeding tubes<br>• Number of 'do not tube-feed' orders<br>• Weight loss<br>• Mortality<br><br>**Data collection:** surrogates had in-person interviews with trained research assistants at enrolment, and telephone interviews at 1 and 3 months. Structured nursing home chart reviews were completed at enrolment, 1 and 3 months, and brief chart reviews at 6 and 9 months for additional follow-up data on tube feeding, weight loss and mortality. |
| Notes | 90/256 (35%) participants had advanced dementia as defined for this systematic review (staged at GDS 7). The study team re-ran the analysis to produce data for this subset of the study population for this review.<br><br>Funding source: NIH-National Institute for Nursing Research RO1 NR009826 |

| *Risk of bias* | | |
|---|---|---|
| **Bias** | **Authors' judgement** | **Support for judgement** |

**Hanson 2011** *(Continued)*

| | | |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "Nursing homes were randomised in pairs matched on variable associated with tube feeding rates… Paired nursing homes were assigned to intervention or control conditions by computerized random number generation conducted by a single investigator (JG)." |
| Allocation concealment (selection bias) | Low risk | "Randomization was completed and allocation concealed prior to enrolment." |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | "Information shared with physicians and other health care providers was specific to intervention or control assignment, and direct health care providers were told the general purpose of the study but did not know specifically what the outcome measures were."<br><br>It was not possible to blind surrogates to the intervention. |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | "Due to cluster randomisation, data collectors were not blinded to group assignment."<br><br>We judged this lack of blinding to be a high risk of bias for all outcomes. |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | Numbers lost to 3-month follow-up in both groups was low (5% and 13%). |
| Selective reporting (reporting bias) | Low risk | All outcomes listed in the Methods section were reported and there was no evidence of selective outcome reporting. |
| Recruitment bias (cluster trials only) | High risk | Nursing homes were randomised before recruitment of all participants and surrogate dyads. |
| Other bias | Low risk | Baseline imbalance between clusters and cluster effects both accounted for in analysis. |

**Hanson 2017**

| ***Study characteristics*** | |
|---|---|
| Methods | **Design:** single-blind cluster-randomised clinical trial<br><br>**Unit of randomisation:** nursing home<br><br>**Setting and timeframe:** 22 nursing homes within 60-minute driving radius of University of North Carolina-Chapel Hill, US. Conducted over a 2-year period (April 2012 to September 2014). |
| Participants | **Participants:** dyads of people with advanced dementia (staged as GDS 5-7) and their family decision-maker<br><br>**Recruitment:** nursing homes sent initial letters and referred those who agreed to contact with researchers. Family decision-makers provided written informed consent for themselves and the resident with advanced dementia.<br><br>**Number of participants:** 302 (151 in intervention and 151 in control). Of these, 76 met the review criteria for advanced dementia (34 in intervention and 42 in control). |
| Interventions | **Intervention condition:** family decision-makers had the 2-part intervention, consisting of an 18-minute goals of care video decision aid and a structured discussion with the nursing home care team. The decision aid provided information on dementia, goals of prolonging life, supporting function, or improving comfort, treatments consistent with each goal, and how to prioritise goals. Decision-makers |

**Hanson 2017** *(Continued)*

| | |
|---|---|
| | saw the decision aid with research staff at the initial study visit and received a print copy of the decision aid and guide called "Questions to Consider in Care Planning". Investigators delivered a 1-hour training session to nurses, social workers, therapists and nutritionists who create care plans. They viewed the goals of care decision aid, learned the VALUE (value family comments, address emotions, listen, understand the patient as a person, and elicit family questions) principles for family communication, and observed a short role play of a goals of care discussion. Research staff also provided them with a written discussion guide, and reminders to meet with decision-makers.<br><br>**Control condition:** family decision-makers in control sites experienced an informational video on interaction with someone with dementia and a usual care plan meeting with staff. Nursing home staff received a 45-minute training on study procedures. All other procedures were identical for both arms. |
| Outcomes | **Outcomes:**<br><br>• Quality of communication<br>• Family report of concordance with clinicians on the primary goal of care<br>• Treatment consistent with preferences (Advance Care Planning Problem score)<br>• Family ratings of symptom management and care<br>• Palliative care domains in care plans<br>• Medical Orders for Scope of Treatment completion<br>• Hospital transfers<br><br>**Data collection:** research assistants interviewed family decision-makers in person at baseline, and by telephone at 3, 6 and 9 months. They also completed structured resident medical chart reviews at baseline, and at 3, 6 and 9 months. On a resident's death, interviews were modified to address care during dying. |
| Notes | Funding source: National Institutes of Health grant R01AG037483 (Hanson, PI); Dr Mitchell was supported by the National Institutes of Health, National Institute on Aging grant K24AG033640. |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | The study statistician randomised 22 nursing homes in blocks of 4, except for a final block of 2, matched by profit versus non-profit status and percent African-American residents. |
| Allocation concealment (selection bias) | Unclear risk | No evidence |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Neither participants nor study personnel were blinded, due to the nature of the intervention. |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Low risk | Research assistants were blinded to allocation of assessed outcomes |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | Less than 20% lost to follow-up in reduced data set |
| Selective reporting (reporting bias) | Unclear risk | Some evidence of this – reporting at 3 months and 9 months for goals of care, and at 6 months and 9 months for other outcomes. |

**Hanson 2017** *(Continued)*

| | | |
|---|---|---|
| Recruitment bias (cluster trials only) | Unclear risk | Unclear whether individuals were recruited before or after randomisation |
| Other bias | Unclear risk | None |

**Hanson 2019**

| ***Study characteristics*** | |
|---|---|
| Methods | **Design:** pilot randomised controlled trial<br><br>**Unit of randomisation:** individual patient/family decision-maker dyad<br><br>**Setting and timeframe:** one acute hospital in North Carolina, USA, over a period of 19 months (March 2016 to August 2017) |
| Participants | **Participants:** dyads of persons with late-stage dementia (staged as GDS 5-7) and family decision-makers<br><br>**Recruitment:** potentially eligible participants were identified within 24 hours of admission, and reviewed by research staff for eligibility. A palliative care physician then confirmed dementia diagnosis and stage with the participant's attending physician and sought permission to approach the family decision-maker about participation. Family decision-makers provided written consent for themselves and the person with late-stage dementia.<br><br>**Number of participants:** 62 (30 in intervention and 32 in control). Of these, 13 met the review criteria for advanced dementia (5 in intervention and 8 in control). |
| Interventions | **Intervention condition:** participant-family dyads received a specialty palliative care consultation while hospitalised and an information booklet, 'Advanced Dementia: A Guide for Families'. Based on their assessments, consultants provided individualised recommendations for palliative care domains, offered to assist with completion of a Medical Orders for Scope of Treatment (MOST) order set, and recommended referrals to post-discharge services. Transitional care included provision of consult recommendations and MOST form to the post-acute primary provider, as well as a 2-week post-discharge follow-up call by a palliative care nurse practitioner. Investigators provided a 1-hour training session to palliative care physicians and nurse practitioners to teach them the dementia protocol and to provide access to an electronic health record-template consult note.<br><br>**Control condition:** dyads received information on care-giving for late-stage dementia from the Alzheimer's Association, and participants received usual hospital care. Specialty palliative care consultation was allowed, if requested by attending physicians. All other procedures were identical for intervention and control. |
| Outcomes | **Outcomes:**<br><br>• 60-day hospital or emergency department visits<br>• Participant comfort (CAD-EOLD)<br>• Family distress (Family distress in advanced dementia)<br>• Palliative care domains addressed in the treatment plan<br>• Access to hospice or community-based palliative care<br>• Discussion of prognosis<br>• Goals of care<br>• Completion of MOST<br>• Treatment decisions<br><br>**Data collection:** research staff masked to study arm collected data using 30- and 60-day post-discharge telephone interviews with family decision-makers. When an enrolled participant died, staff con- |

