National Institute for Health and Care Excellence

Final

End of life care for adults: service delivery

[B] Evidence review: Timing of referral to palliative care services

NICE guideline NG142

Evidence review

October 2019

Final

Developed by the National Guideline Centre, hosted by the Royal College of Physicians

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1.1 Review question: What is the best timing of referral to (or provision of) palliative care services in people thought to be entering their last year of life?

1.2 Introduction

Potential benefits from earlier referral to palliative care have been described, at least for people with metastatic cancer, and include better symptom management and longer survival. However, the specification of supportive and palliative care services varies widely, and the elements of care provided to intervention and control groups in studies are not described. The definition of early or late referral also varies. Some people are referred whilst still receiving disease-modifying treatment, others when a decision has been taken to discontinue such treatment. The time period for people to be referred may be between the last 6 months to a year of life, to only a few weeks.

For diseases or conditions with trajectories that are hard to predict, for example heart failure and COPD, or conditions where recovery from treatment is unlikely but still possible, it is difficult to define the criteria for early or late referral and to compare the effect of one timing against the other. Some conditions, such as some neurological diseases including dementia, may deprive a person of the ability to express their wishes regarding palliative care and, for them, it may be prudent to initiate discussions earlier after diagnosis.

1.3 PICO table

For full details see the review protocol in Appendix A.

Table 1: PICO characteristics of review question

Population	Adults (aged over 18 or over) with progressive life-limiting conditions thought to be entering the last year of life.
Intervention	• Early referral to (or provision of) palliative care services • Late referral to (or provision of) palliative care services
Comparison	'Early' and 'late' as defined by studies
Outcomes	CRITICAL • Quality of life (Continuous) • Preferred and actual place of death (Dichotomous) • Preferred and actual place of care (Dichotomous) IMPORTANT • Length of survival (Continuous) • Length of stay (Continuous) • Hospitalisation (Dichotomous) • Number of hospital visits (Dichotomous) • Number of visits to accident and emergency (Dichotomous) • Number of unscheduled admissions (Dichotomous) • Use of community services (Dichotomous) • Avoidable/inappropriate admissions to ICU (Dichotomous) • Inappropriate attempts at cardiopulmonary resuscitation (Dichotomous)

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	• Staff satisfaction (Continuous) • Patient/carer reported outcomes (satisfaction) (Continuous)
Study design	• Systematic reviews • RCTs • Non-randomised comparative studies, including before and after studies and interrupted-time-series.

1.4 Clinical evidence

1.4.1 Included studies

A search was conducted for randomised trials and non-randomised comparative studies on the effect of timing of referral to (or provision of) palliative care services in people thought to be entering their last year of life.

Five studies were included in the review;[3,7,35,64,68] these are summarised below.

Evidence from these studies is summarised in the clinical evidence summary below (Table 4). See also the study selection flow chart in Appendix B, study evidence tables in Appendix D, forest plots in Appendix E, GRADE tables in Appendix F and excluded studies list in Appendix G.

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1.4.2 Summary of clinical studies included in the evidence review

Table 2: Summary of studies included in the evidence review

Study	Intervention and comparison	Population	Outcomes	Comment
Amano 2015[3]	The palliative care team provided consultation services in both outpatients and inpatients suffering from cancer on the basis of referral from primary responsible physicians. The palliative care team consisted of two palliative physicians and 3 certified palliative care nurses. All patients were followed at least once per week, and the palliative care physician prescribed or gave written recommendations of medication. All patients were monitored continuously until death or transfer to another institution. Early (>3 months before death); Delayed (<3 months before death)	Adults and patients who died from cancer or cause related to cancer during the study. Follow up: 1 year N=265 Japan	Number of unscheduled admissions (inpatient hospice utilisation); Preferred and actual place of death (Hospital death); Number of visits to accident and emergency (People with ≥2 emergency department visits); Number of unscheduled admissions (People with ≥2 hospital admissions); Hospitalisation (People with >14 days of hospitalisation); Avoidable/inappropriate admissions to ICU (People with ICU admission)	
Bakitas 2015[7]	ENABLE - includes initial in-person, standardised outpatient palliative care (PC) consultation by a board-certified PC clinician and six structured weekly telephone coaching sessions by an advanced practice nurse using manualised curriculum (Charting Your Course). Session one to three focus on problem solving, symptom management, self-care, identification and coordination of local resources, communication, decision making, and advance care planning. Session four to six focused on outlook, a life review	Adults with advanced stage solid tumour or hematologic malignancy, oncologist-determined prognosis of 6-24 months, and able to complete baseline questionnaire. Aged >18 years Follow up: 1 year N=207 USA	Quality of life (FACIT-PAL) (Functional Assessment of Chronic Illness Therapy - Palliative Care); Length of survival; Preferred and actual place of death (Deaths at home)	Hospital use reported as decedents' rate. Insufficient information to extract.

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Study	Intervention and comparison	Population	Outcomes	Comment
	approach that encourages participants to frame advance illness challenges as personal growth opportunities. After the six sessions, monthly follow up calls reinforced prior content and identified new challenges or care coordination issues. Sessions generally lasted 30-45 minutes. Nurse coach training included self-study, review of treatment manuals and scripts, and role play with feedback. Received within 30 days of being informed of an advance cancer diagnosis, or after 3 months. Early (within 30 days of diagnosis); Delayed (> 3 months of diagnosis)			
Hui 2014[35]	Referral to palliative care. The Supportive Care Centre operated 5 days per week and saw approximately 25 patients per day. It was staffed by 2 palliative care specialists who were supported by an interdisciplinary team of nurses and a social worker. Patients referred to the palliative care mobile team in the inpatient setting were managed similarly by the same team of palliative care specialists following common clinical pathways. 3-month cut-off Early referral (> 3 months between first palliative care consultation and death); Late referral (< 3 months between first palliative care consultation and death)	All adult patients in the Houston area who died of advanced cancer between 9/1/2009 and 2/28/2010, who had received a palliative care referral, and had contact with the cancer centre within the last 3 months of life. Follow up: 1 year N=732 USA	Number of unscheduled admissions (People with any number of hospital admission); Number of visits to accident and emergency (People with ≥2 emergency room visits); Number of unscheduled admissions (People with any hospital admissions); Number of hospital visits (People with ≥2 hospital admissions); Hospitalisation (People with >14 days of hospitalisation); Preferred and actual place of death (Hospital death); Preferred and actual place of death (ICU death); Avoidable/inappropriate admissions to ICU (People with ICU admission)	

Study	Intervention and comparison	Population	Outcomes	Comment
	6-month cut-off Early referral (> 6 months between first palliative care consultation and death); Late referral (< 6 months between first palliative care consultation and death)			
Nieder 2016[64]	Early referral to (or provision of) palliative care services. Palliative care team involved 3 months before death or earlier. Late referral to (or provision of) palliative care services. Palliative Care Team involved only during the last phase of the incurable disease, < 3 months	All patients who died from non-small cell lung cancer NSCLC in the uptake area of the Nordland Hospital Trust. N=286 Norway.	Hospitalisation (hospitalised in last 3 months); Preferred and actual place of death (hospital death); Length of survival (median survival)	
Poulose 2013[68]	Early referral to (or provision of) palliative care services. Palliative care referral ≥30 days before death. Late referral to (or provision of) palliative care services. Palliative care referral <30 days before death.	Decedents who were referred to and seen by the palliative care specialists. N=842 Singapore	Preferred and actual place of death (death at home) Preferred and actual place of death (inpatient hospice death)	Number of patients referred early or late not provided. Male/female data was reported separately. Death in hospital was not reported

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1.4.3 Quality assessment of clinical studies included in the evidence review

Table 3: Early versus Late Referral: data unsuitable for meta-analysis

Study	Outcome	Intervention results	Intervention group (n)	Comparison results	Comparison group (n)	Risk of bias
Bakitas 2015	Median survival (months)	18.3	50	11.8	59	High
Nieder 2016	Median survival (months)	14	22	6.7	77	Very high

Table 4: Clinical evidence summary: Early (> 3 months between first palliative care consultation and death) versus late (< 3 months between first palliative care consultation and death) referral to palliative care services

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with <3 months	Risk difference with >3 months (95% CI)
Number of unscheduled admissions (Inpatient hospice utilisation)	265 (1 study) 1 years	⨁⨁⊖⊖ LOW[a]	RR 1.58 (1.28 to 1.95)	469 per 1000	272 more per 1000 (from 131 more to 446 more)
Preferred and actual place of death (Hospital death)	730 (3 studies) 1 years	⨁⊖⊖⊖ VERY LOW[a,b,c] due to indirectness, imprecision	RR 0.81 (0.71 to 0.93)	609 per 1000	116 fewer per 1000 (from 43 fewer to 176 fewer)
Number of visits to accident and emergency (People with ≥2 emergency room visits)	631 (2 studies) 1 years	⨁⊖⊖⊖ VERY LOW[a,c] due to imprecision	RR 0.62 (0.62 to 1)	147 per 1000	56 fewer per 1000 (from 56 fewer to 0 more)
Number of unscheduled admissions (People with ≥2 hospital admissions)	631 (2 studies) 1 years	⨁⊖⊖⊖ VERY LOW[a,b,c] due to indirectness, imprecision	RR 0.46 (0.27 to 0.8)	155 per 1000	84 fewer per 1000 (from 31 fewer to 113 fewer)
Hospitalisation (People with >14 days of hospitalisation)					

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Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with <3 months	Risk difference with >3 months (95% CI)
	631 (2 studies) 1 years	⨁⊖⊖⊖ VERY LOW[a,c] due to imprecision	RR 0.77 (0.60 to 0.99)	398 per 1000	92 fewer per 1000 (from 4 fewer to 159 fewer)
Avoidable/inappropriate admissions to ICU (People with any ICU admission)	631 (2 studies) 1 years	⨁⊖⊖⊖ VERY LOW[a,b,c] due to indirectness, imprecision	RR 0.53 (0.27 to 1.02)	107 per 1000	50 fewer per 1000 (from 78 fewer to 2 more)
Number of visits to accident and emergency (People with any number of emergency room visits)	366 (1 study) 1 years	⨁⨁⊖⊖ LOW[a]	RR 0.57 (0.45 to 0.73)	683 per 1000	294 fewer per 1000 (from 184 fewer to 376 fewer)
Number of unscheduled admissions (People with any hospital admission)	366 (1 study) 1 years	⨁⊖⊖⊖ VERY LOW[a,b] due to indirectness	RR 0.59 (0.49 to 0.72)	813 per 1000	333 fewer per 1000 (from 228 fewer to 415 fewer)
Preferred and actual place of death (ICU death)	366 (1 study) 1 years	⨁⊖⊖⊖ VERY LOW[a,b,c] due to indirectness, imprecision	RR 0.62 (0.17 to 2.19)	41 per 1000	15 fewer per 1000 (from 34 fewer to 48 more)
Hospitalised in last 3 months of life	99 (1 study)	⨁⊖⊖⊖ VERY LOW[a,c] due to risk of bias, imprecision	RR 0.75 (0.58 to 0.97)	974 per 1000	244 fewer per 1000 (from 29 fewer to 409 fewer)

[a] Downgraded by 2 increments if the majority of the evidence was from studies with observational/non-randomised study design
[b] Downgraded by 1 increment because the majority of the evidence had indirect outcomes
[c] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

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Table 5: Clinical evidence summary: Early (< 30 days between diagnosis and referral) versus late (> 3 months between diagnosis and referral) referral to palliative care services

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Late	Risk difference with Early (95% CI)
Quality of life (FACIT-PAL) Scale from: 0 to 184.	155 (1 study) 3 months	⊕⊕⊖⊖ LOW[a,b] due to risk of bias, imprecision	-	The mean quality of life (FACIT-PAL) in the control groups was 127.2	The mean quality of life (facet-pal) in the intervention groups was 2.7 higher (1.76 lower to 7.16 higher)
Quality of life (FACIT-PAL) Scale from: 0 to 184.	155 (1 study) 6 months	⊕⊕⊖⊖ LOW[a,b] due to risk of bias, imprecision	-	The mean quality of life (FACIT-PAL) in the control groups was 127.2	The mean quality of life (facet-pal) in the intervention groups was 2.7 higher (1.76 lower to 7.16 higher)
Quality of life (FACIT-PAL) Scale from: 0 to 184.	155 (1 study) 12 months	⊕⊕⊖⊖ LOW[a,b] due to risk of bias, imprecision	-	The mean quality of life (FACIT-PAL) in the control groups was 129.1	The mean quality of life (facet-pal) in the intervention groups was 0.8 higher (3.86 lower to 5.46 higher)
Preferred and actual place of death (participants who died at home)	110 (1 study) until death	⊕⊕⊖⊖ LOW[b,c] due to indirectness, imprecision	RR 1.16 (0.80 to 1.68)		
				467 per 1000	75 more per 1000 (from 93 fewer to 317 more)

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[b] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
[c] Downgraded by 1 increment because the majority of the evidence had indirect outcomes

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Table 6: Clinical evidence summary: Early (> 6 months between first palliative care consultation and death) versus late (< 6months between first palliative care consultation and death) referral to palliative care services

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Late	Risk difference with Early (95% CI)
Number of visits to accident and emergency (People with any number of emergency room visits) (>6 months versus <6 months)	366 (1 study) 1 years	⊕⊖⊖⊖ VERY LOW[a,b] due to imprecision	RR 0.66 (0.49 to 0.88)	628 per 1000	213 fewer per 1000 (from 75 fewer to 320 fewer)
Number of visits to accident and emergency (People with ≥2 emergency room visits) (>6 months versus <6 months)	366 (1 study) 1 years	⊕⊖⊖⊖ VERY LOW[a,b] due to imprecision	RR 0.42 (0.19 to 0.92)	211 per 1000	123 fewer per 1000 (from 17 fewer to 171 fewer)
Number of unscheduled admissions (People with any hospital admission) (>6 months versus <6 months)	366 (1 study) 1 years	⊕⊖⊖⊖ VERY LOW[a,b,c] due to indirectness, imprecision	RR 0.69 (0.54 to 0.87)	748 per 1000	232 fewer per 1000 (from 97 fewer to 344 fewer)
Number of unscheduled admissions (People with ≥2 hospital admissions) (>6 months versus <6 months)	366 (1 study) 1 years	⊕⊖⊖⊖ VERY LOW[a,b,c] due to indirectness, imprecision	RR 0.72 (0.37 to 1.38)	185 per 1000	52 fewer per 1000 (from 116 fewer to 70 more)
Hospitalisation (People with >14 days of hospitalisation) (>6 months versus <6 months)	366 (1 study) 1 years	⊕⊖⊖⊖ VERY LOW[a,b] due to imprecision	RR 0.65 (0.31 to 1.38)	158 per 1000	55 fewer per 1000 (from 109 fewer to 60 more)
Preferred and actual place of death (Hospital death) (>6 months versus <6 months)	366 (1 study) 1 years	⊕⊖⊖⊖ VERY LOW[a,b,c]	RR 0.62 (0.36 to 1.07)	285 per 1000	108 fewer per 1000

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Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Late	Risk difference with Early (95% CI)
		due to indirectness, imprecision			(from 183 fewer to 20 more)
Preferred and actual place of death (ICU death) (>6 months versus <6 months)	366 (1 study) 1 years	⊕⊖⊖⊖ VERY LOW[a,b,c] due to indirectness, imprecision	RR 0.8 (0.18 to 3.51)	37 per 1000	7 fewer per 1000 (from 30 fewer to 93 more)
Avoidable/inappropriate admissions to ICU (People with any ICU admission) (>6 months versus <6 months)	366 (1 study) 1 years	⊕⊖⊖⊖ VERY LOW[a,b,c] due to indirectness, imprecision	RR 0.73 (0.29 to 1.81)	101 per 1000	27 fewer per 1000 (from 71 fewer to 82 more)

[a] Downgraded by 2 increments if the majority of the evidence was from studies with observational/non-randomised study design.
[b] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
[c] Downgraded by 1 increment because the majority of the evidence had indirect outcomes

Table 7: Clinical evidence summary: Early (palliative care provided >30 days before death) versus late (palliative care provided <30 days before death)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
Place of death (males who died at home) (>30 days versus <30 days)	842 (1 study)	⊕⊖⊖⊖ VERY LOW[a,b] due to indirectness	OR 2.21 (1.34 to 3.65)
Place of death (females who died at home) (>30 days versus <30 days)	842 (1 study)	⊕⊖⊖⊖ VERY LOW[a,b] due to indirectness	OR 3.33 (2.07 to 5.36)

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Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)
Place of death (males who died at inpatient hospice) (>30 days versus <30 days)	842 (1 study)	⊕⊖⊖⊖ VERY LOW[a,b,c] due to indirectness, imprecision	OR 2.02 (1.13 to 3.61)
Place of death (females who died at inpatient hospice) (>30 days versus <30 days)	842 (1 study)	⊕⊖⊖⊖ VERY LOW[a,b] due to indirectness	OR 2.69 (1.55 to 4.67)

[a] Downgraded by 2 increments if the majority of the evidence was from studies with observational/non-randomised study design
[b] Downgraded by 1 increment because the majority of the evidence had indirect outcomes
[c] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

See Appendix F for full GRADE tables.