**Hanson 2019** *(Continued)*

| | |
|---|---|
| | ducted family interviews with modifications for care during dying. A separate research staff member conducted chart reviews at 60 days after discharge. |
| Notes | Funding source: funding was provided by the National Institute on Aging Grant R21AG052140 (Hanson, PI) and National Palliative Care Research Center (Hanson, PI). |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | The study biostatistician randomised each dyad in a 1:1 ratio to intervention vs. control arms before the baseline interview |
| Allocation concealment (selection bias) | Low risk | Assigned immediately after randomisation so no allocation concealment required |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Allocation was revealed to the baseline interviewer, family decision-maker and the attending physician, but concealed from the investigators and research staff collecting interview outcome data. |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Low risk | Investigators and research staff collecting outcome data were blinded. |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | Missing data < 20% |
| Selective reporting (reporting bias) | Low risk | All outcomes listed in the Methods section were reported and there was no evidence of selective outcome reporting. |
| Recruitment bias (cluster trials only) | Low risk | Not applicable |
| Other bias | Unclear risk | None |

**Mitchell 2018**

***Study characteristics***

| | |
|---|---|
| Methods | **Design:** cluster-randomised controlled trial<br><br>**Unit of randomisation:** nursing home<br><br>**Setting and timeframe:** 64 nursing homes in the Boston area, conducted over a 4-year period (February 2013 to July 2017) |
| Participants | **Participants:** residents with advanced dementia (staged as GDS 7) and their proxies<br><br>**Recruitment:** at the time of nursing home recruitment and quarterly thereafter, research assistants asked nurses to identify residents with dementia, GDS=7, and available proxies. Proxies of eligible residents were mailed information and telephoned 2 weeks later to solicit their participation. Proxies provided consent for themselves and the residents.<br><br>**Number of participants:** 402 (212 in intervention, 190 in control) |

**Mitchell 2018** *(Continued)*

| | |
|---|---|
| Interventions | **Intervention condition:** an advance care planning video for proxies and provision of a form to the residents' primary care team indicating the proxy's preferred level of care after viewing the video. The 12-minute video was developed by geriatricians and palliative care specialists. Proxies were shown the video on tablets by a research assistant during a baseline in-person interview. The video described the typical features of advanced dementia, accompanied by images of an individual with advanced dementia. Three levels of care options were also presented: intensive, basic, comfort, with images.<br><br>**Control:** proxies were read descriptions of the levels of care and asked their preferences. Their choice was not communicated to providers and they otherwise experienced usual advance care planning practice. |
| Outcomes | **Outcomes:**<br><br>• Directive to forgo hospital transfers, tube-feeding, and intravenous hydration<br>• Documented goals of care discussions between providers and proxies in the prior 3 months<br>• Proportions of proxies preferring comfort care<br>• Burdensome treatment including feeding tube insertions, parenteral therapy and hospital transfers<br><br>**Data collection:** resident data were collected at baseline and quarterly up to 12 months from their charts, except for baseline measures of functional and cognitive status. Proxy data were collected at baseline in-person interviews and quarterly telephone interviews for up to 12 months. Charts reviews were done within 14 days of a resident's death. |
| Notes | Funding source: National Institute on Aging R01 AG043440 and K24AG033640. |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | Randomly assigned one nursing home to each arm using a computer-generated algorithm. |
| Allocation concealment (selection bias) | Low risk | Once a pair was recruited, facilities were assigned de-identified labels that the statistician used to randomly assign one nursing home to each arm using a computer-generated algorithm. |
| Blinding of participants and personnel (performance bias)<br>All outcomes | Low risk | One research assistant conducted all baseline in-person interviews when the video was also shown, and therefore was not masked. Three other research assistants who conducted chart abstractions and follow-up proxy interviews, which included all outcome data, were masked. Proxy participants were only told about the intervention in their own arm, so they were reasonably masked. The investigators, statistician and data programmers were masked. Overall, low risk of bias. |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Low risk | The three research assistants who conducted chart abstractions and follow-up proxy interviews, which included all outcome data, were masked. |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | Only 16/402 were lost to follow-up. Therefore, low risk of bias. |
| Selective reporting (reporting bias) | Low risk | All outcomes listed in the Methods section were reported and there was no evidence of selective outcome reporting. |
| Recruitment bias (cluster trials only) | High risk | Individuals were recruited after randomisation. |

**Mitchell 2018** *(Continued)*

| | | |
|---|---|---|
| Other bias | Low risk | None. |

**Verreault 2018**

| ***Study characteristics*** | |
|---|---|
| Methods | **Design:** non-randomised controlled before-and-after study<br><br>**Unit of randomisation:** not applicable. Unit of allocation was the nursing home.<br><br>**Setting and timeframe:** 4 long-term care facilities in the cities of Quebec and Sherbrooke in Canada, conducted over a 21-month period (September 2012 to June 2014). |
| Participants | **Participants:** residents with dementia (staged as FAST 7e,f) and a close family member<br><br>**Recruitment:** residents with terminal dementia were identified by the research team. No further details provided.<br><br>**Number of participants:** 193 (97 in intervention, 96 in control), Pre-intervention data were collected from 80 residents with dementia who had died in the six months prior to the study (36 in intervention, 44 in control) |
| Interventions | **Intervention condition:** the intervention included five components:<br><br>• training of physicians (3 hours), nurses (7 hours) and nurses' aides (3.5 hours)<br>• clinical monitoring of pain;<br>• regular mouth care routine;<br>• communication with families - early and systematically;<br>• use of nurse facilitator on site to implement and monitor the intervention – released from regular work for 1 year to focus on this study, 1 week of training on palliative care.<br><br>**Control:** care as usual |
| Outcomes | **Outcomes:**<br><br>• Quality of care (Family Perception of Care Scale - FPCS)<br>• Symptom management (SM-EOLD)<br>• Comfort in dying with Dementia (CAD-EOLD)<br><br>**Data collection:** outcomes were measured when a person died. Assessed comfort in the last 48 hours before death both from the family and the nurses' perspectives. The nurses' evaluation was completed within 72 hours of the death in the intervention group, but not in the usual care group in order to avoid contamination. The FPCS, SM-EOLD, and CAD-EOLD questionnaires were mailed to family members 4 weeks after the death of their relative. These 3 questionnaires were sent to families of all residents who died during the 6-month period prior to intervention, in order to obtain baseline information on quality of care (QOC) and quality of dying (QOD) in all participating facilities (experimental and control) before the beginning of the study. |
| Notes | Funding source: grant from the Canadian Institutes of Health Research (CIHR; Project No. 243952). |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | High risk | Not randomised, so high risk |

**Verreault 2018** *(Continued)*

| | | |
|---|---|---|
| Allocation concealment (selection bias) | High risk | Not randomised, so high risk |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Not blinded |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Family and staff were not blinded and were responsible for most of the outcome data. |
| Incomplete outcome data (attrition bias)<br>All outcomes | High risk | 36% of families did not respond and the response rate was higher in the intervention group. |
| Selective reporting (reporting bias) | Unclear risk | Data were collected from both families and nurses; however, it is not clear whether the data presented are family- or nurse-rated. |
| Recruitment bias (cluster trials only) | Low risk | Not applicable |
| Other bias | High risk | Regarding confounding bias, the 4 participating long-term care settings are publicly funded institutions, with similar residents' characteristics, nursing staff ratios and prescribing practices. Private room at baseline is higher in usual care (77% vs 35%) – but is explained by the authors as "due to local differences". Therefore, we judge the risk of confounding bias to be low.<br><br>Regarding selection bias, the decision to allocate sites to the intervention and control groups in the Verreault study was taken by administrative officials without information about the specifics of the study. The choice was mainly based on the capacity to find a local nurse capable and willing to act as a nurse facilitator for the project within the intervention facility. However, participant recruitment followed allocation to the intervention; therefore, the potential for selection bias is high. |

CAD-EOLD: Comfort Assessment in Dying with Dementia; CMAI: Cohen-Mansfield Agitation Index; EOL: end of life; EOLD: End of Life in Dementia; EQ-5D-5L: European Quality of Life Five Dimension; FAST: Functional Assessment Staging Test; FPCS: Family Perception of Care Scale; GDS: Global Deterioration Scale; GHQ-12: 12-item General Health Questionnaire; ICECAP-O: Investigating Choice Experiences Capability Measure for Older People; ICECAP-SCM: Investigating Choice Experiences Capability - Supportive Care Measure; NPI-Q: Neuropsychiatric Inventory–Questionnaire; PAIN-AD: Pain Assessment in Advanced Dementia; PCADQ: Palliative Care for Advanced Dementia Questionnaire; PCECAT: Person-centred Environment and Care Assessment Tool; QOC: quality of care; QOD-LTC: Quality of Dying in Long-Term Care; QoL: quality of life; QUALID: Quality of Life in Late-Stage Dementia; SM-EOLD: Symptom Management at the End-Of-Life in Dementia; SWC-EOLD: Satisfaction With Care at the End-of-Life in Dementia.

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

| Study | Reason for exclusion |
|---|---|
| Ballard 2016 | Not a palliative intervention |
| Ballard 2018 | Not a palliative intervention |
| Bergh 2012 | Not a palliative intervention |
| Bonner 2014 | Carers of people with dementia who have not reached the stage of advanced dementia |

| Study | Reason for exclusion |
|---|---|
| Bonner 2020 | > 80% of study participants not advanced dementia; data not available separately for people with advanced dementia |
| Brazil 2018 | > 80% of study participants not advanced dementia; data not available separately for people with advanced dementia |
| Burns 2009 | Not a palliative intervention |
| Courtright 2016 | Dementia not staged using a validated functional assessment tool |
| De Deyn 2004 | Not a palliative intervention |
| Devanand 2012 | Not a palliative intervention |
| Ernecoff 2019 | Secondary analysis of trial data |
| Finkel 1995 | Not a palliative intervention |
| Fleischhacker 1986 | Not a palliative intervention |
| Grossberg 2013 | Not a palliative intervention |
| Hager 2014 | Not a palliative intervention |
| Hamilton 2017 | Dementia not staged using a validated functional assessment tool |
| Iwasaki 2007 | Not a palliative intervention |
| Kovach 1996 | Dementia not staged using a validated functional assessment tool |
| Kovach 2006 | > 80% of study participants not advanced dementia; data not available separately for people with advanced dementia |
| Kovach 2012 | > 80% of study participants not advanced dementia; data not available separately for people with advanced dementia |
| Levy 2017 | Dementia not staged using a validated functional assessment tool |
| Loizeau 2016 | Ineligible patient population |
| Loizeau 2018 | Ineligible patient population |
| Meeker 2000 | Ineligible study design |
| Mintzer 2006 | Not a palliative intervention |
| Mitchell 2020 | > 80% of study participants not advanced dementia; data not available separately for people with advanced dementia |
| Navratilova 2007 | Not a palliative intervention |
| NCT00921297 | Not a palliative intervention |
| NCT03323411 | Unable to contact authors to clarify inclusion |

| Study | Reason for exclusion |
|---|---|
| NCT03323502 | Dementia not staged using a validated functional assessment tool |
| NCT03798327 | Dementia not staged using a validated functional assessment tool |
| Pieper 2018 | Not a palliative intervention |
| Reinhardt 2004 | > 80% of study participants not advanced dementia; data not available separately for people with advanced dementia |
| Shin 2013 | Not a palliative intervention |
| Street 2000 | Not a palliative intervention |
| Surr 2020 | Not a palliative intervention |
| Tropea 2019 | Dementia not staged using a validated tool |
| Van den Block 2019 | Dementia not staged using a validated tool |
| Wilchesky 2018 | Wrong study design |

## Characteristics of ongoing studies *[ordered by study ID]*

### Arendts 2019

| | |
|---|---|
| Study name | A randomised trial of a Carer End of Life Planning Intervention (CELPI) and its effect on the proportion of people with dementia dying in hospital |
| Methods | Randomised trial |
| Participants | Carers of people living with advanced stage dementia |
| Interventions | An intervention triad of carer education, end of life planning and palliative care.<br><br>**Intervention:** intervention clinician will meet the carer in their homes or at a location of their choice at a time that is convenient to them. The length of the visit is expected to be between one and a half and two hours long. Each participant will receive a single visit.<br><br>**Control:** the control group will be given a specially designed information brochure about dementia that lists contact numbers of services providers. |
| Outcomes | Primary outcome: proportion of deaths in hospital in persons with dementia<br><br>Secondary outcome: number of emergency department attendances by the persons with dementia, determined by electronic health record, confirmed with carer interview |
| Starting date | 16 July 2019 |
| Contact information | Glenn Arendts (glenn.arendts@uwa.edu.au) |
| Notes | Not yet recruiting |

**Smaling 2018**

| | |
|---|---|
| Study name | Effects of the Namaste Care Family programme on quality of life of nursing home residents with advanced dementia and on family care-giving experiences: study protocol of a cluster-randomised controlled trial |
| Methods | Cluster-randomised trial; nursing home unit of randomisation |
| Participants | Nursing home residents with advanced dementia and family caregivers |
| Interventions | **Intervention:** the nursing homes in the intervention group will implement the Namaste Care Family programme, which is a 7-day-a-week programme, intended to be offered in 2-hour sessions, twice a day. Nursing staff and volunteers in the intervention group will receive a 2-hour training from the research team, after the baseline assessment.<br><br>**Control:** Usual care |
| Outcomes | Quality of life of the persons with dementia (QUALID) and positive care-giving experiences (PES) |
| Starting date | September 2016 |
| Contact information | Jenny T van der Steen (jtvandersteen@lumc.nl) |
| Notes | Target study completion: September 2018 |

## DATA AND ANALYSES

### Comparison 1. Organisation and delivery versus usual care

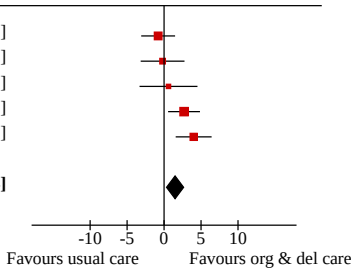
| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1.1 Comfort in dying (CADEOLD) | 5 | 335 | Mean Difference (IV, Fixed, 95% CI) | 1.49 [0.34, 2.64] |
| 1.2 Symptom Management | 0 | 0 | Mean Difference (IV, Fixed, 95% CI) | Not estimable |
| 1.3 Quality of Life | 1 | 15 | Mean Difference (IV, Fixed, 95% CI) | -8.20 [-16.13, -0.27] |
| 1.4 Pain | 0 | 0 | Mean Difference (IV, Fixed, 95% CI) | Not estimable |
| 1.5 Palliative care plan in place | 1 | 99 | Risk Ratio (M-H, Fixed, 95% CI) | 5.84 [1.37, 25.02] |
| 1.6 Review of prescribing antipsychotics | 0 | 0 | Risk Ratio (M-H, Fixed, 95% CI) | Not estimable |
| 1.7 Review of prescribing analgesics | 0 | 0 | Risk Ratio (M-H, Fixed, 95% CI) | Not estimable |
| 1.8 Use of non-palliative interventions | 2 | 292 | Risk Ratio (M-H, Fixed, 95% CI) | 1.11 [0.71, 1.72] |

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1.9 Advance care planning discussion | 1 | 193 | Risk Ratio (M-H, Fixed, 95% CI) | 1.08 [1.00, 1.18] |
| 1.10 Documentation of advance directives | 2 | 112 | Risk Ratio (M-H, Fixed, 95% CI) | 1.46 [0.50, 4.25] |
| 1.11 Decisional conflict | 0 | 0 | Mean Difference (IV, Fixed, 95% CI) | Not estimable |
| 1.12 Goals of care discussion | 1 | 13 | Risk Ratio (M-H, Fixed, 95% CI) | 2.36 [1.00, 5.54] |
| 1.13 Concordance with goals-of-care | 0 | 0 | Risk Ratio (M-H, Fixed, 95% CI) | Not estimable |

## Analysis 1.1. Comparison 1: Organisation and delivery versus usual care, Outcome 1: Comfort in dying (CAD-EOLD)

| Study or Subgroup | MD | SE | Organisation and Delivery Total | Usual Care Total | Weight | Mean Difference IV, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| Agar 2017 | -0.8 | 1.1686 | 52 | 50 | 25.3% | -0.80 [-3.09 , 1.49] |
| Boogaard 2018 | -0.2 | 1.5117 | 57 | 24 | 15.1% | -0.20 [-3.16 , 2.76] |
| Hanson 2019 | 0.6 | 1.998 | 5 | 8 | 8.6% | 0.60 [-3.32 , 4.52] |
| Verreault 2018 | 2.7 | 1.0991 | 70 | 54 | 28.6% | 2.70 [0.55 , 4.85] |
| Froggatt 2020 (1) | 4 | 1.2394 | 9 | 6 | 22.5% | 4.00 [1.57 , 6.43] |
| **Total (95% CI)** | | | **193** | **142** | **100.0%** | **1.49 [0.34 , 2.64]** |