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1.5 Economic evidence

1.5.1 Included studies

No relevant health economic studies were identified.

1.5.2 Excluded studies

No health economic studies that were relevant to this question were excluded due to assessment of limited applicability or methodological limitations.

See also the health economic study selection flow chart in Appendix C.

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1.5.3 Unit costs

Table 8 and Table 9 provide some unit costs for specialist and generalist palliative that were presented to the guideline committee to help them consider the cost effectiveness of early versus later referral to palliative care services. Table 8 provides national average unit costs of specialist palliative care services in hospital and in the community where unit costs were available. Table 9 provides the unit costs of staff time for people who might provide general palliative care in a hospital and in a community setting. The cost of patient contact as opposed to per working hour has been reported where available. Once a person has been referred to receive palliative care services, the frequency of the services they receive will be very specific to the individual and their circumstances; therefore it was not possible to determine the cost of generalist or specialist palliative care over a specified time interval, for example one week or one month.

Table 8: Unit costs for NHS Specialist Palliative Care Services

Service description	Code	Currency Description	National Average Unit Cost
Specialist Palliative Care Services in Hospital			
Day case and Regular Day/Night	SD02A	Inpatient Specialist Palliative Care, Same Day, 19 years and over	£108
Inpatient	SD01A	Inpatient Specialist Palliative Care, 19 years and over	£396
Inpatient	SD03A	Hospital Specialist Palliative Care Support, 19 years and over	£100
Outpatient	SD04A	Medical Specialist Palliative Care Attendance, 19 years and over	£136
Outpatient	SD05A	Non-Medical Specialist Palliative Care Attendance, 19 years and over	£94
Specialist Palliative Care Services in the Community			
Nursing	N21AF	Specialist Nursing, Palliative/Respite Care, Adult, Face to face	£92
Nursing	N21AN	Specialist Nursing, Palliative/Respite Care, Adult, Non face to face	£39

Source: NHS reference costs (2015-16) [20]

Table 9: Unit costs for Generalist Palliative Care Services

Staff Member	Unit Cost of Staff Time[(a)]
Generalist Palliative Care Services in Hospital	
Hospital-based scientific and professional staff	£24-£77 per working hour (Band 2 – Band 8b)
Hospital-based nurses	£86-£130 per hour of patient contact (Band 5 – 7)
Hospital-based doctors	£29-£106 (FY1 – Consultant)
Generalist Palliative Care Services in the Community	
General practitioner	£199 per hour of patient contact
Community-based scientific and professional Staff	£23-£74 per working hour (Band 2 – Band 8b)

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Staff Member	Unit Cost of Staff Time[(a)]
Community nurse	£22-£73 per working hour (Band 2 – Band 8b)
Nurse (GP practice)	£36 per working hour
Social Worker (adult services)	£55 per hour of client-related work
Home care worker	£24 per hour of face-to-face contact (weekday) £27 per hour of face-to-face contact (day-time weekend) £25 per hour of face-to-face contact (nigh-time weekday) £27 per hour of face-to-face contact (night-time weekend)
Family support worker	£52 per hour of client related work

Source: Curtis (2016)[19]

(a) Staff costs without qualifications have been reported.

1.6 Resource costs

Recommendations made based on this review (see section **Error! Reference source not found.**) are not expected to have a substantial impact on resources.

1.7 Evidence statements

1.7.1 Clinical evidence statements

Early (> 3 months between first palliative care consultation and death) versus late (< 3 months between first palliative care consultation and death) referral to palliative care services

Three studies compared referral to palliative care services at > 3 months versus < 3 months between first palliative care consultation and death. One study found no evidence of clinical difference in number of unscheduled admissions (inpatient hospice utilisation), preferred and actual place of death (hospital death) and hospitalisation (people with >14 days of hospitalisation) (n=265; very low quality).There was evidence of clinically important benefit of early referral, with fewer people having 2 or more hospital admissions and people with any number of ICU admissions (n=265, very low quality). However there was also evidence of clinically important benefit of late referral in terms of number of people with 2 or more emergency room visits (n=265; very low quality).

A second study reported a clinically important benefit of early referral was observed for the outcomes of number of visits to accident and emergency, unscheduled admissions to hospital, hospitalisation (people with >14 days of hospitalisation), preferred and actual place of death (hospital death and ICU death) and avoidable/inappropriate admissions to ICU (n=366; very low quality).

Another study found a clinically important benefit of early referral was observed for the outcomes of hospitalised in last 3 months of life, death in hospital and median survival (n=99; very low quality).

Early (< 30 days between diagnosis and referral) versus late (> 3 months between diagnosis and referral) referral to palliative care services

One study compared referral to palliative care services at < 30 days versus > 3 months between diagnosis and referral. There was no evidence of clinically important difference between groups for quality of life (measured with FACIT-PAL scale) at any time point (n=155;

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low quality). There was also no clinically important difference in terms of people dying at home between the two groups (n=110; low quality).

Early (> 6 months between first palliative care consultation and death) versus late (< 6 months between first palliative care consultation and death) referral to palliative care services

One study compared referral to palliative care services at >6 months versus <6 months between first palliative care consultation and death. Clinically important benefit of early referral was observed for the outcomes of number of visits to accident and emergency, unscheduled admissions to hospital, hospitalisation (people with >14 days of hospitalisation), preferred and actual place of death (hospital death) and avoidable/inappropriate admissions to ICU (n=366; very low quality). There was no clinically important difference between groups for the outcome of preferred and actual place of death (ICU death) (n=366; very low quality).

Early (>30 days between first palliative care consultation and death) versus late (<30 days between first palliative care consultation and death) referral to palliative care services

One study compared referral to palliative care services at > 30 days versus < 30 days between first palliative care consultation and death. Clinically important benefit of early referral was observed for the outcomes of death occurring at home or inpatient hospice with early referral (n=842; very low quality).

1.7.2 Health economic evidence statements

No relevant economic evaluations were identified.

1.8 The committee's discussion of the evidence

1.8.1 Interpreting the evidence

1.8.1.1 The outcomes that matter most

The Committee identified quality of life, and preferred and actual place of care and death, as the critical outcomes to measure the impact of early or late referral to the provision of palliative care services. These critical outcomes were identified as outcomes that would reflect a direct benefit to the patient as they are about maintaining or improving their quality of life and upholding their choices in the last year of life. The following outcomes were identified as important for decision making and focus on the impact and use of health resources as well as the impact on the patient; length of hospital stay, length of survival, hospitalisation, number of hospital visits, number of visits to accident and emergency, number of unscheduled admissions, use of community services, avoidable/inappropriate admissions to ICU, inappropriate attempts at cardiopulmonary resuscitation and staff, patient and carer satisfaction.

See tables 7 and 8 in the Methods chapter for a detailed explanation of why the committee selected these outcomes.

Five studies reported actual place of death, which was used as an indirect outcome for actual place of death compared to preferred place of death. None of the studies reported actual and preferred place of care.

For the important outcomes, one study reported the number of hospital visits. Two studies reported the outcome length of survival. Two studies reported the number of visits to

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accident and emergency. Three studies reported the outcome of hospitalisation but none reported whether these were unscheduled or avoidable. Two studies reported number of admissions to hospital and admission to ICU, although there were no details on these being unscheduled, inappropriate or avoidable. No studies reported the use of community services, length of stay, satisfaction of patient or family, inappropriate resuscitation or staff satisfaction.

1.8.1.2 The quality of the evidence

The quality of the evidence ranged from very low to low. This was due to study design, selection and performance bias, resulting in a high risk of bias rating, as well as the imprecise nature of the results extracted and analysed in this review. Indirectness in some outcomes (for example: actual and final place of death; hospitalisation) further contributed to the final GRADE rating.

1.8.1.3 Benefits and harms

Over 30 days and under 30 days

Clinical benefit was identified for early compared to late referral for place of death (at home or inpatient hospice (> 30 days versus < 30 days). No clinical differences were identified for early (< 30 days) compared to late referral (> 3 months). There were clinical benefits for early (> 3 months) versus late referral (< 3 month), with fewer hospital and ICU admissions, higher survival and death occurring more in hospital or the ICU.

Over 6 months and under 6 months

There was a clinical benefit of early referral (> 6 months versus late (< 6 months) for number of visits to accident and emergency, unscheduled admissions to hospital, people with >14 days of hospitalisation, hospital death and avoidable/inappropriate admissions to ICU. No clinically important differences were found between the groups for preferred and actual place of death (ICU death). The results were conflicting across the studies for an increase or reduction in emergency room visits.

Overall there were more benefits for early referral than late but the committee agreed the evidence was too limited to make a recommendation for a particular time point to have early referral.

The definition of early and late referral varied across the studies and it was not always clear why the time points where chosen. Two studies had the cut-off of 3 months (with more than 3 months before death considered early and after 3 months delayed), however it is unknown why this cut-off was chosen. One study included the cut-off of 3 months (with more than 3 months before death considered early and after 3 months delayed) and 6 months (with more than 6 months before death considered early and after 6 months delayed). In another study ‘early’ and ‘late’ referral was defined as < 30 days or > 3 months from diagnosis, but no information was reported on the time to death.

The committee commented that the difference in time of referral was only a few months in the studies and this could explain the absence of evidence for any clinically important differences between the two groups for the majority of the outcomes. One study used 30 days as the cut-off point (with earlier than 30 days considered early and after this considered late). Again this was considered to be a very short time-scale in which to make any clear conclusions of when an appropriate time for referral would be.

The committee agreed that some of the studies were conducted in different healthcare systems than the UK and this made it difficult to generalise the results to the NHS. Two of the studies were conducted in the US where there are marked differences in the organisation of end of life care and the provision compared to the UK. In addition one study centre was located in a specialist centre making it harder to extrapolate any conclusions from this setting. The other studies were conducted in Norway, Japan and Singapore which have

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different healthcare systems to the UK. Furthermore, all studies included cancer patients further limiting the generalisability to other populations.

Overall, the Committee commented that the time between referral to palliative care services and death observed in the studies included in the review was quite short, however, this could be explained at least in part by the challenge of identifying people in the last year of life who would benefit from a referral to palliative care services. The Committee also commented that people who consented to receive early palliative care could be inherently different in severity of illness or in social or cultural factors influencing the make-up of the study populations. The Committee was aware of other studies of early referral to palliative services, however in these studies the comparison was standard care, rather than late referral. The protocol specified including studies which defined 'early' and 'late' in order to make useful recommendations.

The Committee concluded there were no negative consequences of early referral to palliative care services but no substantial evidence of benefit either. The Committee concluded that the evidence on benefit of early referral (or provision of) palliative care services for people in the last year of life was not sufficient to formulate a recommendation. However, the Committee agreed to formulate a recommendation to offer initial holistic needs assessment soon after identification of being in the last year of life and for it to be carried out by someone knowledgeable who would be able to identify when and how to carry it out. This was extended to include a recommendation about carer's needs assessment. The Committee agreed it was important to assess the Carers needs as well. Neglecting the carers needs inevitably impacts on the care the person in the last year of life receives (also see evidence review H on carers support services).

1.8.2 Cost effectiveness and resource use

No economic evidence was identified for this question.

Referral for early palliative care would cost more in terms of resources spent on palliative care services as people would receive the services for a longer period of time. However the committee acknowledged that receiving palliative care earlier could lead to some people deciding to withdraw from disease modifying or life prolonging treatments earlier. Providing early palliative care could be an efficient use of resources if the costs of providing the services for longer were lower than the costs saved from people withdrawing from (sometimes not cost effective, highly expensive with limited clinical effectiveness) treatments earlier.

Regardless of this view, the committee felt there were a number of sizeable issues with comparing 'early' palliative care to 'late' palliative care. A main issue being the inability to define what is meant by the term 'early'. The significant challenge that exists in identifying when a person is in their last year of life, and even if identified, estimating their life expectancy with accuracy, makes knowing when to begin offering 'early' palliative care options extremely problematic. The committee noted that some conditions do not have predictable progression trajectories. It is extremely difficult to estimate the life expectancy of a person who has a condition where it is common for peaks and troughs in symptom severity to occur for example COPD or Heart Failure, or a condition where recovery from treatment may be unlikely but still possible.

Potential cost savings of early palliative care is dependent on the health care teams having access to resources which are not currently standardised within the NHS. Including these costs may suggest that a saving is not achievable in the short term as significant investment is required in improving resources. Estimating the costs that could be saved from people withdrawing from treatment earlier is even more challenging. Deciding to withdraw from treatment is a personal decision that will vary by condition, by individual circumstance and individual choice.

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Without a clear definition of 'early' palliative care and without evidence on the effect that early palliative care has on treatment withdrawal in the entire end of life population, the committee were not able to estimate this effect. The committee were therefore unable to determine the cost effectiveness of early palliative care and did not feel they had enough information to be able to formulate a recommendation on the timing of an assessment.

The committee agreed that as soon as the health system identifies someone as a carer there should be a system in place that triggers an immediate referral for a carer's needs assessment to occur as soon after the identification as possible. Early referral for a carer's assessment will ensure that the carer is supported by and can benefit from the local carer support services available as early as possible.

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Appendices

Appendix A: Review protocols

Table 10: Review protocol: Early versus late referral to palliative care services

Question number: 6

Relevant section of Scope: Service delivery models for end of life care, including both acute, community and third sector settings covering:

- types of services (supportive and palliative care) provided by generalists and specialists during the course of the last year of life,
- who delivers the services and how, multidisciplinary team composition,
- timing and review of service provision,
- Location of services, for example, place of care,
- out of hours, weekend and 24/7 availability of services

ID	Field	Content
I	Review question	What is the best timing of referral to (or provision of) palliative care services in people thought to be entering their last year of life?
II	Type of review question	Intervention review. A review of health economic evidence related to the same review question was conducted in parallel with this review. For details see the health economic review protocol for this NICE guideline.
III	Objective of the review	To identify the best timing of referral to (or provision of) palliative care services in people thought to be entering their last year of life
IV	Eligibility criteria – population / disease / condition / issue / domain	Adults (aged over 18 or over) with progressive life-limiting conditions thought to be entering the last year of life.
V	Eligibility criteria – intervention(s) / exposure(s) / prognostic factor(s)	• Early referral to (or provision of) palliative care services 'Early' as defined by studies
VI	Eligibility criteria – comparator(s) / control or reference (gold) standard	• Late referral to (or provision of) palliative care services 'Late' as defined by studies
VII	Outcomes and prioritisation	CRITICAL • Quality of life (Continuous) • Preferred and actual place of death (Dichotomous) • Preferred and actual place of care (Dichotomous) IMPORTANT • Length of stay (Continuous)

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		• Length of survival (Dichotomous) • Hospitalisation (Dichotomous) • Number of hospital visits (Dichotomous) • Number of visits to accident and emergency (Dichotomous) • Number of unscheduled admissions (Dichotomous) • Use of community services (Dichotomous) • Avoidable/inappropriate admissions to ICU (Dichotomous) • Inappropriate resuscitation (Dichotomous) • Staff satisfaction (Continuous) • Patient/carer reported outcomes (satisfaction) (Continuous)
VIII	Eligibility criteria – study design	• Systematic reviews • RCTs • Non-randomised comparative studies, including before and after studies.
IX	Other inclusion exclusion criteria	• Children and young people (17 years or younger) in their last year of life • Studies will only be included if they reported one of more of the outcomes listed above • Descriptive (non-comparative) studies will be excluded
X	Proposed sensitivity / subgroup analysis, or meta-regression	Subgroup analyses if there is heterogeneity: • Younger adults (aged 18-25) • Frail elderly • People with dementia • People with hearing loss • People with advanced heart and lung disease • People in prisons • Socioeconomic inequalities (people from lower income brackets) • Homeless people/vulnerably housed • Travellers • People with learning difficulties • People with disabilities • People with mental health problems • Migrant workers • LGBT • People in whom life-prolonging therapies are still an active option
XI	Selection process – duplicate screening / selection / analysis	Quality assurance will be undertaken by a senior research fellow prior to completion. Review strategy/other analysis: • Information on identification tools used as part of a service will be extracted. • Due to the expected complexity of the service models implemented in the studies, studies will be reported separately if necessary. In such case, studies on the populations included in the subgroup list will be highlighted to the Committee and will be considered when making the recommendations
XII	Data management (software)	• Pairwise meta-analyses were performed using Cochrane Review Manager (RevMan5).

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		• GRADEpro was used to assess the quality of evidence for each outcome. • Endnote was used for: o Bibliography, citations, sifting and reference management • Evibase was used for o Data extraction and quality assessment / critical appraisal
XIII	Information sources – databases and dates	Clinical search databases to be used: Medline, Embase, Cochrane Library, Current Nursing and Allied Health Literature (CINAHL), PsycINFO, Healthcare Management Information Consortium (HMIC), Social Policy and Practice (SSP), Applied Social Sciences Index and Abstracts (ASSIA) Date: All years Health economics search databases to be used: Medline, Embase, NHSEED, HTA Date: Medline, Embase from 2014 NHSEED, HTA – All years Language: Restrict to English only
XIV	Identify if an update	Not applicable.
XV	Author contacts	https://www.nice.org.uk/guidance/indevelopment/gid-cgwave0799
XVI	Highlight if amendment to previous protocol	For details please see section 4.5 of Developing NICE guidelines: the manual.
XVII	Search strategy – for one database	For details please see Appendix B
XVIII	Data collection process – forms / duplicate	A standardised evidence table format will be used, and published as Appendix A of the evidence report.
XIX	Data items – define all variables to be collected	For details please see evidence tables in Appendix D (clinical evidence tables) or health economic evidence tables where applicable.
XX	Methods for assessing bias at outcome / study level	Standard study checklists were used to critically appraise individual studies. For details please see section 6.2 of Developing NICE guidelines: the manual The risk of bias across all available evidence was evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/ [Please document any deviations/alternative approach when GRADE isn't used or if a modified GRADE approach has been used for non-intervention or non-comparative studies.]
XXI	Criteria for quantitative synthesis	For details please see section 6.4 of Developing NICE guidelines: the manual.
XXII	Methods for quantitative analysis – combining studies and exploring (in)consistency	For details please see the separate Methods report for this guideline.

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XXIII	Meta-bias assessment – publication bias, selective reporting bias	For details please see section 6.2 of Developing NICE guidelines: the manual. [Consider exploring publication bias for review questions where it may be more common, such as pharmacological questions, certain disease areas.. Describe any steps taken to mitigate against publication bias, such as examining trial registries.]
XXIV	Confidence in cumulative evidence	For details please see sections 6.4 and 9.1 of Developing NICE guidelines: the manual.
XXV	Rationale / context – what is known	For details please see the introduction to the evidence review.
XXVI	Describe contributions of authors and guarantor	A multidisciplinary committee [https://www.nice.org.uk/guidance/indevelopment/gid-cgwave0799] developed the evidence review. The committee was convened by the National Guideline Centre (NGC) and chaired by Mark Thomas in line with section 3 of Developing NICE guidelines: the manual. Staff from NGC undertook systematic literature searches, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate, and drafted the evidence review in collaboration with the committee. For details please see Developing NICE guidelines: the manual.
XXVII	Sources of funding / support	NGC is funded by NICE and hosted by the Royal College of Physicians.
XXVIII	Name of sponsor	NGC is funded by NICE and hosted by the Royal College of Physicians.
XXIX	Roles of sponsor	NICE funds NGC to develop guidelines for those working in the NHS, public health and social care in England.
XXX	PROSPERO registration number	Not registered

Table 11: Health economic review protocol

Review question	**All questions – health economic evidence**
Objectives	To identify health economic studies relevant to any of the review questions.
Search criteria	• Populations, interventions and comparators must be as specified in the clinical review protocol above. • Studies must be of a relevant health economic study design (cost–utility analysis, cost-effectiveness analysis, cost–benefit analysis, cost–consequences analysis, comparative cost analysis). • Studies must not be a letter, editorial or commentary, or a review of health economic evaluations. (Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.) • Unpublished reports will not be considered unless submitted as part of a call for evidence. • Studies must be in English.
Search strategy	A health economic study search will be undertaken using population-specific terms and a health economic study filter – see Appendix G *[in the Full guideline]*
Review strategy	Studies not meeting any of the search criteria above will be excluded. Studies published before 2007, abstract-only studies and studies from non-OECD countries or the USA will also be excluded.

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Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in Appendix H of Developing NICE guidelines: the manual (2014).[63]

Inclusion and exclusion criteria

- If a study is rated as both 'Directly applicable' and with 'Minor limitations' then it will be included in the guideline. A health economic evidence table will be completed and it will be included in the health economic evidence profile.
- If a study is rated as either 'Not applicable' or with 'Very serious limitations' then it will usually be excluded from the guideline. If it is excluded then a health economic evidence table will not be completed and it will not be included in the health economic evidence profile.
- If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both then there is discretion over whether it should be included.

Where there is discretion

The health economist will make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the guideline committee if required. The ultimate aim is to include health economic studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be included, then the health economist, in discussion with the committee if required, may decide to include only the most applicable studies and to selectively exclude the remaining studies. All studies excluded on the basis of applicability or methodological limitations will be listed with explanation as excluded health economic studies in Appendix M.

The health economist will be guided by the following hierarchies.

Setting:

- UK NHS (most applicable).
- OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden).
- OECD countries with predominantly private health insurance systems (for example, Switzerland).
- Studies set in non-OECD countries or in the USA will be excluded before being assessed for applicability and methodological limitations.

Health economic study type:

- Cost–utility analysis (most applicable).
- Other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequences analysis).
- Comparative cost analysis.
- Non-comparative cost analyses including cost-of-illness studies will be excluded before being assessed for applicability and methodological limitations.

Year of analysis:

- The more recent the study, the more applicable it will be.
- Studies published in 2007 or later but that depend on unit costs and resource data entirely or predominantly from before 2007 will be rated as 'Not applicable'.
- Studies published before 2007 will be excluded before being assessed for applicability and methodological limitations.

Quality and relevance of effectiveness data used in the health economic analysis:

- The more closely the clinical effectiveness data used in the health economic analysis match with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline.

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Appendix B: Literature search strategies

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual 2014, updated 2017 https://www.nice.org.uk/guidance/pmg20/resources/developing-nice-guidelines-the-manual-pdf-72286708700869

For more detailed information, please see the Methodology Review.

B.1 Clinical search literature search strategy

Searches for were constructed using a PICO framework where population (P) terms were combined with Intervention (I) and in some cases Comparison (C) terms. Outcomes (O) are rarely used in search strategies for interventions as these concepts may not be well described in title, abstract or indexes and therefore difficult to retrieve. Search filters were applied to the search where appropriate.

Table 12: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (Ovid)	1946 – 04 January 2019	Exclusions
Embase (Ovid)	1974 – 04 January 2019	Exclusions
The Cochrane Library (Wiley)	Cochrane Reviews to Issue 1 of 12, January 2019 CENTRAL to Issue 1 of 12, January 2019 DARE, and NHSEED to Issue 2 of 4 2015 HTA to Issue 4 of 4 2016	None
CINAHL, Current Nursing and Allied Health Literature (EBSCO)	Inception – 04 January 2019	Limiters - English Language; Exclude MEDLINE records; Publication Type: Clinical Trial, Journal Article, Meta Analysis, Randomized Controlled Trial, Systematic Review: Age Groups: All Adult; Language: English
PsycINFO (ProQuest)	Inception – 04 January 2019	Study type
HMIC. Healthcare Management Information Consortium (Ovid)	1979 – 04 January 2019	Exclusions
SPP, Social Policy and Practice	1981 – 04 January 2019	Study types
ASSIA, Applied Social Sciences Index and Abstracts (ProQuest)	1987 – 04 January 2019	None

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Medline (Ovid) search terms

1.	Palliative care/
2.	Terminal care/
3.	Hospice care/
4.	palliat*.ti,ab.
5.	((terminal* or long term or longterm) adj2 (care* or caring)).ti,ab.
6.	Nursing Homes/
7.	((care or nursing) adj2 (home or homes)).ti,ab.
8.	Respite Care/
9.	((respite or day) adj2 (care or caring)).ti,ab.
10.	Hospices/
11.	hospice*.ti,ab.
12.	exp Advance Care Planning/
13.	(advance* adj2 (plan* or decision* or directive*)).ti,ab.
14.	living will*.ti,ab.
15.	*Patient care planning/
16.	*"Continuity of Patient Care"/
17.	((advance* or patient*) adj3 (care or caring) adj3 (continu* or plan*)).ti,ab.
18.	*Physician-Patient Relations/
19.	*Long-Term Care/
20.	*"Delivery of Health Care"/
21.	((dying or death) adj2 (care or caring)).ti,ab.
22.	or/1-21
23.	Terminally Ill/
24.	((terminal* or long term or longterm) adj2 ill*).ti,ab.
25.	((dying or terminal) adj (phase* or stage*)).ti,ab.
26.	life limit*.ti,ab.
27.	*Attitude to Death/
28.	(attitude* adj3 (death* or dying*)).ti,ab.
29.	(end adj2 life).ti,ab.
30.	EOLC.ti,ab.
31.	((last or final) adj2 (year or month*) adj2 life).ti,ab.
32.	((dying or death) adj2 (patient* or person* or people)).ti,ab.
33.	or/23-32
34.	22 and 33
35.	letter/
36.	editorial/

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37.	news/
38.	exp historical article/
39.	Anecdotes as Topic/
40.	comment/
41.	case report/
42.	(letter or comment*).ti.
43.	or/35-43
44.	randomized controlled trial/ or random*.ti,ab.
45.	43 not 44
46.	animals/ not humans/
47.	exp Animals, Laboratory/
48.	exp Animal Experimentation/
49.	exp Models, Animal/
50.	exp Rodentia/
51.	(rat or rats or mouse or mice).ti.
52.	or/45-51
53.	34 not 52
54.	(exp child/ or exp pediatrics/ or exp infant/) not (exp adolescent/ or exp adult/ or exp middle age/ or exp aged/)
55.	53 not 54
56.	limit 55 to English language
57.	"referral and consultation"/
58.	(referral* or referred or referring or refer or refers or consult*).ti,ab.
59.	(recommend* or direct*).ti,ab.
60.	or/57-59
61.	(commission* adj2 (support* or service* or model*)).ti,ab.
62.	((service* or program* or co-ordinat* or co ordinat* or coordinat*) adj2 (model* or deliver* or strateg* or support* or access* or method* or system* or policies or policy or availab*)).ti,ab.
63.	Critical Pathways/
64.	((critical or clinic* or service* or care) adj2 path*).ti,ab.
65.	Patient Care Bundles/
66.	(care adj2 (bundle* or service* or package* or standard*)).ti,ab.
67.	or/61-66
68.	(assess* or criteria* or predict* or recogni* or identif* or refer*).ti,ab.
69.	56 and 67 and 68
70.	gold standard*.ti,ab.
71.	56 and 70
72.	(amber adj2 bundle).ti,ab.
73.	69 or 71 or 72
74.	patient care team/
75.	interdisciplinary communication/
76.	(((interdisciplin* or inter-disciplin* or interprofession* or inter-profession* or multidisciplin* or multi-disciplin* or multi-profession* or multiprofession* or transprofession* or trans-profession*) adj2 (team* or staff* or meeting* or manag* or appointment* or system* or program* or practic* or advic* or advis* or caring or

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	intervention* or ward* or round* or panel* or forum* or fora or communicat* or collaborat* or relat*)) or MDT or IDT).ti,ab.
77.	(((integrat* or network*) adj2 (team* or staff* or meeting* or manag* or appointment* or system* or program* or practic* or advic* or advis* or caring or intervention* or ward* or round* or panel* or forum* or fora or communicat* or collaborat* or relat*)) or MDT or IDT).ti,ab.
78.	(key adj2 work*).ti,ab.
79.	((healthcare or care) adj2 (lead or leader or leads or facilitat*)).ti,ab.
80.	((healthcare or care) adj1 profession*).ti,ab.
81.	*Case Management/
82.	(case adj2 manage*).ti,ab.
83.	(co-ordinator* or coordinator* or coordinate* or co-ordinate*).ti,ab.
84.	Or/74-83
85.	interdisciplinary communication/
86.	exp Communication Barriers/
87.	(communicat* or discuss* or speak* or talk* or convers* or contact).ti,ab.
88.	((handover or hand over or share or shared or sharing or transfer*) adj3 information*).ti,ab.
89.	(followup or follow up).ti,ab.
90.	(palliativ* adj2 (care or caring)).ti,ab.
91.	Or/85-90
92.	56 and 84 and 91
93.	Social Welfare/ec, ed, es, eh, ma, st, sn, td [Economics, Education, Ethics, Ethnology, Manpower, Standards, Statistics & Numerical Data, Trends]
94.	Charities/ec, ed, es, ma, mt, og, st, sn, sd, td, ut [Economics, Education, Ethics, Manpower, Methods, Organization & Administration, Standards, Statistics & Numerical Data, Supply & Distribution, Trends, Utilization]
95.	Home Care Services/ec, ed, es, ma, mt, og, st, sn, sd, td, ut [Economics, Education, Ethics, Manpower, Methods, Organization & Administration, Standards, Statistics & Numerical Data, Supply & Distribution, Trends, Utilization]
96.	Community Health Nursing/ec, ed, es, ma, mt, og, st, sn, sd, td, ut [Economics, Education, Ethics, Manpower, Methods, Organization & Administration, Standards, Statistics & Numerical Data, Supply & Distribution, Trends, Utilization]
97.	Telemedicine/ec, es, ma, mt, og, st, sn, td, ut [Economics, Ethics, Manpower, Methods, Organization & Administration, Standards, Statistics & Numerical Data, Trends, Utilization]
98.	exp remote consultation/
99.	*telemedicine/ or *telepathology/ or *teleradiology/ or *telerehabilitation/
100.	(telemedicine or tele medicine or telehealth or tele health or virtual hospital* or helpline* or help line* or rapid response team* or telepathology or teleradiology or telerehabilitatio).ti,ab.
101.	((tele* or remote) adj2 consult*).ti,ab.
102.	Mobile Health Units/ec, es, ma, og, st, sn, sd, td, ut [Economics, Ethics, Manpower, Organization & Administration, Standards, Statistics & Numerical Data, Supply & Distribution, Trends, Utilization]
103.	(mobile adj2 (health or care) adj2 unit*).ti,ab.
104.	(hospital-based home care or HBHC or hospital-based hospice care or acute hospital care).ti,ab.
105.	(hospital adj3 (domicil* or home)).ti,ab.
106.	home hospitali*ation.ti,ab.
107.	exp Home Care Agencies/