Heterogeneity: Chi² = 10.60, df = 4 (P = 0.03); I² = 62%
Test for overall effect: Z = 2.53 (P = 0.01)
Test for subgroup differences: Not applicable

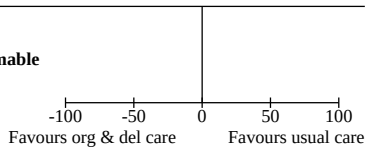



**Footnotes**
(1) Staff-rated CAD-EOLD

## Analysis 1.2. Comparison 1: Organisation and delivery versus usual care, Outcome 2: Symptom Management

| Study or Subgroup | Organisation and Delivery Mean | SD | Total | Usual Care Mean | SD | Total | Weight | Mean Difference IV, Fixed, 95% CI |
|---|---|---|---|---|---|---|---|---|
| **Total (95% CI)** | | | **0** | | | **0** | | **Not estimable** |

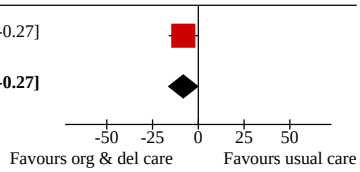
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



## Analysis 1.3. Comparison 1: Organisation and delivery versus usual care, Outcome 3: Quality of Life

| Study or Subgroup | MD | SE | Organisation and Delivery Total | Usual Care Total | Weight | Mean Difference IV, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| Froggatt 2020 | -8.2 | 4.0485 | 9 | 6 | 100.0% | -8.20 [-16.13 , -0.27] |
| **Total (95% CI)** | | | **9** | **6** | **100.0%** | **-8.20 [-16.13 , -0.27]** |

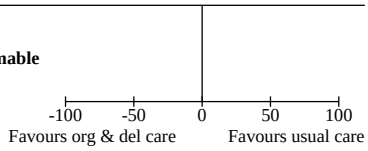
Heterogeneity: Not applicable
Test for overall effect: Z = 2.03 (P = 0.04)
Test for subgroup differences: Not applicable




## Analysis 1.4. Comparison 1: Organisation and delivery versus usual care, Outcome 4: Pain

| Study or Subgroup | Organisation and Delivery Mean | SD | Total | Usual Care Mean | SD | Total | Weight | Mean Difference IV, Fixed, 95% CI |
|---|---|---|---|---|---|---|---|---|
| **Total (95% CI)** | | | **0** | | | **0** | | **Not estimable** |

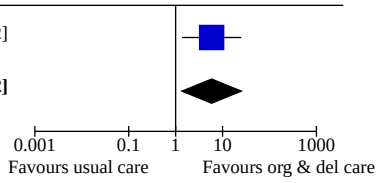
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable




## Analysis 1.5. Comparison 1: Organisation and delivery versus usual care, Outcome 5: Palliative care plan in place

| Study or Subgroup | Organisation and Delivery Events | Total | Usual Care Events | Total | Weight | Risk Ratio M-H, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| Ahronheim 2000 | 11 | 48 | 2 | 51 | 100.0% | 5.84 [1.37 , 25.02] |
| **Total (95% CI)** | | **48** | | **51** | **100.0%** | **5.84 [1.37 , 25.02]** |
| Total events: | 11 | | 2 | | | |

Heterogeneity: Not applicable
Test for overall effect: Z = 2.38 (P = 0.02)
Test for subgroup differences: Not applicable




## Analysis 1.6. Comparison 1: Organisation and delivery versus usual care, Outcome 6: Review of prescribing antipsychotics

| Study or Subgroup | Organisation and Delivery Events | Total | Usual Care Events | Total | Weight | Risk Ratio M-H, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| **Total (95% CI)** | | **0** | | **0** | | **Not estimable** |
| Total events: | 0 | | 0 | | | |

Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable

## Analysis 1.7. Comparison 1: Organisation and delivery versus usual care, Outcome 7: Review of prescribing analgesics

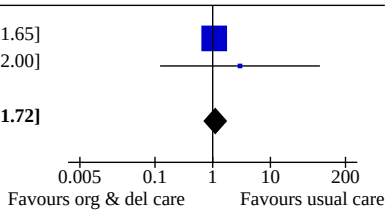
| Study or Subgroup | Organisation and Delivery Events | Total | Usual Care Events | Total | Weight | Risk Ratio M-H, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| **Total (95% CI)** | | **0** | | **0** | | **Not estimable** |
| Total events: | 0 | | 0 | | | |

Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable


## Analysis 1.8. Comparison 1: Organisation and delivery versus usual care, Outcome 8: Use of non-palliative interventions

| Study or Subgroup | Organisation and Delivery Events | Total | Usual Care Events | Total | Weight | Risk Ratio M-H, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| Ahronheim 2000 (1) | 22 | 48 | 22 | 51 | 97.7% | 1.06 [0.68 , 1.65] |
| Verreault 2018 (2) | 1 | 97 | 0 | 96 | 2.3% | 2.97 [0.12 , 72.00] |
| **Total (95% CI)** | | **145** | | **147** | **100.0%** | **1.11 [0.71 , 1.72]** |
| Total events: | 23 | | 22 | | | |

Heterogeneity: Chi² = 0.40, df = 1 (P = 0.53); I² = 0%
Test for overall effect: Z = 0.45 (P = 0.65)
Test for subgroup differences: Not applicable

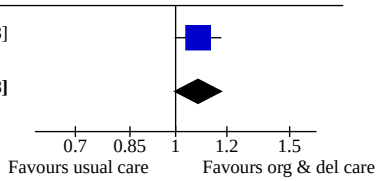



**Footnotes**
(1) Used data for tube-feeding
(2) Used data for parenteral therapy

## Analysis 1.9. Comparison 1: Organisation and delivery versus usual care, Outcome 9: Advance care planning discussion

| Study or Subgroup | Organisation and Delivery Events | Total | Usual Care Events | Total | Weight | Risk Ratio M-H, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| Verreault 2018 | 93 | 97 | 85 | 96 | 100.0% | 1.08 [1.00 , 1.18] |
| **Total (95% CI)** | | **97** | | **96** | **100.0%** | **1.08 [1.00 , 1.18]** |
| Total events: | 93 | | 85 | | | |

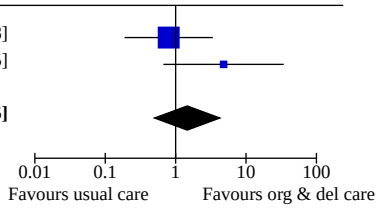
Heterogeneity: Not applicable
Test for overall effect: Z = 1.88 (P = 0.06)
Test for subgroup differences: Not applicable



## Analysis 1.10. Comparison 1: Organisation and delivery versus usual care, Outcome 10: Documentation of advance directives

| Study or Subgroup | Organisation and Delivery Events | Total | Usual Care Events | Total | Weight | Risk Ratio M-H, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| Ahronheim 2000 (1) | 3 | 48 | 4 | 51 | 83.5% | 0.80 [0.19 , 3.38] |
| Hanson 2019 (1) | 3 | 5 | 1 | 8 | 16.5% | 4.80 [0.67 , 34.35] |
| **Total (95% CI)** | | **53** | | **59** | **100.0%** | **1.46 [0.50 , 4.25]** |
| Total events: | 6 | | 5 | | | |

Heterogeneity: Chi² = 2.08, df = 1 (P = 0.15); I² = 52%
Test for overall effect: Z = 0.69 (P = 0.49)
Test for subgroup differences: Not applicable

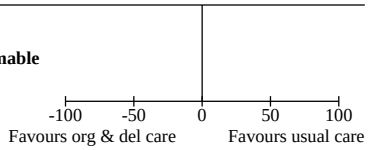



**Footnotes**
(1) Used data on do not tube-feed

## Analysis 1.11. Comparison 1: Organisation and delivery versus usual care, Outcome 11: Decisional conflict

| Study or Subgroup | Organisation and Delivery Mean | SD | Total | Usual Care Mean | SD | Total | Weight | Mean Difference IV, Fixed, 95% CI |
|---|---|---|---|---|---|---|---|---|
| **Total (95% CI)** | | | **0** | | | **0** | | **Not estimable** |

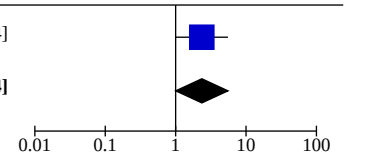
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable




## Analysis 1.12. Comparison 1: Organisation and delivery versus usual care, Outcome 12: Goals of care discussion

| Study or Subgroup | Organisation and Delivery Events | Total | Usual Care Events | Total | Weight | Risk Ratio M-H, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| Hanson 2019 (1) | 5 | 5 | 3 | 8 | 100.0% | 2.36 [1.00 , 5.54] |
| **Total (95% CI)** | | **5** | | **8** | **100.0%** | **2.36 [1.00 , 5.54]** |
| Total events: | 5 | | 3 | | | |

Heterogeneity: Not applicable
Test for overall effect: Z = 1.97 (P = 0.05)
Test for subgroup differences: Not applicable




**Footnotes**
(1) Unpublished data obtained from study authors

## Analysis 1.13. Comparison 1: Organisation and delivery versus usual care, Outcome 13: Concordance with goals-of-care

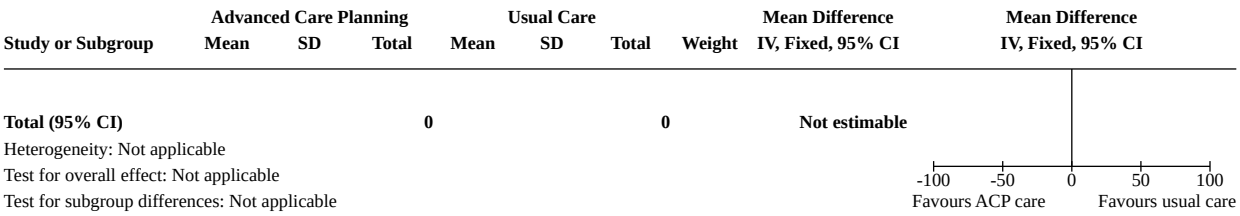
| Study or Subgroup | Organisation and Delivery Events | Total | Usual Care Events | Total | Weight | Risk Ratio M-H, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| **Total (95% CI)** | | **0** | | **0** | | **Not estimable** |
| Total events: | 0 | | 0 | | | |

Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable

**Comparison 2. Advance care planning versus usual care**

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 2.1 Comfort in dying (CAD-EOLD) | 0 | 0 | Mean Difference (IV, Fixed, 95% CI) | Not estimable |
| 2.2 Symptom management (SM-EOLD) | 1 | 67 | Mean Difference (IV, Fixed, 95% CI) | -1.80 [-6.49, 2.89] |
| 2.3 Quality of life | 0 | 0 | Mean Difference (IV, Fixed, 95% CI) | Not estimable |
| 2.4 Pain | 0 | 0 | Mean Difference (IV, Fixed, 95% CI) | Not estimable |
| 2.5 Palliative care plan in place | 0 | 0 | Risk Ratio (M-H, Fixed, 95% CI) | Not estimable |
| 2.6 Review of prescribing antipsychotics | 0 | 0 | Risk Ratio (M-H, Fixed, 95% CI) | Not estimable |
| 2.7 Review of prescribing analgesics | 0 | 0 | Risk Ratio (M-H, Fixed, 95% CI) | Not estimable |
| 2.8 Use of non-palliative interventions | 0 | 0 | Risk Ratio (M-H, Fixed, 95% CI) | Not estimable |
| 2.9 Advance care planning discussion | 1 | 67 | Risk Ratio (IV, Fixed, 95% CI) | 1.04 [0.87, 1.24] |
| 2.10 Documentation of advance directives | 2 | 384 | Risk Ratio (IV, Fixed, 95% CI) | 1.23 [1.07, 1.41] |
| 2.11 Decisional conflict | 1 | 79 | Mean Difference (IV, Fixed, 95% CI) | -0.30 [-0.63, 0.03] |
| 2.12 Goals of care discussion | 2 | 384 | Risk Ratio (IV, Fixed, 95% CI) | 1.33 [1.11, 1.59] |
| 2.13 Concordance with goals of care | 1 | 63 | Risk Ratio (IV, Fixed, 95% CI) | 1.39 [1.08, 1.79] |

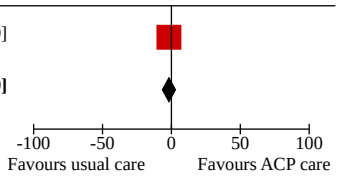
**Analysis 2.1. Comparison 2: Advance care planning versus usual care, Outcome 1: Comfort in dying (CAD-EOLD)**



## Analysis 2.2. Comparison 2: Advance care planning versus usual care, Outcome 2: Symptom management (SM-EOLD)

| Study or Subgroup | MD | SE | Advanced Care Planning Total | Usual Care Total | Weight | Mean Difference IV, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| Hanson 2017 (1) | -1.8 | 2.3918 | 30 | 37 | 100.0% | -1.80 [-6.49 , 2.89] |
| **Total (95% CI)** | | | **30** | **37** | **100.0%** | **-1.80 [-6.49 , 2.89]** |

Heterogeneity: Not applicable
Test for overall effect: Z = 0.75 (P = 0.45)
Test for subgroup differences: Not applicable

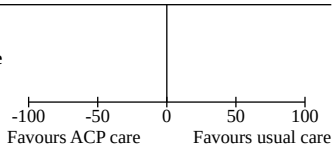



**Footnotes**
(1) Unpublished data obtained from study authors

## Analysis 2.3. Comparison 2: Advance care planning versus usual care, Outcome 3: Quality of life

| Study or Subgroup | Advanced Care Planning Mean | SD | Total | Usual Care Mean | SD | Total | Weight | Mean Difference IV, Fixed, 95% CI |
|---|---|---|---|---|---|---|---|---|
| **Total (95% CI)** | | | **0** | | | **0** | | **Not estimable** |

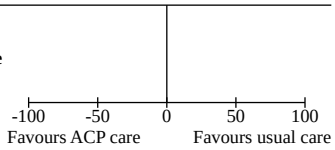
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable




## Analysis 2.4. Comparison 2: Advance care planning versus usual care, Outcome 4: Pain

| Study or Subgroup | Advanced Care Planning Mean | SD | Total | Usual Care Mean | SD | Total | Weight | Mean Difference IV, Fixed, 95% CI |
|---|---|---|---|---|---|---|---|---|
| **Total (95% CI)** | | | **0** | | | **0** | | **Not estimable** |

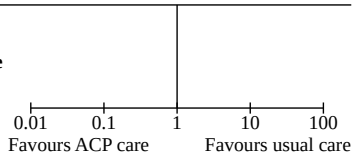
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable




## Analysis 2.5. Comparison 2: Advance care planning versus usual care, Outcome 5: Palliative care plan in place

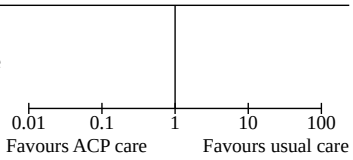
| Study or Subgroup | Advanced Care Planning Events | Total | Usual Care Events | Total | Weight | Risk Ratio M-H, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| **Total (95% CI)** | | **0** | | **0** | | **Not estimable** |
| Total events: | 0 | | 0 | | | |

Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



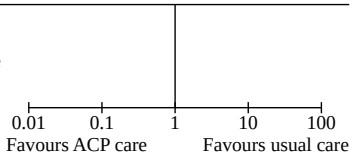
## Analysis 2.6. Comparison 2: Advance care planning versus usual care, Outcome 6: Review of prescribing antipsychotics

| Study or Subgroup | Advanced Care Planning Events | Advanced Care Planning Total | Usual Care Events | Usual Care Total | Weight | Risk Ratio M-H, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| **Total (95% CI)** | | **0** | | **0** | | **Not estimable** |
| Total events: | 0 | | 0 | | | |
| Heterogeneity: Not applicable | | | | | | |
| Test for overall effect: Not applicable | | | | | | |
| Test for subgroup differences: Not applicable | | | | | | |



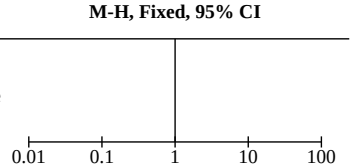

## Analysis 2.7. Comparison 2: Advance care planning versus usual care, Outcome 7: Review of prescribing analgesics

| Study or Subgroup | Advanced Care Planning Events | Advanced Care Planning Total | Usual Care Events | Usual Care Total | Weight | Risk Ratio M-H, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| **Total (95% CI)** | | **0** | | **0** | | **Not estimable** |
| Total events: | 0 | | 0 | | | |
| Heterogeneity: Not applicable | | | | | | |
| Test for overall effect: Not applicable | | | | | | |
| Test for subgroup differences: Not applicable | | | | | | |