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108.	(social adj (welfare or care)).ti,ab.
109.	(nurs* adj4 (home-visit* or home visit* or home-based or home based)).ti,ab.
110.	((district* or communit* or home or visit*) adj nurs*).ti,ab.
111.	(community adj2 (health care or healthcare or nursing or nurse*)).ti,ab.
112.	((hospitali*ation* or admission* or readmission* or admit*) adj3 (reduc* or avoid* or prevent* or inappropiate or increase* or risk*)).ti,ab.
113.	Or/93-112
114.	*"Continuity of Patient Care"/
115.	*Aftercare/ or *Patient discharge/ or *Patient handoff/ or *Patient transfer/ or *Transitional care/
116.	Patient Discharge Summaries/
117.	((patient* or person* or people or nursing* or clinic*) adj (discharg* or handover* or hand* over* or handoff* or hand off* or signout* or sign* out* or signover* or sign* over*)).ti,ab.
118.	((care or caring or serv*) adj2 (continu* or change* or transition* or transfer*)).ti,ab.
119.	(discharg* adj2 (facilitat* or rapid* or pathway* or path way* or plan* or program*)).ti,ab.
120.	Or/114-119
121.	(advance* adj2 (plan* or decision* or directive*)).ti,ab.
122.	living will*.ti,ab.
123.	Or/121-122
124.	*Caregiver/
125.	*Spouse/
126.	*Family/
127.	(spouse* or wife or wives or husband* or carer* or caregiver* or care giver* or significant other* or friend* or partner* or family or families or individual* or sibling* or brother* or sister* or relative or relatives or mothers* or daughters* or father* or son or sons or uncle* or aunt* or grand mother* or grandmother* or grandfather* or grand father* or aunt* or uncle* or cousin* or niece* or nephew*).ti,ab.
128.	Or/124-127
129.	((replacement or break* or holiday* or respite) adj3 (care* or service*)).ti,ab.
130.	((communit* or support* or psychosocial* or psycholog*) adj3 (service* or group* or system*)).ti,ab.
131.	((group* or support* or psychosocial* or psycholog*) adj3 (selfhelp or self help or therap*)).ti,ab.
132.	((psychosocial* or psycholog*) adj2 support*).ti,ab.
133.	*Self-Help/
134.	*Social support/
135.	*Counseling/
136.	(counseling or counselling*).ti,ab.
137.	(buddy* or buddies).ti,ab.
138.	((health* or medical*) adj2 check*).ti,ab.
139.	((spouse* or wife or wives or husband* or carer* or caregiver* or care giver* or significant other* or friend* or partner* or family or families or individual* or sibling* or brother* or sister* or relative or relatives or mothers* or daughters* or father* or son or sons or uncle* or aunt* or grand mother* or grandmother* or grandfather* or grand father* or aunt* or uncle* or cousin* or niece* or nephew*) adj3 (education or educate or educating or information or literature or leaflet* or booklet* or pamphlet* or website* or knowledge)).ti,ab.
140.	Or/129-139

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141.	56 and 128 and 140
142.	56 and (60 or 84 or 113 or 120 or 123)
143.	73 or 92 or 141 or 142

Embase (Ovid) search terms

1.	*Palliative therapy/
2.	*Terminal care/
3.	*Hospice care/
4.	palliat*.ti,ab.
5.	((terminal* or long term or longterm) adj2 (care* or caring)).ti,ab.
6.	*Nursing home/
7.	((care or nursing) adj2 (home or homes)).ti,ab.
8.	*Respite Care/
9.	((respite or day) adj2 (care or caring)).ti,ab.
10.	*Hospice/
11.	hospice*.ti,ab.
12.	*Patient care planning/
13.	(advance* adj2 (plan* or decision* or directive*)).ti,ab.
14.	living will*.ti,ab.
15.	*Patient care/
16.	((advance* or patient*) adj3 (care or caring) adj3 (continu* or plan*)).ti,ab.
17.	*Attitude to Death/
18.	(attitude* adj3 (death* or dying*)).ti,ab.
19.	*Doctor patient relation/
20.	*Long term care/
21.	*Health care delivery/
22.	or/1-21
23.	*Terminally ill patient/
24.	((terminal* or long term or longterm) adj2 ill*).ti,ab.
25.	((dying or terminal) adj (phase* or stage*)).ti,ab.
26.	life limit*.ti,ab.
27.	*Attitude to Death/
28.	(attitude* adj3 (death* or dying*)).ti,ab.
29.	(end adj2 life).ti,ab.
30.	EOLC.ti,ab.
31.	((last or final) adj2 (year or month*) adj2 life).ti,ab.
32.	((dying or death) adj2 (patient* or person* or people)).ti,ab.
33.	or/23-32
34.	22 and 33
35.	letter.pt. or letter/
36.	note.pt.
37.	editorial.pt.
38.	case report/ or case study/
39.	(letter or comment*).ti.
40.	or/35-39
41.	randomized controlled trial/ or random*.ti,ab.

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42.	40 not 41
43.	animal/ not human/
44.	nonhuman/
45.	exp Animal Experiment/
46.	exp Experimental Animal/
47.	animal model/
48.	exp Rodent/
49.	(rat or rats or mouse or mice).ti.
50.	or/42-49
51.	34 not 50
52.	(exp child/ or exp pediatrics/ or exp infant/) not (exp adolescent/ or exp adult/ or exp middle age/ or exp aged/)
53.	51 not 52
54.	limit 53 to English language
55.	exp patient referral/
56.	(referral* or referred or referring or refer or refers or consult*).ti,ab.
57.	(recommend* or direct*).ti,ab.
58.	or/55-57
59.	54 and 58
60.	(commission* adj2 (support* or service* or model*)).ti,ab.
61.	((service* or program* or co-ordinat* or co ordinat* or coordinat*) adj2 (model* or deliver* or strateg* or support* or access* or method* or system* or policies or policy or availab*)).ti,ab.
62.	*Clinical Pathway/
63.	((critical or clinic* or service* or care) adj2 path*).ti,ab.
64.	*Care Bundle/
65.	(care adj2 (bundle* or service* or package* or standard*)).ti,ab.
66.	or/60-65
67.	(assess* or criteria* or predict* or recogni* or identif* or refer*).ti,ab.
68.	54 and 66 and 67
69.	gold standard*.ti,ab.
70.	54 and 69
71.	(amber adj2 bundle).ti,ab.
72.	68 or 70 or 71
73.	interdisciplinary communication/
74.	patient care team*.ti,ab.
75.	(((interdisciplin* or inter-disciplin* or interprofession* or inter-profession* or multidisciplin* or multi-disciplin* or multi-profession* or multiprofession* or transprofession* or trans-profession*) adj2 (team* or staff* or meeting* or manag* or appointment* or system* or program* or practic* or advic* or advis* or caring or intervention* or ward* or round* or panel* or forum* or fora or communicat* or collaborat* or relat*)) or MDT or IDT).ti,ab.
76.	(((integrat* or network*) adj2 (team* or staff* or meeting* or manag* or appointment* or system* or program* or practic* or advic* or advis* or caring or intervention* or ward* or round* or panel* or forum* or fora or communicat* or collaborat* or relat*)) or MDT or IDT).ti,ab.
77.	(key adj2 work*).ti,ab.
78.	((healthcare or care) adj2 (lead or leader or leads or facilitat*)).ti,ab.

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79.	((healthcare or care) adj1 profession*).ti,ab.
80.	*Case Management/
81.	(case adj2 manage*).ti,ab.
82.	(co-ordinator* or coordinator* or coordinate* or co-ordinate*).ti,ab.
83.	Or/73-82
84.	interdisciplinary communication/
85.	(communicat* or discuss* or speak* or talk* or convers* or contact).ti,ab.
86.	((handover or hand over or share or shared or sharing or transfer*) adj3 information*).ti,ab.
87.	(followup or follow up).ti,ab.
88.	(palliativ* adj2 (care or caring)).ti,ab.
89.	Or/84-88
90.	54 and 83 and 89
91.	*social welfare/
92.	*community health nursing/ or *community care/
93.	*senior center/
94.	*telemedicine/ or *telehealth/
95.	*teleconsultation/
96.	(telehealth or tele health or virtual hospital* or helpline* or help line* or rapid response team* or mobile health unit*).ti,ab.
97.	*home care/ or *home health agency/ or *home monitoring/ or *home oxygen therapy/ or *home physiotherapy/ or *home rehabilitation/ or *home respiratory care/ or *respite care/ or *visiting nursing service/
98.	*health care personnel/ or *health auxiliary/ or *nursing home personnel/
99.	(telemedicine or tele medicine or telehealth or tele health or virtual hospital* or helpline* or help line* or rapid response team* or telepathology or teleradiology or telerehabilitatio).ti,ab.
100.	((tele* or remote) adj2 consult*).ti,ab.
101.	(mobile adj2 (health or care) adj2 unit*).ti,ab.
102.	(hospital-based home care or HBHC or hospital-based hospice care or acute hospital care).ti,ab.
103.	(hospital adj3 (domicil* or home)).ti,ab.
104.	home hospitali*ation.ti,ab.
105.	(social adj (welfare or care)).ti,ab.
106.	(nurs* adj4 (home-visit* or home visit* or home-based or home based)).ti,ab.
107.	((district* or communit* or home or visit*) adj nurs*).ti,ab.
108.	(community adj2 (health care or healthcare or nursing or nurse*)).ti,ab.
109.	((hospitali*ation* or admission* or readmission* or admit*) adj3 (reduc* or avoid* or prevent* or inappropiate or increase* or risk*)).ti,ab.
110.	Or/91-109
111.	*patient care/ or *case management/ or *patient care planning/ or *rapid response team/
112.	*aftercare/
113.	*hospital discharge/
114.	*clinical handover/
115.	*transitional care/
116.	*patient care planning/
117.	*medical record/

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118.	((patient* or person* or people or nursing* or clinic*) adj (discharg* or handover* or hand* over* or handoff* or hand off* or signout* or sign* out* or signover* or sign* over*)).ti,ab.
119.	((care or caring or serv*) adj2 (continu* or change* or transition* or transfer*)).ti,ab.
120.	(discharg* adj2 (facilitat* or rapid* or pathway* or path way* or plan* or program*)).ti,ab.
121.	Or/111-120
122.	(advance* adj2 (plan* or decision* or directive*)).ti,ab.
123.	living will*.ti,ab.
124.	Or/122-123
125.	*Caregiver/
126.	*Spouse/
127.	*Family/
128.	(spouse* or wife or wives or husband* or carer* or caregiver* or care giver* or significant other* or friend* or partner* or family or families or individual* or sibling* or brother* or sister* or relative or relatives or mothers* or daughters* or father* or son or sons or uncle* or aunt* or grand mother* or grandmother* or grandfather* or grand father* or aunt* or uncle* or cousin* or niece* or nephew*).ti,ab.
129.	Or/125-128
130.	((replacement or break* or holiday* or respite) adj3 (care* or service*)).ti,ab.
131.	((communit* or support* or psychosocial* or psycholog*) adj3 (service* or group* or system*)).ti,ab.
132.	((group* or support* or psychosocial* or psycholog*) adj3 (selfhelp or self help or therap*)).ti,ab.
133.	((psychosocial* or psycholog*) adj2 support*).ti,ab.
134.	*Self-Help/
135.	*Social support/
136.	*Counseling/
137.	(counseling or counselling*).ti,ab.
138.	(buddy* or buddies).ti,ab.
139.	((health* or medical*) adj2 check*).ti,ab.
140.	((spouse* or wife or wives or husband* or carer* or caregiver* or care giver* or significant other* or friend* or partner* or family or families or individual* or sibling* or brother* or sister* or relative or relatives or mothers* or daughters* or father* or son or sons or uncle* or aunt* or grand mother* or grandmother* or grandfather* or grand father* or aunt* or uncle* or cousin* or niece* or nephew*) adj3 (education or educate or educating or information or literature or leaflet* or booklet* or pamphlet* or website* or knowledge)).ti,ab.
141.	or/130-140
142.	54 and 129 and 141
143.	54 and (83 or 110 or 121 or 124)
144.	59 or 72 or 90 or 142 or 143

Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Palliative Care] this term only
#2.	MeSH descriptor: [Terminal Care] this term only
#3.	MeSH descriptor: [Hospice Care] this term only
#4.	palliat*:ti,ab
#5.	((terminal* or long term or longterm) near/2 (care* or caring)):ti,ab
#6.	MeSH descriptor: [Nursing Homes] explode all trees

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#7.	((care or nursing) near/2 (home or homes)):ti,ab
#8.	MeSH descriptor: [Respite Care] this term only
#9.	((respite or day) near/2 (care or caring)):ti,ab
#10.	MeSH descriptor: [Hospices] this term only
#11.	hospice*:ti,ab
#12.	MeSH descriptor: [Advance Care Planning] explode all trees
#13.	(advance* near/2 (plan* or decision* or directive*)):ti,ab
#14.	living will*:ti,ab
#15.	MeSH descriptor: [Patient Care Planning] this term only
#16.	MeSH descriptor: [Continuity of Patient Care] this term only
#17.	((advance* or patient*) near/3 (care or caring) near/3 (continu* or plan*)):ti,ab
#18.	MeSH descriptor: [Physician-Patient Relations] this term only
#19.	MeSH descriptor: [Long-Term Care] this term only
#20.	MeSH descriptor: [Delivery of Health Care] this term only
#21.	((dying or death) near/2 (care or caring)):ti,ab
#22.	(or #1-#21)
#23.	MeSH descriptor: [Terminally Ill] explode all trees
#24.	((terminal* or long term or longterm) near/2 ill*):ti,ab
#25.	((dying or terminal) near (phase* or stage*)):ti,ab
#26.	life limit*:ti,ab
#27.	MeSH descriptor: [Attitude to Death] this term only
#28.	(attitude* near/3 (death* or dying*)):ti,ab
#29.	(end near/2 life):ti,ab
#30.	EOLC:ti,ab
#31.	((last or final) near/2 (year or month*) near/2 life):ti,ab
#32.	((dying or death) near/2 (patient* or person* or people)):ti,ab
#33.	(or #24-#32)
#34.	#22 and #33
#35.	MeSH descriptor: [Referral and Consultation] explode all trees
#36.	(referral* or referred or referring or refer or refers or consult*):ti,ab
#37.	(recommend* or direct*):ti,ab
#38.	(or #34-#36)
#39.	#34 and #38
#40.	(commission* near/2 (support* or service* or model*)):ti,ab
#41.	((service* or program* or co-ordinat* or co ordinat* or coordinat*) near/2 (model* or deliver* or strateg* or support* or access* or method* or system* or policies or policy or availab*)):ti,ab
#42.	MeSH descriptor: [Critical Pathways] explode all trees
#43.	((critical or clinic* or service* or care) near/2 path*):ti,ab
#44.	MeSH descriptor: [Patient Care Bundles] explode all trees
#45.	(care near/2 (bundle* or service* or package* or standard*)):ti,ab
#46.	(or #40-#45)
#47.	(assess* or criteria* or predict* or recogni* or identif* or refer*):ti,ab
#48.	#34 and #46 and #47
#49.	gold standard*:ti,ab
#50.	#34 and #49