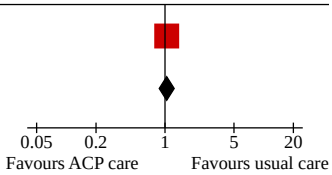

## Analysis 2.8. Comparison 2: Advance care planning versus usual care, Outcome 8: Use of non-palliative interventions

| Study or Subgroup | Advanced Care Planning Events | Advanced Care Planning Total | Usual Care Events | Usual Care Total | Weight | Risk Ratio M-H, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| **Total (95% CI)** | | **0** | | **0** | | **Not estimable** |
| Total events: | 0 | | 0 | | | |
| Heterogeneity: Not applicable | | | | | | |
| Test for overall effect: Not applicable | | | | | | |
| Test for subgroup differences: Not applicable | | | | | | |




## Analysis 2.9. Comparison 2: Advance care planning versus usual care, Outcome 9: Advance care planning discussion

| Study or Subgroup | log[RR] | SE | Advanced Care Planning Total | Usual Care Total | Weight | Risk Ratio IV, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| Hanson 2017 (1) | 0.0398 | 0.089 | 30 | 37 | 100.0% | 1.04 [0.87 , 1.24] |
| **Total (95% CI)** | | | **30** | **37** | **100.0%** | **1.04 [0.87 , 1.24]** |
| Heterogeneity: Not applicable | | | | | | |
| Test for overall effect: Z = 0.45 (P = 0.65) | | | | | | |
| Test for subgroup differences: Not applicable | | | | | | |



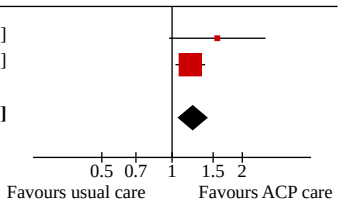

**Footnotes**

(1) Unpublished data obtained from study authors

## Analysis 2.10. Comparison 2: Advance care planning versus usual care, Outcome 10: Documentation of advance directives

| Study or Subgroup | log[RR] | SE | Advanced Care Planning Total | Usual Care Total | Weight | Risk Ratio IV, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| Hanson 2017 (1) | 0.4461 | 0.2428 | 30 | 37 | 8.6% | 1.56 [0.97 , 2.51] |
| Mitchell 2018 (1) | 0.1803 | 0.0747 | 167 | 150 | 91.4% | 1.20 [1.03 , 1.39] |
| **Total (95% CI)** | | | **197** | **187** | **100.0%** | **1.23 [1.07 , 1.41]** |

Heterogeneity: Chi² = 1.09, df = 1 (P = 0.30); I² = 9%
Test for overall effect: Z = 2.85 (P = 0.004)
Test for subgroup differences: Not applicable

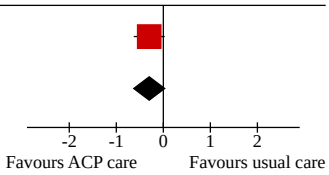



**Footnotes**
(1) Used data on do not tube-feed

## Analysis 2.11. Comparison 2: Advance care planning versus usual care, Outcome 11: Decisional conflict

| Study or Subgroup | MD | SE | Advanced Care Planning Total | Usual Care Total | Weight | Mean Difference IV, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| Hanson 2011 | -0.3 | 0.1678 | 40 | 39 | 100.0% | -0.30 [-0.63 , 0.03] |
| **Total (95% CI)** | | | **40** | **39** | **100.0%** | **-0.30 [-0.63 , 0.03]** |

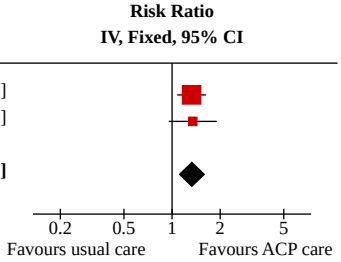
Heterogeneity: Not applicable
Test for overall effect: Z = 1.79 (P = 0.07)
Test for subgroup differences: Not applicable




## Analysis 2.12. Comparison 2: Advance care planning versus usual care, Outcome 12: Goals of care discussion

| Study or Subgroup | log[RR] | SE | Advanced Care Planning Total | Usual Care Total | Weight | Risk Ratio IV, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| Hanson 2017 (1) | 0.2812 | 0.1056 | 30 | 37 | 73.7% | 1.32 [1.08 , 1.63] |
| Mitchell 2018 | 0.2981 | 0.1766 | 167 | 150 | 26.3% | 1.35 [0.95 , 1.90] |
| **Total (95% CI)** | | | **197** | **187** | **100.0%** | **1.33 [1.11 , 1.59]** |

Heterogeneity: Chi² = 0.01, df = 1 (P = 0.93); I² = 0%
Test for overall effect: Z = 3.15 (P = 0.002)
Test for subgroup differences: Not applicable

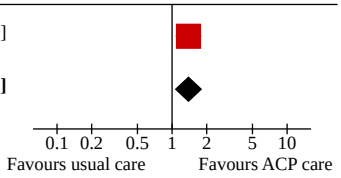



**Footnotes**
(1) Unpublished data obtained from study authors

## Analysis 2.13. Comparison 2: Advance care planning versus usual care, Outcome 13: Concordance with goals of care

| Study or Subgroup | log[RR] | SE | Advanced Care Planning Total | Usual Care Total | Weight | Risk Ratio IV, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| Hanson 2017 (1) | 0.3285 | 0.1298 | 27 | 36 | 100.0% | 1.39 [1.08 , 1.79] |
| **Total (95% CI)** | | | **27** | **36** | **100.0%** | **1.39 [1.08 , 1.79]** |

Heterogeneity: Not applicable
Test for overall effect: Z = 2.53 (P = 0.01)
Test for subgroup differences: Not applicable




**Footnotes**
(1) Unpublished data obtained from study authors

# APPENDICES

## Appendix 1. Sources searched and search strategies

| Source | Search strategy | Hits retrieved |
|---|---|---|
| 1. ALOIS (www.medicine.ox.ac.uk/alois)<br><br>[Date of most recent search: 07 October 2020] | palliative OR terminal OR hospice OR dying OR "end of life" | Jan 2015: 16<br>Feb 2016: 0<br>Feb 2018: 20<br>Oct 2019: 9<br>Oct 2020: 80<br>**TOTAL: 125** |
| 2. MEDLINE In-process and other non-indexed citations and MEDLINE 1950-present (Ovid SP)<br><br>[Date of most recent search: 07 October 2020] | 1. exp Dementia/<br>2. Delirium/<br>3. Wernicke Encephalopathy/<br>4. Delirium, Dementia, Amnestic, Cognitive Disorders/<br>5. dement*.mp.<br>6. alzheimer*.mp.<br>7. (lewy* adj2 bod*).mp.<br>8. deliri*.mp.<br>9. (chronic adj2 cerebrovascular).mp.<br>10. ("organic brain disease" or "organic brain syndrome").mp.<br>11. ("normal pressure hydrocephalus" and "shunt*").mp.<br>12. "benign senescent forgetfulness".mp.<br>13. (cerebr* adj2 deteriorat*).mp.<br>14. (cerebral* adj2 insufficient*).mp.<br>15. (pick* adj2 disease).mp.<br>16. (creutzfeldt or jcd or cjd).mp.<br>17. huntington*.mp.<br>18. binswanger*.mp.<br>19. korsako*.mp.<br>20. or/1-19<br>21. exp Palliative Care/<br>22. "Hospice and Palliative Care Nursing"/ | Jan 2015: 494<br>Feb 2016: 48<br>Feb 2019: 174<br>Suppl: 344<br>Oct 2019: 103<br>Oct 2020: 102<br>**TOTAL: 1265** |

(Continued)

23. Terminal Care/

24. "end of life".ti,ab.

25. palliative.ti,ab.

26. (dying adj3 (care or comfort or relief or strateg* or plan or intervention or pain)).ti,ab.

27. "symptom control".ti,ab.

28. (bereavement adj2 support).ti,ab.

29. or/21-28

30. 20 and 29

31. (control adj2 (group or groups or patient* or cohort*)).ti,ab.

32. (controlled adj study).ti,ab.

33. comparative study.ti,ab.

34. clinical trial/

35. multicenter study/

36. "before-and-after".ti,ab.

37. CBA.ti,ab.

38. Interrupted Time Series Analysis/

39. Interrupted time series.ti,ab.

40. ("non-random?sed trial*" or "non-random?sed stud*").ti,ab.

41. ("nonrandom?sed trial*" or "nonrandom?sed stud*").ti,ab.

42. Controlled Before-After Studies/

43. pragmatic clinical trial.pt.

44. (quasiexperiment* or quasi experiment* or pseudo experiment* or pseudo-experiment*).ti,ab.

45. ((pretest or pre test) and (posttest or post test)).ti,ab.

46. repeated measur*.ti,ab.

47. randomized controlled trial.pt.

48. controlled clinical trial.pt.

49. random$.ti,ab.

50. groups.ab.

51. drug therapy.fs.

52. placebo.ab.

53. rct.ti,ab.

54. or/31-53

55. 30 and 54

*(Continued)*

| | | |
|---|---|---|
| 3. Embase<br>(Ovid SP)<br>[Date of most recent search: 07 October 2020] | 1. exp *dementia/<br>2. dement*.ti,ab.<br>3. alzheimer*.ti,ab.<br>4. (lewy* adj2 bod*).ti,ab.<br>5. (frontotemporal* or FTD or FTLD).ti,ab.<br>6. or/1-5<br>7. exp palliative nursing/ or exp palliative therapy/<br>8. hospice care/ or hospice/ or hospice nursing/ or hospice patient/<br>9. terminal care/<br>10. death/ or dying/<br>11. palliative.ti,ab.<br>12. hospice*.ti,ab.<br>13. terminal.ti,ab.<br>14. "end of life".ti,ab.<br>15. (dying adj3 (care or comfort or relief or strateg* or plan or intervention or pain)).ti,ab.<br>16. ("symptom control" and (dying or death)).ti,ab.<br>17. (bereavement adj2 support).ti,ab.<br>18. or/7-17<br>19. 6 and 18<br>20. (control adj2 (group or groups or patient* or cohort*)).ti,ab.<br>21. (controlled adj study).ti,ab.<br>22. comparative study.ti,ab.<br>23. clinical trial/<br>24. multicenter study/<br>25. "before-and-after".ti,ab.<br>26. CBA.ti,ab.<br>27. Interrupted Time Series Analysis/<br>28. Interrupted time series.ti,ab.<br>29. ("non-random?sed trial*" or "non-random?sed stud*").ti,ab.<br>30. ("nonrandom?sed trial*" or "nonrandom?sed stud*").ti,ab.<br>31. Controlled Before-After Studies/<br>32. (quasiexperiment* or quasi experiment* or pseudo experiment* or pseudo-experiment*).ti,ab.<br>33. ((pretest or pre test) and (posttest or post test)).ti,ab. | Jan 2015: 276<br>Feb 2016: 37<br>Feb 2019: 176<br>Suppl: 802<br>Oct 2019: 84<br>Oct 2020: 99<br>**TOTAL: 1474** |

(Continued)

| | | |
|---|---|---|
| | 34. repeated measur*.ti,ab. | |
| | 35. randomized controlled trial/ | |
| | 36. controlled clinical trial/ | |
| | 37. (randomly adj3 (divide* or shared or allocat*)).ti,ab. | |
| | 38. placebo.ab. | |
| | 39. "double-blind*".ti,ab. | |
| | 40. "single blind*".ti,ab. | |
| | 41. RCT.ti,ab. | |
| | 42. (randomized or randomised).ti. | |
| | 43. or/20-42 | |
| | 44. 19 and 43 | |
| 4. PsycINFO | 1. dement*.ti,ab. | Jan 2015: 276 |
| (Ovid SP) | 2. alzheimer*.ti,ab. | Feb 2016: 15 |
| [Date of most recent search: 07 October 2020] | 3. exp Dementia/ | Feb 2019: 34 |
| | 4. (lewy* adj2 bod*).ti,ab. | Suppl: 62 |
| | 5. (frontotemporal* or FTD or FTLD).ti,ab. | Oct 2019: 23 |
| | 6. or/1-5 | Oct 2020: 26 |
| | 7. exp Hospice/ or exp "Death and Dying"/ or exp Palliative Care/ or exp Terminally Ill Patients/ | **TOTAL: 436** |
| | 8. hospice*.ti,ab. | |
| | 9. terminal*.ti,ab. | |
| | 10. "end of life".ti,ab. | |
| | 11. (dying adj3 (care or comfort or relief or strateg* or plan or intervention or pain)).ti,ab. | |
| | 12. ("symptom control" and (dying or death)).ti,ab. | |
| | 13. (bereavement adj2 support).ti,ab. | |
| | 14. palliative.ti,ab. | |
| | 15. or/7-14 | |
| | 16. 6 and 15 | |
| | 17. (control adj2 (group or groups or patient* or cohort*)).ti,ab. | |
| | 18. (controlled adj study).ti,ab. | |
| | 19. comparative study.ti,ab. | |
| | 20. clinical trial/ | |
| | 21. "before-and-after".ti,ab. | |
| | 22. CBA.ti,ab. | |

(Continued)

| | | |
|---|---|---|
| | 23. Interrupted time series.ti,ab.<br>24. ("non-random?sed trial*" or "non-random?sed stud*").ti,ab.<br>25. ("nonrandom?sed trial*" or "nonrandom?sed stud*").ti,ab.<br>26. (quasiexperiment* or quasi experiment* or pseudo experiment* or pseudo-experiment*).ti,ab.<br>27. ((pretest or pre test) and (posttest or post test)).ti,ab.<br>28. repeated measur*.ti,ab.<br>29. exp Intervention/ or exp Clinical Trials/<br>30. placebo.ab.<br>31. randomly.ab.<br>32. (randomised or randomized or RCT or trial).ti,ab.<br>33. "double-blind*".ti,ab.<br>34. "single blind*".ti,ab.<br>35. or/17-34<br>36. 16 and 35 | |
| 5. CINAHL (EBSCOhost)<br>[Date of most recent search: 07 October 2020] | S1 (MH “Dementia”)<br>S2 TX dement*<br>S3 TX alzheimer*<br>S4 TX “lew* bod*”<br>S5 TX FTLD OR FTD OR frontotemporal<br>S6 S1 OR S2 OR S3 OR S4 OR S5<br>S7 (MH "Palliative Care") OR (MH "Hospice and Palliative Nursing") OR (MH "Terminal Care") OR (MH "Hospice Care”)<br>S8 TX "end of life”<br>S9 TX palliative OR terminal* OR hospice* OR bereavement<br>S10 S7 OR S8 OR S9<br>S11 S6 AND S10<br>S12 (MH "Controlled Before-After Studies")<br>S13 TX "before and after stud*"<br>S14 (MH "Pretest-Posttest Design") OR (MH "Pretest-Posttest Control Group Design")<br>S15 TX (pretest and posttest)<br>S16 TX (pre-test and post-test)<br>S17 TX interrupted time series<br>S18 (MH "Interrupted Time Series Analysis") | Jan 2015: 75<br>Feb 2016: 16<br>Feb 2019: 48<br>Suppl: 62<br>Oct 2019: 16<br>Oct 2020:<br>**TOTAL: 238** |