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#51.	(amber near/2 bundle):ti,ab
#52.	#48 or #50 or #51
#53.	MeSH descriptor: [Patient Care Team] explode all trees
#54.	MeSH descriptor: [Interdisciplinary Communication] explode all trees
#55.	(((interdisciplin* or inter-disciplin* or interprofession* or inter-profession* or multidisciplin* or multi-disciplin* or multi-profession* or multiprofession* or transprofession* or trans-profession*) near/2 (team* or staff* or meeting* or manag* or appointment* or system* or program* or practic* or advic* or advis* or caring or intervention* or ward* or round* or panel* or forum* or fora or communicat* or collaborat* or relat*)) or MDT or IDT):ti,ab
#56.	((integrat* or network*) near/2 (team* or staff* or meeting* or manag* or appointment* or system* or program* or practic* or advic* or advis* or caring or intervention* or ward* or round* or panel* or forum* or fora or communicat* or collaborat* or relat*)):ti,ab
#57.	(key near/2 work*):ti,ab
#58.	((healthcare or care) near/2 (lead or leader or leads or facilitat*)):ti,ab
#59.	((healthcare or care) near/1 profession*):ti,ab
#60.	MeSH descriptor: [Case Management] this term only
#61.	(case near/2 manage*):ti,ab
#62.	(co-ordinator* or coordinator* or coordinate* or co-ordinate*):ti,ab
#63.	(or #53-#62)
#64.	MeSH descriptor: [Interdisciplinary Communication] explode all trees
#65.	MeSH descriptor: [Communication Barriers] explode all trees
#66.	(communicat* or discuss* or speak* or talk* or convers* or contact):ti,ab
#67.	((handover or hand over or share or shared or sharing or transfer*) near/3 information*):ti,ab
#68.	(followup or follow up):ti,ab
#69.	(palliativ* near/2 (care or caring)):ti,ab
#70.	(or #64-#69)
#71.	34 and 63 and 69
#72.	MeSH descriptor: [Social Welfare] explode all trees
#73.	MeSH descriptor: [Charities] explode all trees
#74.	MeSH descriptor: [Adult Day Care Centers] explode all trees
#75.	MeSH descriptor: [Community Health Nursing] explode all trees
#76.	MeSH descriptor: [Home Care Services] explode all trees
#77.	MeSH descriptor: [Senior Centers] explode all trees
#78.	MeSH descriptor: [Telemedicine] this term only
#79.	MeSH descriptor: [Remote Consultation] explode all trees
#80.	(telehealth or tele health or virtual hospital* or helpline* or help line* or rapid response team*):ti,ab
#81.	MeSH descriptor: [Mobile Health Units] explode all trees
#82.	((community based or community dwelling home or rural) near/3 (care or health care or healthcare)):ti,ab
#83.	(hospital-based home care or HBHC or hospital-based hospice care or acute hospital care):ti,ab
#84.	((hospitali*ation* or admission* or readmission* or admit*) near/3 (reduc* or avoid* or prevent* or inappropiate or increase* or risk*)):ti,ab
#85.	(home based versus hospital based):ti,ab
#86.	(hospital near/3 (domicil* or home)):ti,ab

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#87.	(home hospitali*ation):ti,ab
#88.	MeSH descriptor: [Home Care Services, Hospital-Based] explode all trees
#89.	MeSH descriptor: [Home Health Nursing] explode all trees
#90.	MeSH descriptor: [Homemaker Services] explode all trees
#91.	MeSH descriptor: [Home Care Agencies] explode all trees
#92.	MeSH descriptor: [Home Health Aides] explode all trees
#93.	(social care):ti,ab
#94.	MeSH descriptor: [Nurses, Community Health] explode all trees
#95.	(nurs* near/4 (home-visit* or home visit* or home-based or home based)):ti,ab
#96.	((district* or communit* or home or visit*) near nurs*):ti,ab
#97.	(Or #72-#96)
#98.	MeSH descriptor: [Continuity of Patient Care] this term only
#99.	MeSH descriptor: [Aftercare] this term only
#100.	MeSH descriptor: [Patient Discharge] this term only
#101.	MeSH descriptor: [Patient Handoff] this term only
#102.	MeSH descriptor: [Patient Transfer] this term only
#103.	MeSH descriptor: [Transitional Care] this term only
#104.	MeSH descriptor: [Patient Discharge Summaries] this term only
#105.	((patient* or person* or people or nursing* or clinic*) near (discharg* or handover* or hand* over* or handoff* or hand off* or signout* or sign* out* or signover* or sign* over*)):ti,ab
#106.	((care or caring or serv*) near/2 (continu* or change* or transition* or transfer*)):ti,ab
#107.	(discharg* near/2 (facilitat* or rapid* or pathway* or path way* or plan* or program*)):ti,ab
#108.	(or #98-#107)
#109.	MeSH descriptor: [Advance Care Planning] explode all trees
#110.	(advance* near/2 (plan* or decision* or directive*)):ti,ab
#111.	living will*:ti,ab
#112.	(or #109-#111)
#113.	MeSH descriptor: [Caregivers] this term only
#114.	MeSH descriptor: [Spouses] this term only
#115.	MeSH descriptor: [Family] this term only
#116.	(spouse* or wife or wives or husband* or carer* or caregiver* or care giver* or significant other* or friend* or partner* or family or families or individual* or sibling* or brother* or sister* or relative or relatives or mothers* or daughters* or father* or son or sons or uncle* or aunt* or grand mother* or grandmother* or grandfather* or grand father* or aunt* or uncle* or cousin* or niece* or nephew*):ti,ab
#117.	(or #113-#116)
#118.	((replacement or break* or holiday* or respite) near/3 (care* or service*)):ti,ab
#119.	((communit* or support* or psychosocial* or psycholog*) near/3 (service* or group* or system*)):ti,ab
#120.	((group* or support* or psychosocial* or psycholog*) near/3 (selfhelp or self help or therap*)):ti,ab
#121.	((psychosocial* or psycholog*) near/2 support*):ti,ab
#122.	MeSH descriptor: [Self-Help Groups] this term only
#123.	MeSH descriptor: [Social Support] explode all trees
#124.	MeSH descriptor: [Counseling] this term only
#125.	(counseling or counselling*):ti,ab

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#126.	(buddy* or buddies):ti,ab
#127.	(health or medical*) near/3 check*:ti,ab
#128.	(spouse* or wife or wives or husband* or carer* or caregiver* or care giver* or significant other* or friend* or partner* or family or families or individual* or sibling* or brother* or sister* or relative or relatives or mothers* or daughters* or father* or son or sons or uncle* or aunt* or grand mother* or grandmother* or grandfather* or grand father* or aunt* or uncle* or cousin* or niece* or nephew*) near/3 (education or educate or educating or information or literature or leaflet* or booklet* or pamphlet* or website* or knowledge):ti,ab
#129.	(or #118-#128)
#130.	#34 and #117 and #129
#131.	#34 and (#63 or #97 or #108 or #112)
#132.	#39 or #52 or #71 or #130 or #131

CINAHL (EBSCO) search terms

S1.	MH Palliative care
S2.	MH Terminal care
S3.	MH Hospice care
S4.	TI palliat* OR AB palliat*
S5.	MW Terminally ill
S6.	TI (terminal* or long term or longterm) AND TI (care* or caring)
S7.	AB (terminal* or long term or longterm) AND AB (care* or caring)
S8.	TI (dying or terminal) AND TI (phase* or stage*)
S9.	AB (dying or terminal) AND AB (phase* or stage*)
S10.	TI life limit* OR AB life limit*
S11.	MH Nursing homes
S12.	TI (care or nursing) AND TI (home or homes)
S13.	AB (care or nursing) AND AB (home or homes)
S14.	MH Respite care
S15.	TI (respite or day) AND TI (care or caring)
S16.	AB (respite or day) AND AB (care or caring)
S17.	MH Hospices
S18.	TI Hospice* OR AB Hospice*
S19.	(MH "Patient Care Plans")
S20.	(MH "Continuity of Patient Care")
S21.	TI (advance* or patient*) AND TI (care or caring) AND TI (continu* or plan*)
S22.	AB (advance* or patient*) AND AB (care or caring) AND AB (continu* or plan*)
S23.	MH Attitude to Death
S24.	TI attitude* AND TI (death* or dying)
S25.	AB attitude* AND AB (death* or dying)
S26.	MH Physician-Patient Relations
S27.	(MH "Long Term Care")
S28.	(MH "Health Care Delivery")
S29.	TI end AND TI life OR AB end AND AB life
S30.	TI EOLC OR AB EOLC
S31.	TI (last or final) AND TI (year or month) AND TI life
S32.	AB (last or final) AND AB (year or month) AND AB life

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S33.	TI (dying or death) AND TI (patient* or person* or people)
S34.	AB (dying or death) AND AB (patient* or person* or people)
S35.	TI (terminal* or long term or longterm) AND TI (ill*)
S36.	AB (terminal* or long term or longterm) AND AB (ill*)
S37.	TI (dying or death) AND TI (care or caring)
S38.	AB (dying or death) AND AB (care or caring)
S39.	S1 OR S2 OR S3 OR S4 OR S6 OR S7 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S26 OR S27 OR S28 OR S37 OR S38
S40.	S5 OR S8 OR S9 OR S10 OR S23 OR S24 OR S25 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36
S41.	S39 AND S40
S42.	(MH "Referral and Consultation+")
S43.	TI (referral* or referred or referring or refer or refers or consult*) OR AB (referral* or referred or referring or refer or refers or consult*)
S44.	TI (recommend* or direct*) OR AB (recommend* or direct*)
S45.	S42 OR S43 OR S44
S46.	S41 AND S45
S47.	TI commission* AND TI ((support* or service* or model*))
S48.	AB commission* AND AB ((support* or service* or model*))
S49.	TI (service* or program* or co-ordinat* or co ordinat* or coordinat*) AND TI (model* or deliver* or strateg* or support* or access* or method* or system* or policies or policy or availab*)
S50.	AB (service* or program* or co-ordinat* or co ordinat* or coordinat*) AND AB (model* or deliver* or strateg* or support* or access* or method* or system* or policies or policy or availab*)
S51.	TI (critical or clinic* or service* or care) AND TI path*
S52.	AB (critical or clinic* or service* or care) AND AB path*
S53.	TI care AND TI (bundle* or service* or package* or standard*)
S54.	AB care AND AB (bundle* or service* or package* or standard*)
S55.	S47 OR S48 OR 49 OR S50 OR S51 OR S52 OR S53 OR S54
S56.	TI (assess* or criteria* or predict* or recogni* or identif* or refer*) OR AB (assess* or criteria* or predict* or recogni* or identif* or refer*)
S57.	S41 AND S55 AND S56
S58.	TI gold standard* OR AB gold standard*
S59.	S41 AND S58
S60.	TI amber AND TI bundle
S61.	AB amber AND AB bundle
S62.	S60 OR S61
S63.	S57 OR S59 OR 62
S64.	(MH "Multidisciplinary Care Team+")
S65.	MDT OR IDT
S66.	((interdisciplin* or inter-disciplin* or interprofession* or inter-profession* or multidisciplin* or multi-disciplin* or multi-profession* or multiprofession* or transprofession* or trans-profession*) n2 (team* or staff* or meeting* or manag* or appointment* or system* or program* or practic* or advic* or advis* or caring or intervention* or ward* or round* or panel* or forum* or fora or communicat* or collaborat* or relat*))

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S67.	((integrat* or network*) n2 (team* or staff* or meeting* or manag* or appointment* or system* or program* or practic* or advic* or advis* or caring or intervention* or ward* or round* or panel* or forum* or fora or communicat* or collaborat* or relat*))
S68.	TI (key n2 work*) OR AB (key n2 work*)
S69.	TI (((healthcare or care) n2 (lead or leader or leads or facilitat*))) OR AB (((healthcare or care) n2 (lead or leader or leads or facilitat*)))
S70.	TI (((healthcare or care) n1 profession*)) OR AB (((healthcare or care) n1 profession*))
S71.	MH Case Management
S72.	TI (case n2 manage*) OR AB (case n2 manage*)
S73.	TI ((co-ordinator* or coordinator* or coordinate* or co-ordinate*)*)) OR AB ((co-ordinator* or coordinator* or coordinate* or co-ordinate*))
S74.	S64 OR S65 OR S66 OR S67 OR S68 OR S69 OR S70 OR S71 OR S72 OR S73
S75.	MeSH descriptor: [Interdisciplinary Communication] explode all trees
S76.	MeSH descriptor: [Communication Barriers] explode all trees
S77.	(communicat* or discuss* or speak* or talk* or convers* or contact):ti,ab
S78.	((handover or hand over or share or shared or sharing or transfer*) near/3 information*):ti,ab
S79.	(followup or follow up):ti,ab
S80.	(palliativ* near/2 (care or caring)):ti,ab
S81.	S75 OR S76 OR S77 OR S78 OR S79 OR S80
S82.	S41 AND S74 AND S81
S83.	(MM "Social Welfare")
S84.	(MH "Charities")
S85.	(MM "Adult Day Center (Saba CCC)") OR (MM "Housing for the Elderly") OR (MM "Older Adult Care (Saba CCC)")
S86.	(MH "Community Health Nursing+") OR (MM "Community Health Centers")
S87.	(MH "Home Health Care+") OR (MM "Home Health Aides") OR (MM "Home Health Care Information Systems") OR (MM "Home Health Aide Service (Saba CCC)")
S88.	(MM "Housing for the Elderly") OR (MM "Rural Health Centers") OR (MM "Community Health Centers")
S89.	(MH "Telemedicine+") OR (MH "Telehealth+")
S90.	(MM "Remote Consultation") OR (MM "Telephone Consultation (Iowa NIC)") OR (MM "Services for Australian Rural and Remote Allied Health")
S91.	telehealth or tele health or virtual hospital* or helpline* or help line* or rapid response team* or senior center*
S92.	(MM "Rural Health Personnel") OR (MM "Mobile Health Units")
S93.	remote consultation
S94.	((community based or community dwelling home or rural) n3 (care or health care or healthcare))
S95.	hospital-based home care or HBHC or hospital-based hospice care or acute hospital care
S96.	((hospitali?ation* or admission* or readmission* or admit*) n3 (reduc* or avoid* or prevent* or inappropiate or increase* or risk*))
S97.	home based versus hospital based
S98.	(hospital n3 (domicil* or home))
S99.	home hospitali?ation
S100.	home care service*
S101.	(MM "Home Health Agencies") OR (MM "Nursing Home Personnel")

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S102.	(MM "Homemaker Services") OR (MM "Health Services for the Aged")
S103.	(MH "Home Health Care+") OR (MM "Home Care Equipment and Supplies") OR (MH "Nursing Homes") OR (MM "National Association for Home Care & Hospice") OR (MM "Nursing Home Patients")
S104.	social care
S105.	(MM "Hospitals, Community")
S106.	(MM "Home Nursing") OR (MM "Home Nursing, Professional")
S107.	(nurs* n4 (home-visit* or home visit* or home-based or home based))
S108.	((district* or communit* or home or visit*) n nurs*)
S109.	S83 OR S84 OR S85 OR S86 OR S87 OR S88 OR S89 OR S90 OR S91 OR S92 OR S93 OR S94 OR S95 OR S96 OR S97 OR S98 OR S99 OR S100 OR S101 OR S102 OR S103 OR S104 OR S105 OR S106 OR S107 OR S108
S110.	MH Continuity of Patient Care OR MH Aftercare OR MH Patient discharge OR MH Patient handoff OR MH Patient transfer OR MH Transitional care
S111.	(MM "Discharge Planning") OR (MM "Patient Discharge Summaries")
S112.	TI (((patient* or person* or people or nursing* or clinic*)) AND TX ((discharg* or handover* or hand* over* or handoff* or hand off* or signout* or sign* out* or signover* or sign* over*))
S113.	AB (((patient* or person* or people or nursing* or clinic*)) AND AB ((discharg* or handover* or hand* over* or handoff* or hand off* or signout* or sign* out* or signover* or sign* over*))
S114.	AB ((care or caring or serv*)) AND AB ((continu* or change* or transition* or transfer*))
S115.	TI ((care or caring or serv*)) AND TI ((continu* or change* or transition* or transfer*))
S116.	TI discharg* AND TI (facilitat* or rapid* or pathway* or path way* or plan* or program*))
S117.	AB discharg* AND AB (facilitat* or rapid* or pathway* or path way* or plan* or program*))
S118.	S110 OR S111 OR S112 OR S113 OR S114 OR S115 OR S116 OR S117
S119.	TI advance* AND TI (plan* or decision* or directive*)
S120.	AB advance* AND AB (plan* or decision* or directive*)
S121.	S119 OR S120
S122.	S41 AND (S74 OR S109 OR S118 OR S121)
S123.	S46 OR S63 OR S82 OR S122