*(Continued)*

| | | |
|---|---|---|
| | S19 TX CBA<br>S20 TX repeated measures<br>S21 (MH "Equivalence Trials")<br>S22 (MH "Equivalence Trials")<br>S23 TX "non-randomised"<br>S24 TX "non-randomized"<br>S25 TX "nonrandomized"<br>S26 TX "nonrandomised"<br>S27 TX nRCT<br>S28 TX pseudo-experiment*<br>S29 TX quasi-experiment*<br>S30 TX quasiexperiment*<br>S31 TX pseudoexperiment*<br>S32 (MH "Randomized Controlled Trials")<br>S33 TX randomised<br>S34 TX randomized<br>S35 AB placebo<br>S36 AB randomly<br>S37 AB "double blind*"<br>S38 AB "single blind*"<br>S39 AB RCT<br>S40 S12 OR S13 OR 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 OR S36 OR S37 OR S38 OR S39<br>S33 S40 AND S11 | |
| 6. ISI Web of Science – all databases [includes: Web of Science (1945-present); BIOSIS Previews (1926-present); MEDLINE (1950-present); Journal Citation Reports]<br>[Date of most recent search: 07 October 2020] | TOPIC: (dement* OR alzheimer* OR "lew* bod*" OR frontotemporal OR FTD OR FTLD OR "severe* cognit* impair*") AND TOPIC: (palliative* OR terminal* OR hospice* OR dying OR "end of life" OR bereavement) AND TOPIC: "non-randomised" OR "nonrandomised" OR "non-randomized" OR nonrandomized OR nRCT OR CBA OR "controlled before-after" OR "before and after stud*" OR "interrupted time series" OR "repeated measures" OR "quasi-experiment*" OR quasiexperiment* OR "pseudo-experiment*" OR pseudoexperiment* OR "comparative trial" OR "comparative study" OR randomised OR randomized OR randomly OR RCT<br>Timespan: All years.<br>Search language=Auto | Jan 2015: 463<br>Feb 2016: 37<br>Feb 2019: 180<br>Suppl: 71<br>Oct 2019: 63<br>Oct 2020:<br>**TOTAL: 904** |
| 7. LILACS (BIREME) | demência OR dementia OR demencia OR alzheimer$ [Words] and paliativos OR palliative OR hospice OR terminal OR terminalidade OR morrer OR dying OR morte [Words] | Jan 2015: 1<br>Feb 2016: 1 |

(Continued)

| | | |
|---|---|---|
| [Date of most recent search: 07 October 2020] | | Feb 2019: 0<br>Suppl: 100<br>Oct 2019: 0<br>Oct 2020: 0<br>**TOTAL: 102** |
| 8. CENTRAL (The Cochrane Library, Wiley)<br>[Date of most recent search: 07 October 2020] | #1 dement*<br>#2 alzheimer*<br>#3 MeSH descriptor: [Dementia] explode all trees<br>#4 "lew* bod*" or DLB or LBD<br>#5 frontotemporal* or FTD or FTLD<br>#6 #1 or #2 or #3 or #4 or #5<br>#7 palliative<br>#8 terminal*<br>#9 hospice*<br>#10 "end of life"<br>#11 dying<br>#12 bereavement<br>#13 MeSH descriptor: [Palliative Care] explode all trees<br>#14 MeSH descriptor: [Hospice and Palliative Care Nursing] explode all trees<br>#15 MeSH descriptor: [Terminal Care] explode all trees<br>#16 MeSH descriptor: [Palliative Medicine] explode all trees<br>#17 #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16<br>#18 #17 and #6 | Jan 2015: 131<br>Feb 2016: 25<br>Feb 2019: 166<br>Oct 2019: 61<br>Oct 2020:<br>**TOTAL: 457** |
| 9. Clinicaltrials.gov (www.clinicaltrials.gov)<br>[Date of most recent search: 07 October 2020] | [condition] dementia OR alzheimer OR alzheimers AND [search terms] palliative OR terminal OR hospice OR dying OR "end of life"<br>Study type: interventional<br>Dates: ALL | Jan 2015: 66<br>Feb 2016: 8<br>Feb 2019: 84<br>Oct 2019: 2<br>Oct 2020: 29<br>**TOTAL: 189** |
| 10. ICTRP Search Portal (http://apps.who.int/trialsearch) [includes: Australian New Zealand Clinical Trials Registry; ClinicalTrilas.gov; ISRCTN; Chinese Clinical Trial Registry; Clini- | [condition] dementia OR alzheimer OR alzheimers AND [intervention] palliative OR terminal OR hospice OR dying OR "end of life"<br>Recruitment status: ALL<br>Dates: ALL | Jan 2015: 6<br>Feb 2016: 0<br>Feb 2019: 21<br>Oct 2019: 3<br>Oct 2020: 0 |

| | |
|---|---|
| *(Continued)*<br>cal Trials Registry – India; Clinical Research Information Service – Republic of Korea; German Clinical Trials Register; Iranian Registry of Clinical Trials; Japan Primary Registries Network; Pan African Clinical Trial Registry; Sri Lanka Clinical Trials Registry; The Netherlands National Trial Register]<br><br>[Date of most recent search: 07 October 2020] | **TOTAL: 30** |
| TOTAL before de-duplication | **5211** |
| TOTAL after de-duplication and first assessment (if done) by CDCIG information specialist | **2210** |

## WHAT'S NEW

| Date | Event | Description |
|---|---|---|
| 7 October 2020 | New search has been performed | The most recent search for this review was performed on 7 October 2020. New studies added, conclusions unchanged. |
| 7 October 2020 | New citation required but conclusions have not changed | New studies added and content extensively revised. Conclusions unchanged. |

## HISTORY

Protocol first published: Issue 2, 2015
Review first published: Issue 12, 2016

| Date | Event | Description |
|---|---|---|
| 28 October 2019 | New search has been performed | A search for this review was performed on 28 October 2019 |

## CONTRIBUTIONS OF AUTHORS

SW screened and selected studies, inspected the abstracts and full texts, transferred data to Review Manager 5, conducted statistical analysis and wrote the review.

EM screened and selected studies, inspected the abstracts and full texts, extracted data, checked accuracy of data entry in RevMan, assessed risk of bias and commented on all sections of the review.

EoS contributed to decisions on inclusion where consultation was required, and contributed to the drafting of the review.

DD provided a methodological perspective, advice on writing the review, and commented on all sections of the final review.

ES contributed to decisions on inclusion where consultation was required, and commented on all sections of the final review.

SC extracted data, assessed risk of bias and commented on all sections of the final review.

PC extracted data and assessed risk of bias.

All authors contributed to the outcome prioritisation process.

## DECLARATIONS OF INTEREST

We have no known conflicts of interest to declare.

## SOURCES OF SUPPORT

### Internal sources

- No sources of support provided

### External sources

- The Health Research Board, Ireland

  Cochrane Review Training Fellowship (recipient: Edel Murphy)
- NIHR, UK

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## DIFFERENCES BETWEEN PROTOCOL AND REVIEW

The interventions in the seven new included studies have allowed us to reflect on the nature of the palliative interventions tested in our review population. The types of interventions outlined in the original protocol still apply but we have concluded that it is best to report on the interventions under two categories, namely:

**Organisation and delivery of care,** encompassing the assessment and management of physical, psychological and spiritual symptoms of the person, management of transitions from one care setting to another, and education and training on living and dying, for family members, clinicians and professional care staff.

**Advance care planning** interventions for family or surrogate carers.

As a result, our comparisons are now:

- Organisation and delivery of care interventions versus usual care
- Advance care planning interventions versus usual care
- Organisation and delivery palliative care interventions versus advance care planning interventions.

In the original review, we reported on 31 outcomes reported across the two included studies, with no outcome common to both studies. With the addition of seven new included studies, the number of outcomes reported across all studies exceeds 75. We believe that reporting on all outcomes in the updated review will not synthesise information in a useful way for palliative patients, their family or professional carer staff or clinicians. Thus, drawing on the EAPC definition of palliative care (Van der Steen 2014), and on the 'How the intervention might work' section of the original review, we agreed to group outcomes into four categories, and within these categories, to focus on these specific outcomes, based on a rationale drawn from those two sources, as follows:

### Primary outcomes

*Patient- and family-centred outcomes*

- patient comfort in dying
- symptom management

### Secondary outcomes

*Patient- and family-centred outcomes*

- quality of life
- pain
- palliative care plan in place/palliative domains in care plan

*Prescribing patterns*

- review of prescribing of antipsychotic medications
- review of prescribing of analgesics

*Non-palliative interventions*

- use of non-palliative interventions; for example, use of enteral (tube) feeding; use of parenteral therapy (use of injections or IV fluids); use of antibiotics; hospital admission with a non-palliative intent

*Advance care planning (ACP)*

- discussion with patient and/or family on ACP directives occurred
- documentation of advance directives; for example, do not tube feed; do not resuscitate (DNR); do not use parenteral therapy; do not hospitalise (DNH); do not use antibiotics
- decisional conflict in carers
- goals of care discussion occurred
- care consistent with goals (concordance)

## INDEX TERMS

### Medical Subject Headings (MeSH)

Caregivers; Decision Making; Dementia [*nursing]; Family; Outcome Assessment, Health Care; Palliative Care [*methods]; Randomized Controlled Trials as Topic

### MeSH check words

Aged; Humans