PsycINFO (ProQuest) search terms

1.	(ti,ab(commission* NEAR/2 (support* OR service* OR model*)) OR ((service* OR program* OR co-ordinat* OR coordinat*) NEAR/2 (model* OR deliver* OR strateg* OR support* OR access* OR method* OR system* OR policies OR policy OR availab*))) AND (SU.EXACT("Palliative Care") OR SU.EXACT("Terminally Ill Patients") OR SU.EXACT("Hospice") OR ti,ab(palliat*) OR ti,ab((terminal* OR long-term OR longterm) NEAR/2 (care* OR caring OR ill*)) OR ti,ab((dying OR terminal) NEAR/1 (phase* OR stage*)) OR ti,ab(life-limit*) OR SU.EXACT("Nursing Homes") OR ti,ab((care OR nursing) NEAR/2 (home OR homes)) OR SU.EXACT("Respite Care") OR ti,ab((respite OR day) NEAR/2 (care OR caring)) OR ti,ab(hospice*) OR MJSUB.EXACT("Treatment Planning") OR MJSUB.EXACT("Continuum of Care") OR ti,ab((advance* OR patient*) NEAR/3 (care OR caring) NEAR/3 (continu* OR plan*)) OR MJSUB.EXACT("Long Term Care") OR ti,ab(attitude* NEAR/3 (death* OR dying*)) OR ti,ab(end NEAR/2 life) OR ti,ab(EOLC) OR ti,ab((last OR final) NEAR/2 (year OR month*) NEAR/2 life) OR ti,ab((dying OR death) NEAR/2 (patient* OR person* OR people OR care OR caring)))

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2.	Adolescence (13-17 Yrs), Adulthood (18 Yrs & Older), Aged (65 Yrs & Older), Middle Age (40-64 Yrs), Thirties (30-39 Yrs), Very Old (85 Yrs & Older), Young Adulthood (18-29 Yrs)
3.	1 and 2
4.	Conference Proceedings, Journal Article, Peer Reviewed Journal
5.	3 and 4

HMIC (Ovid) search terms

1.	exp End of life care/
2.	(terminal* adj ill*).ti,ab.
3.	((dying or terminal) adj (phase* or stage*)).ti,ab.
4.	life limit*.ti,ab.
5.	(end adj2 life).ti,ab.
6.	EOLC.ti,ab.
7.	((last or final) adj2 (year or month*) adj2 life).ti,ab.
8.	((dying or death) adj2 (patient* or person* or people or care or caring)).ti,ab.
9.	or/2-8
10.	(exp child/ or exp Paediatrics/ or exp infant/) not (exp adolescent/ or exp adult/ or exp middle age/ or exp older people/)
11.	9 not 10
12.	limit 11 to English
13.	limit 12 to (audiovis or book or chapter dh helmis or circular or microfiche dh helmis or multimedias or website)
14.	limit 12 to (audiocass or books or cdrom or chapter or dept pubs or diskettes or folio pamp or "map" or marc or microfiche or multimedia or pamphlet or parly or press or press rel or thesis or trustdoc or video or videos or website)
15.	13 or 14
16.	12 not 15
17.	euthanasia/
18.	euthanasia.ti,ab.
19.	17 or 18
20.	16 not 19

SPP (Ovid) search terms

1.	palliat*.ti,ab.
2.	((dying or terminal) adj (phase* or stage*)).ti,ab.
3.	life limit*.ti,ab.
4.	hospice*.ti,ab.
5.	(advance* adj2 (plan* or decision* or directive*)).ti,ab.
6.	living will*.ti,ab.
7.	((advance* or patient*) adj3 (care or caring) adj3 (continu* or plan*)).ti,ab.
8.	(attitude* adj3 (death* or dying*)).ti,ab.
9.	(end adj2 life).ti,ab.
10.	EOLC.ti,ab.
11.	((last or final) adj2 (year or month*) adj2 life).ti,ab.
12.	((dying or death) adj2 (patient* or person* or people or care or caring)).ti,ab.
13.	(nursing adj2 (home or homes)).ti,ab.
14.	(terminal* adj2 ill*).ti,ab.

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15.	(respite adj2 (care or caring)).ti,ab.
16.	or/1-15
17.	(child* or infant*).ti,ab.
18.	(adult* or adolescent*).ti,ab.
19.	17 not 18
20.	16 not 19
21.	limit 20 to (journal or journal article or online resource or online report or report)

ASSIA (ProQuest) search terms

1.	palliat*.ti,ab. ((ti,ab(commission* N/2 (support* or service* or model*)) OR ti,ab((service* or program* or co-ordinat* or coordinat*) N/2 (model* or deliver* or strateg* or support* or access* or method* or system* or policies or policy or availab*))) AND ((SU.EXACT("Care" OR "Clinical nursing" OR "Community homes" OR "Community nursery nursing" OR "Community nursing" OR "Compassionate care" OR "Continuing care" OR "District nursing" OR "Family centred care" OR "Geriatric wards" OR "Group care" OR "Health visiting" OR "Home care" OR "Home from home care" OR "Home health aides" OR "Home helps" OR "Hospices" OR "Hostel wards" OR "Informal care" OR "Integrated care pathways" OR "Intentional care" OR "Intermediate care" OR "Intermediate care centres" OR "Lack of care" OR "Learning disability nursing" OR "Length of stay" OR "Liaison nursing" OR "Long stay wards" OR "Long term care" OR "Long term home care" OR "Long term residential care" OR "Nurse led care" OR "Nursing" OR "Occupational health nursing" OR "Ontological care" OR "Out of home care" OR "Outreach nursing" OR "Palliative care" OR "Paranursing" OR "Pastoral care" OR "Patient care" OR "Primary nursing" OR "Private residential care" OR "Process centred care" OR "Quality of care" OR "Radical health visiting" OR "Residential care" OR "Residential group care" OR "Respite care" OR "Shared care" OR "Social care" "Temporary care" OR "Terminal care" OR "Wards") OR (SU.EXACT("Terminally ill elderly people") OR SU.EXACT("Terminally ill fathers") OR SU.EXACT("Terminally ill elderly men") OR SU.EXACT("Terminally ill elderly women") OR SU.EXACT("Terminally ill young adults") OR SU.EXACT("Terminally ill parents") OR SU.EXACT("Terminally ill women") OR SU.EXACT("Terminally ill widowed sisters") OR SU.EXACT("Terminally ill colleagues") OR SU.EXACT("Terminally ill young girls") OR SU.EXACT("Terminally ill people") OR SU.EXACT("Terminally ill men")) OR SU.EXACT("Advance directives" OR "Do not resuscitate orders" OR "Durable power of attorney for health care" OR "Living wills" OR "Treatment preferences" OR "Treatment needs")) OR (ti,ab((advance* or patient*) N/3 (care or caring) N/3 (continu* or plan*)) or ti,ab(attitude* N/3 (death* or dying*)) or ti,ab(end N/2 life) or ti,ab(EOLC) or ti,ab((last or final) N/2 (year or month*) N/2 life) or ti,ab((dying or death) N/2 (patient* or person* or people or care or caring))))) OR SU.EXACT("End of life decisions")

B.2 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to end of life care in NHS Economic Evaluation Database (NHS EED – this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA) with no date restrictions. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase for health economics, economic modelling and quality of life studies.

Table 13: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	2014 – 04 January 2019	Exclusions Health economics studies

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Database	Dates searched	Search filter used
		Health economics modelling studies Quality of life studies
Embase	2014 – 04 January 2019	Exclusions Health economics studies Health economics modelling studies Quality of life studies
Centre for Research and Dissemination (CRD)	HTA - Inception – 04 January 2019 NHSEED - Inception to March 2015	None

Medline (Ovid) search terms

1.	Palliative care/
2.	Terminal care/
3.	Hospice care/
4.	palliat*.ti,ab.
5.	Terminally Ill/
6.	((terminal* or long term or longterm) adj2 (care* or caring or ill*)).ti,ab.
7.	((dying or terminal) adj (phase* or stage*)).ti,ab.
8.	life limit*.ti,ab.
9.	Nursing Homes/
10.	((care or nursing) adj2 (home or homes)).ti,ab.
11.	Respite Care/
12.	((respite or day) adj2 (care or caring)).ti,ab.
13.	Hospices/
14.	hospice*.ti,ab.
15.	exp Advance Care Planning/
16.	(advance* adj2 (plan* or decision* or directive*)).ti,ab.
17.	living will*.ti,ab.
18.	*Patient care planning/
19.	*"Continuity of Patient Care"/
20.	((advance* or patient*) adj3 (care or caring) adj3 (continu* or plan*)).ti,ab.
21.	*Attitude to Death/
22.	(attitude* adj3 (death* or dying*)).ti,ab.
23.	*Physician-Patient Relations/
24.	*Long-Term Care/
25.	*"Delivery of Health Care"/
26.	(end adj2 life).ti,ab.
27.	EOLC.ti,ab.
28.	((last or final) adj2 (year or month*) adj2 life).ti,ab.
29.	((dying or death) adj2 (patient* or person* or people or care or caring)).ti,ab.
30.	or/1-29
31.	letter/

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32.	editorial/
33.	news/
34.	exp historical article/
35.	Anecdotes as Topic/
36.	comment/
37.	case report/
38.	(letter or comment*).ti.
39.	or/31-38
40.	randomized controlled trial/ or random*.ti,ab.
41.	39 not 40
42.	animals/ not humans/
43.	exp Animals, Laboratory/
44.	exp Animal Experimentation/
45.	exp Models, Animal/
46.	exp Rodentia/
47.	(rat or rats or mouse or mice).ti.
48.	or/41-47
49.	30 not 48
50.	limit 49 to English language
51.	(exp child/ or exp pediatrics/ or exp infant/) not (exp adolescent/ or exp adult/ or exp middle age/ or exp aged/)
52.	50 not 51
53.	economics/
54.	value of life/
55.	exp "costs and cost analysis"/
56.	exp Economics, Hospital/
57.	exp Economics, medical/
58.	Economics, nursing/
59.	economics, pharmaceutical/
60.	exp "Fees and Charges"/
61.	exp budgets/
62.	budget*.ti,ab.
63.	cost*.ti.
64.	(economic* or pharmaco?economic*).ti.
65.	(price* or pricing*).ti,ab.
66.	(cost* adj2 (effectiv* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
67.	(financ* or fee or fees).ti,ab.
68.	(value adj2 (money or monetary)).ti,ab.
69.	or/53-68
70.	exp models, economic/
71.	*Models, Theoretical/
72.	*Models, Organizational/
73.	markov chains/
74.	monte carlo method/
75.	exp Decision Theory/

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76.	(markov* or monte carlo).ti,ab.
77.	econom* model*.ti,ab.
78.	(decision* adj2 (tree* or analy* or model*)).ti,ab.
79.	or/70-78
80.	quality-adjusted life years/
81.	sickness impact profile/
82.	(quality adj2 (wellbeing or well being)).ti,ab.
83.	sickness impact profile.ti,ab.
84.	disability adjusted life.ti,ab.
85.	(qal* or qtime* or qwb* or daly*).ti,ab.
86.	(euroqol* or eq5d* or eq 5*).ti,ab.
87.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
88.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
89.	(hui or hui1 or hui2 or hui3).ti,ab.
90.	(health* year* equivalent* or hye or hyes).ti,ab.
91.	discrete choice*.ti,ab.
92.	rosser.ti,ab.
93.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
94.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
95.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
96.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
97.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
98.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
99.	or/80-98
100.	52 and (69 or 79 or 99)

Embase (Ovid) search terms

1.	*Palliative therapy/
2.	*Terminal care/
3.	*Hospice care/
4.	palliat*.ti,ab.
5.	*Terminally ill patient/
6.	((terminal* or long term or longterm) adj2 (care* or caring or ill*)).ti,ab.
7.	((dying or terminal) adj (phase* or stage*)).ti,ab.
8.	life limit*.ti,ab.
9.	*Nursing home/
10.	((care or nursing) adj2 (home or homes)).ti,ab.
11.	*Respite Care/
12.	((respite or day) adj2 (care or caring)).ti,ab.
13.	*Hospice/
14.	hospice*.ti,ab.
15.	*Patient care planning/
16.	(advance* adj2 (plan* or decision* or directive*)).ti,ab.
17.	living will*.ti,ab.

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18.	*Patient care/
19.	((advance* or patient*) adj3 (care or caring) adj3 (continu* or plan*)).ti,ab.
20.	*Attitude to Death/
21.	(attitude* adj3 (death* or dying*)).ti,ab.
22.	*Doctor patient relation/
23.	*Long term care/
24.	*Health care delivery/
25.	(end adj2 life).ti,ab.
26.	EOLC.ti,ab.
27.	((last or final) adj2 (year or month*) adj2 life).ti,ab.
28.	((dying or death) adj2 (patient* or person* or people or care or caring)).ti,ab.
29.	or/1-28
30.	letter.pt. or letter/
31.	note.pt.
32.	editorial.pt.
33.	case report/ or case study/
34.	(letter or comment*).ti.
35.	or/30-34
36.	randomized controlled trial/ or random*.ti,ab.
37.	35 not 36
38.	animal/ not human/
39.	nonhuman/
40.	exp Animal Experiment/
41.	exp Experimental Animal/
42.	animal model/
43.	exp Rodent/
44.	(rat or rats or mouse or mice).ti.
45.	or/37-44
46.	29 not 45
47.	limit 46 to English language
48.	(exp child/ or exp pediatrics/ or exp infant/) not (exp adolescent/ or exp adult/ or exp middle age/ or exp aged/)
49.	47 not 48
50.	health economics/
51.	exp economic evaluation/
52.	exp health care cost/
53.	exp fee/
54.	budget/
55.	funding/
56.	budget*.ti,ab.
57.	cost*.ti.

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58.	(economic* or pharmaco?economic*).ti.
59.	(price* or pricing*).ti,ab.
60.	(cost* adj2 (effectiv* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
61.	(financ* or fee or fees).ti,ab.
62.	(value adj2 (money or monetary)).ti,ab.
63.	or/50-62
64.	statistical model/
65.	exp economic aspect/
66.	64 and 65
67.	*theoretical model/
68.	*nonbiological model/
69.	stochastic model/
70.	decision theory/
71.	decision tree/
72.	monte carlo method/
73.	(markov* or monte carlo).ti,ab.
74.	econom* model*.ti,ab.
75.	(decision* adj2 (tree* or analy* or model*)).ti,ab.
76.	or/66-75
77.	quality-adjusted life years/
78.	"quality of life index"/
79.	short form 12/ or short form 20/ or short form 36/ or short form 8/
80.	sickness impact profile/
81.	(quality adj2 (wellbeing or well being)).ti,ab.
82.	sickness impact profile.ti,ab.
83.	disability adjusted life.ti,ab.
84.	(qal* or qtime* or qwb* or daly*).ti,ab.
85.	(euroqol* or eq5d* or eq 5*).ti,ab.
86.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
87.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
88.	(hui or hui1 or hui2 or hui3).ti,ab.
89.	(health* year* equivalent* or hye or hyes).ti,ab.
90.	discrete choice*.ti,ab.
91.	rosser.ti,ab.
92.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
93.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
94.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
95.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
96.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
97.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.

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98.	or/77-97
99.	49 and (63 or 76 or 98)

NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Palliative Care IN NHSEED,HTA
#2.	MeSH DESCRIPTOR Terminal Care IN NHSEED,HTA
#3.	MeSH DESCRIPTOR Hospice Care IN NHSEED,HTA
#4.	(palliat*) IN NHSEED, HTA
#5.	MeSH DESCRIPTOR Terminally Ill IN NHSEED,HTA
#6.	(((terminal* or long term or longterm) adj2 (care* or caring or ill*))) IN NHSEED, HTA
#7.	(((dying or terminal) adj (phase* or stage*))) IN NHSEED, HTA
#8.	(life limit*) IN NHSEED, HTA
#9.	MeSH DESCRIPTOR Nursing Homes IN NHSEED,HTA
#10.	(((care or nursing) adj2 (home or homes))) IN NHSEED, HTA
#11.	MeSH DESCRIPTOR Respite Care IN NHSEED,HTA
#12.	(((respite or day) adj2 (care or caring))) IN NHSEED, HTA
#13.	MeSH DESCRIPTOR Hospices IN NHSEED,HTA
#14.	(hospice*) IN NHSEED, HTA
#15.	MeSH DESCRIPTOR Advance Care Planning EXPLODE ALL TREES IN NHSEED,HTA
#16.	((advance* adj2 (plan* or decision* or directive*))) IN NHSEED, HTA
#17.	(living will*) IN NHSEED, HTA
#18.	MeSH DESCRIPTOR Patient Care Planning IN NHSEED,HTA
#19.	MeSH DESCRIPTOR Continuity of Patient Care IN NHSEED,HTA
#20.	(((advance* or patient*) adj3 (care or caring) adj3 (continu* or plan*))) IN NHSEED, HTA
#21.	MeSH DESCRIPTOR Attitude to Death IN NHSEED,HTA
#22.	((attitude* adj3 (death* or dying*))) IN NHSEED, HTA
#23.	MeSH DESCRIPTOR Physician-Patient Relations IN NHSEED,HTA
#24.	MeSH DESCRIPTOR Long-Term Care IN NHSEED,HTA
#25.	MeSH DESCRIPTOR Delivery of Health Care IN NHSEED,HTA
#26.	((end adj2 life)) IN NHSEED, HTA
#27.	(EOLC) IN NHSEED, HTA
#28.	(((last or final) adj2 (year or month*) adj2 life)) IN NHSEED, HTA
#29.	(((dying or death) adj2 (patient* or person* or people or care or caring))) IN NHSEED, HTA
#30.	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29
#31.	(#30) IN NHSEED
#32.	(#30) IN HTA

.

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Appendix C: Clinical evidence selection

Figure 1: Flow chart of clinical study selection for the review of information sharing

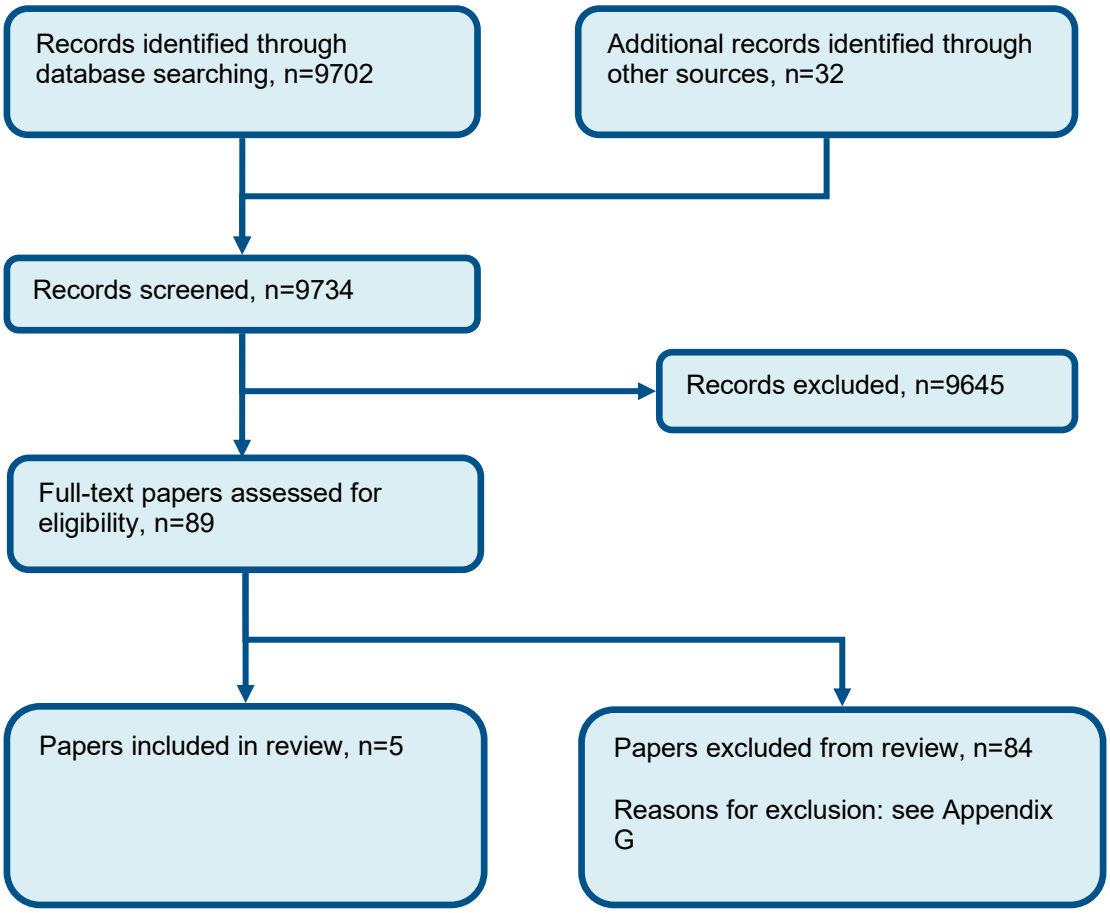

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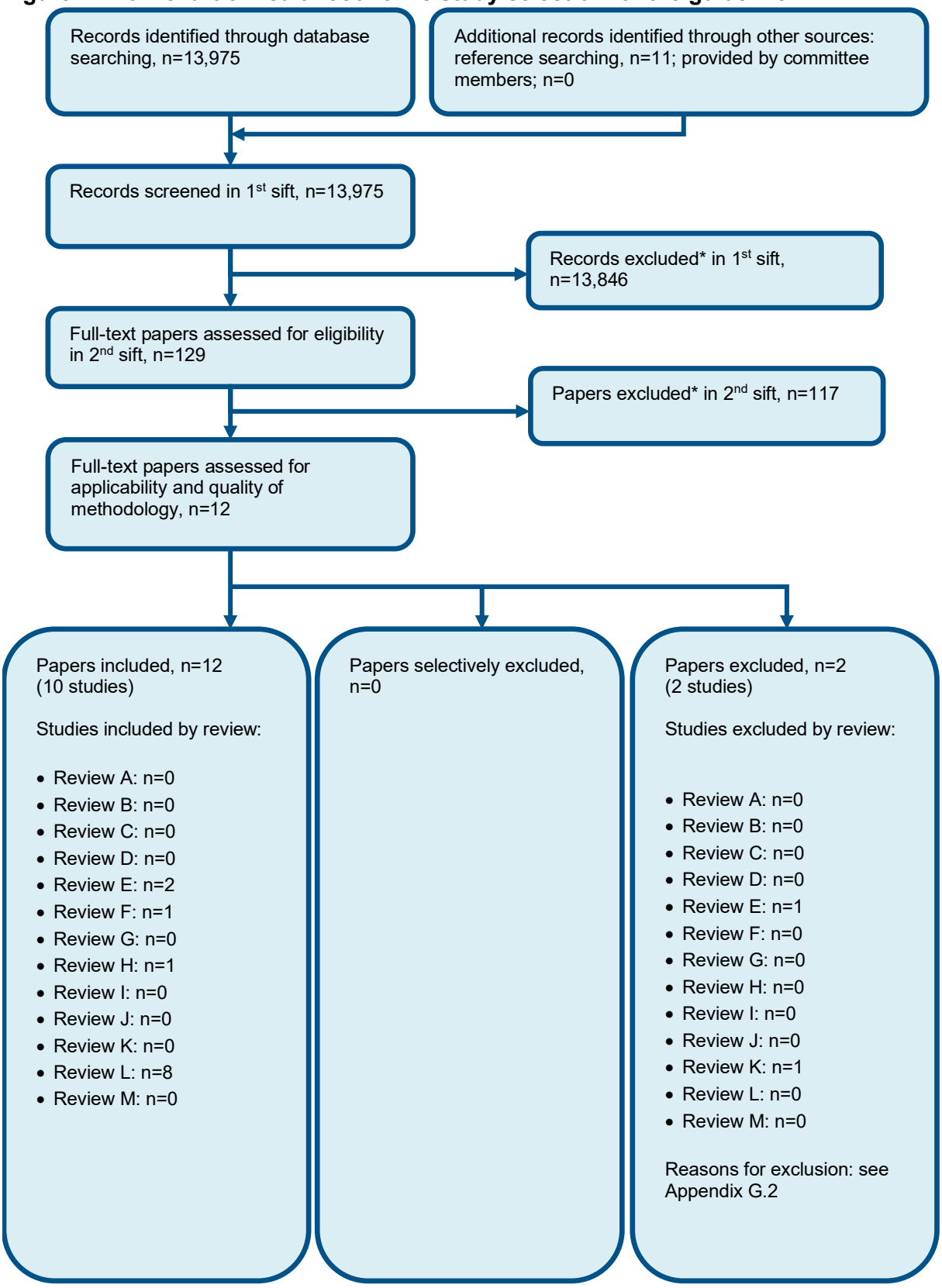
Figure 2: Flow chart of health economic study selection for the guideline



* Non-relevant population, intervention, comparison, design or setting; non-English language

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Appendix D: Clinical evidence tables

Study	Amano 2015[3]
Study type	Non-randomised comparative study
Number of studies (number of participants)	1 (n=265)
Countries and setting	Conducted in Japan; Setting: Cancer-designated hospital in Japan
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 1 year (2013/2014)
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Adults (aged 18 years or over)
Subgroup analysis within study	Not applicable
Inclusion criteria	Adults and patients who died from cancer or cause related to cancer during the study
Exclusion criteria	One patient who had been treated with high dose betamethasone for rheumatoid arthritis and died from infection was excluded
Recruitment/selection of patients	Consecutive cancer decedents
Age, gender and ethnicity	Age - Mean (SD): intervention group 65(15), control group 69(11). Gender (M:F): 159/106. Ethnicity: not stated
Further population details	1. Any specific population: Not applicable
Extra comments	Most common type of cancer was lung followed by gastric in both groups
Indirectness of population	No indirectness
Interventions	(n=54) Intervention 1: Early referral to (or provision of) palliative care services. Early palliative care referral (> 3 months before death). The palliative care team provided consultation services in both outpatients and inpatients suffering from cancer on the basis of referral from primary responsible physicians. The palliative care team consisted of two palliative physicians and 3 certified palliative care nurses. All patients were followed at least once per week, and the palliative care physician prescribed or gave written recommendations of medication. All patients were monitored continuously until death or transfer to another institution. Duration > 3 months. Concurrent medication/care: Not stated. (n=211) Intervention 2: Late referral to (or provision of) palliative care services. Late referral to palliative care

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Study	Amano 2015[3]
	services (< 3 months). The palliative care team provided consultation services in both outpatients and inpatients suffering from cancer on the basis of referral from primary responsible physicians. The palliative care team consisted of two palliative physicians and 3 certified palliative care nurses. All patients were followed at least once per week, and the palliative care physician prescribed or gave written recommendations of medication. All patients were monitored continuously until death or transfer to another institution. Duration < 3 months. Concurrent medication/care: Not stated
Funding	No funding (Authors received no financial support for the research, authorship and publication of this article)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: EARLY REFERRAL TO PALLIATIVE CARE SERVICES (> 3 MONTHS) versus LATE REFERRAL TO PALLIATIVE CARE SERVICES (< 3 MONTHS)

Protocol outcome 1: Number of visits to accident and emergency
- Actual outcome for Adults (aged 18 years or over): ≥ 2 emergency department visits within last 30 days of life; Group 1: 6/54, Group 2: 10/211; Risk of bias: High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness. Baseline details: Groups were different in terms of age

Protocol outcome 2: Number of unscheduled admissions
- Actual outcome for Adults (aged 18 years or over): ≥ 2 hospital admissions within last 30 days of life; Group 1: 2/54, Group 2: 19/211; Risk of bias: High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: Serious indirectness. Comments: no details on the admissions being unscheduled; Baseline details: Groups were different in terms of age
- Actual outcome for Adults (aged 18 years or over): Hospitalisation for ≥14 days within last 30 days of life; Group 1: 29/54, Group 2: 142/211; Risk of bias: High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness

Protocol outcome 3: Use of community services
- Actual outcome for Adults (aged 18 years or over): Inpatient hospice utilisation up to death; Group 1: 40/54, Group 2: 99/211; Risk of bias: High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness

Protocol outcome 4: Preferred and actual place of death
- Actual outcome for Adults (aged 18 years or over): Hospital death within last 30 days of life; Group 1: 54/54, Group 2: 211/211; Risk of bias: High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: Serious indirectness

Protocol outcome 5: Avoidable/inappropriate admissions to ICU

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Study	Amano 2015[3]
- Actual outcome for Adults (aged 18 years or over): Any ICU admission within last 30 days of life; Group 1: 3/54, Group 2: 21/211; Risk of bias: High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: Serious indirectness	
Protocol outcomes not reported by the study	Quality of life; Hospitalisation; Number of hospital visits; Length of survival; Staff satisfaction; Inappropriate resuscitation; Patient/carer reported outcomes (satisfaction); Preferred and actual place of care; Length of stay

Study	Bakitas 2015[7]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=207)
Countries and setting	Conducted in USA; Setting: Questionnaires administered by telephone.
Line of therapy	Adjunctive to current care
Duration of study	Other: October 2010 to March 2013
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Adults (aged 18 years or over)
Subgroup analysis within study	Not applicable
Inclusion criteria	Aged >18 years with advanced stage solid tumour or hematologic malignancy, oncologist-determined prognosis of 6-24 months, and able to complete baseline questionnaire.
Exclusion criteria	Impaired cognition, psychiatric or substance use disorder.
Recruitment/selection of patients	Research coordinators reviewed all outpatient Clinicians' schedules and tumour board (group of doctors and other health care providers with different specialties that meets regularly at the hospital to discuss cancer cases) lists using eligibility criteria.
Age, gender and ethnicity	Age - Mean (SD): 64(10). Gender (M:F): 109/98. Ethnicity: 96.5% White
Further population details	1. Any specific population: Not applicable
Indirectness of population	No indirectness
Interventions	(n=104) Intervention 1: Early referral to (or provision of) palliative care services. ENABLE - includes initial in-person, standardised outpatient palliative care (PC) consultation by a board certified PC clinician and six

Study	Bakitas 2015[7]
	structured weekly telephone coaching sessions by an advanced practice nurse using manualised curriculum (Charting Your Course). Session one to three focus on problem solving, symptom management, self-care, identification and coordination of local resources, communication, decision making, and advance care planning. Session four to six focused on outlook, a life review approach that encourages participants to frame advance illness challenges as personal growth opportunities. After the six sessions, monthly follow up calls reinforced prior content and identified new challenges or care coordination issues. Sessions generally lasted 30-45 minutes. Nurse coach training included self-study, review of treatment manuals and scripts, and role play with feedback. Received within 30 days of being informed of an advance cancer diagnosis. Duration October 2010 to March 2013. Concurrent medication/care: Usual oncology care. (n=103) Intervention 2: Late referral to (or provision of) palliative care services. ENABLE - includes initial in-person, standardised outpatient palliative care (PC) consultation by a board certified PC clinician and six structured weekly telephone coaching sessions by an advanced practice nurse using manualised curriculum (Charting Your Course). Session one to three focus on problem solving, symptom management, self-care, identification and coordination of local resources, communication, decision making, and advance care planning. Session four to six focused on outlook, a life review approach that encourages participants to frame advance illness challenges as personal growth opportunities. After the six sessions, monthly follow up calls reinforced prior content and identified new challenges or care coordination issues. Sessions generally lasted 30-45 minutes. Nurse coach training included self-study, review of treatment manuals and scripts, and role play with feedback. Received 3 months after being informed of an advance cancer diagnosis. Duration October 2010 to March 2013. Concurrent medication/care: Usual oncology care.
Funding	Academic or government funding (Grant from Nation Institute for Nursing research; a Cancer and Leukemia Group B Foundation Clinical Scholar Award; Foundation for informed medical decision)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: EARLY REFERRAL TO (OR PROVISION OF) PALLIATIVE CARE SERVICES versus LATE REFERRAL TO (OR PROVISION OF) PALLIATIVE CARE SERVICES

Protocol outcome 1: Quality of life
- Actual outcome for Adults (aged 18 years or over): FACET-Pal at 3 months ; Group 1: mean 129.9 (SD 14); n=72, Risk of bias: High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Group 1 number missing: 32, Group 2 number missing: 20
- Actual outcome for Adults (aged 18 years or over): FACET-Pal at 6 months ; Group 1: mean 129.9 (SD 14); n=57, Risk of bias: High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Group 1 number missing: 47, Group 2 number missing: 47
- Actual outcome for Adults (aged 18 years or over): FACET-Pal at 12 months ; Group 1: mean 129.9 (SD 14.4); n=29, Risk of bias: High, Selection -

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Study	Bakitas 2015[7]
Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Group 1 number missing: 75, Group 2 number missing: 75 Protocol outcome 2: Preferred and actual place of death - Actual outcome for Adults (aged 18 years or over): Participants who died at home ; Group 1: 27; n=50, Group 1: 28; n=60 Risk of bias: Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: Serious indirectness; Group 1 number missing: 54, Group 2 number missing: 43 Protocol outcome 3: Length of survival - Actual outcome for Adults (aged 18 years or over): survival ; Group 1: median 18.3; n=50, Group 1: median 11.8; n=59 Risk of bias: High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Hospitalisation; Number of hospital visits; Number of visits to accident and emergency; Number of unscheduled admissions; Use of community services; Preferred and actual place of death; Length of survival; Staff satisfaction; Avoidable/inappropriate admissions to ICU; Inappropriate resuscitation; Patient/carer reported outcomes (satisfaction); Preferred and actual place of care; Length of stay

Study	Hui 2014[35]
Study type	Non-randomised comparative study
Number of studies (number of participants)	1 (n=366)
Countries and setting	Conducted in USA; Setting: The Supportive Care Centre operated 5 days per week and saw approximately 25 patients per day. It was staffed by 2 palliative care specialists who were supported by an interdisciplinary team of nurses and a social worker.
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 1 year (2009-2010)
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Adults (aged 18 years or over):
Subgroup analysis within study	Not applicable
Inclusion criteria	All adult patients in the Houston area who died of advanced cancer between 9/1/2009 and 2/28/2010, who had received a palliative care referral, and had contact with the cancer centre within the last 3 months of life.
Exclusion criteria	Patients who transferred care to outside oncologists, relocated to another city or lost to follow-up

Study	Hui 2014[35]
Recruitment/selection of patients	The inclusion/exclusion criteria were specifically chosen such that the investigators were able to reliably capture their medical information in the last months of life
Age, gender and ethnicity	Age - Median (range): 61 (23-87). Gender (M:F): 174/192. Ethnicity: 228 white, 82 black, 53 Hispanic, 19 Asian, 4 others
Further population details	1. Any specific population: Not applicable
Extra comments	Most common type of cancer was gastrointestinal, followed by respiratory in both the intervention and control group.
Indirectness of population	No indirectness
Interventions	(n=120) Intervention 1: Early referral to (or provision of) palliative care services. Early referral to palliative care (> 3 months between first palliative care consultation and death). The Supportive Care Centre operated 5 days per week and saw approximately 25 patients per day. It was staffed by 2 palliative care specialists who were supported by an interdisciplinary team of nurses and a social worker. Patients referred to the palliative care mobile team in the inpatient setting were managed similarly by the same team of palliative care specialists following common clinical pathways. Duration > 3 months. Concurrent medication/care: Not stated Comments: The 3-month cut-off was chosen because the median time from referral to death to the outpatient clinic was 3 months. (n=246) Intervention 2: Late referral to (or provision of) palliative care services. Late referral to palliative care services (< 3 months between first palliative care consultation and death). The Supportive Care Centre operated 5 days per week and saw approximately 25 patients per day. It was staffed by 2 palliative care specialists who were supported by an interdisciplinary team of nurses and a social worker. Patients referred to the palliative care mobile team in the inpatient setting were managed similarly by the same team of palliative care specialists following common clinical pathways. Duration < 3 months. Concurrent medication/care: Not stated Comments: The 3-month cut-off was chosen because the median time from referral to death to the outpatient clinic was approximately 3 months. (n=68) Intervention 3: Early referral to (or provision of) palliative care services. Early referral to palliative care services (> 6 months between first palliative care consultation and death). The Supportive Care Centre operated 5 days per week and saw approximately 25 patients per day. It was staffed by 2 palliative care specialists who were supported by an interdisciplinary team of nurses and a social worker. Patients referred to the palliative care mobile team in the inpatient setting were managed similarly by the same team of palliative care specialists following common clinical pathways. Duration > 6 months. Concurrent medication/care: Not stated

Study	Hui 2014[35]
	Comments: The 6-month cut-off was chosen because the median time from referral to hospice to death was 6 months (n=298) Intervention 4: Late referral to (or provision of) palliative care services. Late referral to palliative care services (< 6 months from first consultation to death). The Supportive Care Centre operated 5 days per week and saw approximately 25 patients per day. It was staffed by 2 palliative care specialists who were supported by an interdisciplinary team of nurses and a social worker. Patients referred to the palliative care mobile team in the inpatient setting were managed similarly by the same team of palliative care specialists following common clinical pathways. Duration < 6 months. Concurrent medication/care: Not stated Comments: The 6 months cut-off was chosen as the median time from referral to hospice to death was approximately 6 months
Funding	Other (No relevant financial disclosure for all authors)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: EARLY REFERRAL TO PALLIATIVE CARE SERVICES (> 3 MONTHS BEFORE DEATH) versus LATE REFERRAL TO PALLIATIVE CARE SERVICES (<3 MONTHS BEFORE DEATH)

Protocol outcome 1: Hospitalisation
- Actual outcome for Adults (aged 18 years or over): People with more than 14 days of hospitalisation within 30 days of life; Group 1: 14/120, Group 2: 40/246; Risk of bias: High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness

Protocol outcome 2: Number of visits to accident and emergency
- Actual outcome for Adults (aged 18 years or over): People with any number of emergency room visit within 30 days of life; Group 1: 47/120, Group 2: 168/246; Risk of bias: High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness
- Actual outcome for Adults (aged 18 years or over): People with 2 or more number of emergency room visits within 30 days of life; Group 1: 12/120, Group 2: 57/246; Risk of bias: High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness

Protocol outcome 3: Number of unscheduled admissions
- Actual outcome for Adults (aged 18 years or over): People with any hospital admission within 30 days of life; Group 1: 58/120, Group 2: 200/246; Risk of bias: High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: Serious indirectness
- Actual outcome for Adults (aged 18 years or over): People with 2 or more hospital admissions within 30 days of life; Group 1: 12/120, Group 2: 52/246; Risk of bias: High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;

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Study	Hui 2014[35]
Indirectness of outcome: Serious indirectness Protocol outcome 4: Preferred and actual place of death - Actual outcome for Adults (aged 18 years or over): Hospital death within 30 days of life; Group 1: 20/120, Group 2: 77/246; Risk of bias: High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: Serious indirectness - Actual outcome for Adults (aged 18 years or over): ICU death within 30 days of life; Group 1: 3/120, Group 2: 10/246; Risk of bias: High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: Serious indirectness Protocol outcome 5: Avoidable/inappropriate admissions to ICU - Actual outcome for Adults (aged 18 years or over): People with any ICU admission within 30 days of life; Group 1: 7/120, Group 2: 28/246; Risk of bias: High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: Serious indirectness RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: EARLY REFERRAL TO PALLIATIVE CARE SERVICES (> 6 MONTHS BEFORE DEATH) versus LATE REFERRAL TO PALLIATIVE CARE SERVICES (< 6 MONTHS BEFORE DEATH) Protocol outcome 1: Hospitalisation - Actual outcome for Adults (aged 18 years or over): People with more than 14 days of hospitalisation at within 30 days of life; Group 1: 7/68, Group 2: 47/298; Risk of bias: High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness Protocol outcome 2: Number of visits to accident and emergency - Actual outcome for Adults (aged 18 years or over): People with any number of emergency room visit at within 30 days of life; Group 1: 28/68, Group 2: 187/298; Risk of bias: High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness - Actual outcome for Adults (aged 18 years or over): People with 2 or more number of emergency room visits at within 30 days of life; Group 1: 6/68, Group 2: 63/298; Risk of bias: High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness Protocol outcome 3: Number of unscheduled admissions - Actual outcome for Adults (aged 18 years or over): People with any hospital admission at within 30 days of life; Group 1: 35/68, Group 2: 223/298; Risk of bias: High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: Serious indirectness - Actual outcome for Adults (aged 18 years or over): People with 2 or more hospital admissions at within 30 days of life; Group 1: 9/68, Group 2: 55/298; Risk of bias: High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low;	

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Study	Hui 2014[35]
Indirectness of outcome: Serious indirectness Protocol outcome 4: Preferred and actual place of death - Actual outcome for Adults (aged 18 years or over): Hospital death within 30 days of life; Group 1: 12/68, Group 2: 85/298; Risk of bias: High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: Serious indirectness - Actual outcome for Adults (aged 18 years or over): ICU death within 30 days of life; Group 1: 2/68, Group 2: 11/298; Risk of bias: High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: Serious indirectness Protocol outcome 5: Avoidable/inappropriate admissions to ICU - Actual outcome for Adults (aged 18 years or over): People with any ICU admission at within 30 days of life; Group 1: 5/68, Group 2: 30/298; Risk of bias: High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: Serious indirectness	
Protocol outcomes not reported by the study	Quality of life; Number of hospital visits; Use of community services; Length of survival; Staff satisfaction; Inappropriate resuscitation; Patient/carer reported outcomes (satisfaction); Preferred and actual place of care; Length of stay.

Study	Nieder 2016[64]
Study type	Non-randomised comparative study
Number of studies (number of participants)	1 (n=286)
Countries and setting	Conducted in Norway; Setting: Nordland Hospital Trust area.
Line of therapy	Not applicable
Duration of study	Other: January 1, 2006 to December 31, 2014
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Retrospective study of all patients who died from Non-small cell lung cancer. The majority of the patients (67%) died within 12 months from diagnosis.
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	All patients who died from NSCLC.
Exclusion criteria	Not reported

Study	Nieder 2016[64]
Recruitment/selection of patients	Used electronic patient records of Nordland Hospital Trust to identify all patients treated for histologically confirmed NSCLC and selected those who died from their disease during the time period January 1, 2006 to December 31, 2014. The initial diagnosis could have been made earlier.
Age, gender and ethnicity	Age - Median (range): 64 (47-89) early palliative care group; 66 (48-89) late palliative care. Gender (M:F): 59/40. Ethnicity: Not reported
Further population details	1. Any specific population: Not applicable
Indirectness of population	Serious indirectness: Only 67% died within 12 months from diagnosis.
Interventions	(n=22) Intervention 1: Early referral to (or provision of) palliative care services. Palliative care team involved 3 months before death or earlier. Duration Not applicable. Concurrent medication/care: Not reported. Indirectness: No indirectness Comments: Unclear earliest palliative care. (n=77) Intervention 2: Late referral to (or provision of) palliative care services. Palliative Care Team involved only during the last phase of the incurable disease, < 3 months. Duration Not applicable. Concurrent medication/care: Not reported. Indirectness: No indirectness
Funding	No funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: EARLY REFERRAL TO (OR PROVISION OF) PALLIATIVE CARE SERVICES versus LATE REFERRAL TO (OR PROVISION OF) PALLIATIVE CARE SERVICES

Protocol outcome 1: Hospitalisation
- Actual outcome: Hospitalisation in the last three months of life; Group 1: 16/22 (73%), Group 2: 75/77 (97%)
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness; Baseline details: Significantly different age reported and number of treatment lines. However this significant difference also includes the analysis for patients who received no palliative care as well

Protocol outcome 2: Preferred and actual place of death
- Actual outcome: Hospital death; Group 1: 7/22 (32%), Group 2: 37/77 (48%)
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: Serious indirectness, Comments: Place of death reported but does not report preferred place of death for comparison; Baseline details: Significantly different age reported and number of treatment lines. However this significant difference also includes the analysis for patients who received no palliative care as well

Protocol outcome 3: length of survival

Study	Nieder 2016[64]
- Actual outcome: Overall survival; Group 1: Median 14.0 months Group 2: Median 6.7 months, p=0.001 Risk of bias: All domain – Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness; Baseline details: Significantly different age reported and number of treatment lines. However this significant difference also includes the analysis for patients who received no palliative care as well	
Protocol outcomes not reported by the study	Quality of life; Number of hospital visits; Number of visits to accident and emergency; Number of unscheduled admissions; Use of community services; Preferred and actual place of death; Staff satisfaction; Avoidable/inappropriate admissions to ICU; Inappropriate resuscitation; Patient/carer reported outcomes (satisfaction); Length of stay

Study	Poulose 2013[68]
Study type	Non-randomised comparative study
Number of studies (number of participants)	1 (n=842)
Countries and setting	Conducted in China; Setting: National Cancer Centre Singapore.
Line of therapy	Not applicable
Duration of study	Other: January 1, 2007, to December 31, 2007
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Retrospective study of all patients who died following referral to specialist palliative care. 86.6% of patients had a diagnosis of terminal cancer. Median time of death was 29 days after referral.
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Decedents who were referred to and seen by the palliative care specialists.
Exclusion criteria	Not reported
Recruitment/selection of patients	Used electronic patient records of National Cancer Centre Singapore to identify all patients referred to the service from January 1, 2007, to December 31, 2007, and seen by the palliative care specialists.
Age, gender and ethnicity	Age - Median (range): 67 (13-101). Gender (M:F): 405/437. Ethnicity: Chinese 87%
Further population details	1. Any specific population: Not applicable
Indirectness of population	Serious indirectness: Median time from referral to death 29 day – range 1-1235.
Interventions	(n=NA) Intervention 1: Early referral to (or provision of) palliative care services. Palliative care referral ≥30 days before death. Duration Not applicable. Concurrent medication/care: Not reported. Indirectness: No indirectness Comments: Number of patients with early referral not reported

Study	Poulose 2013[68]
	(n=NA) Intervention 2: Late referral to (or provision of) palliative care services. Palliative care referral <30 days before death. Duration Not applicable. Concurrent medication/care: Not reported. Indirectness: No indirectness. Comments: Number of patients with late referral not reported
Funding	Dr. Do was supported by an A*STAR infrastructure grant to the Program in Health Services and Systems Research, Duke-NUS Graduate Medical School Singapore.
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: EARLY REFERRAL TO (OR PROVISION OF) PALLIATIVE CARE SERVICES versus LATE REFERRAL TO (OR PROVISION OF) PALLIATIVE CARE SERVICES Protocol outcome 1: Preferred and actual place of death - Actual outcome for Adults (aged 18 years or over): Home death (males); Group 1: OR 2.21 (1.34-3.67), Group 2: OR 1; Risk of bias: High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: Serious indirectness - Actual outcome for Adults (aged 18 years or over): Home death (females); Group 1: OR 3.33 (2.07-5.35), Group 2: OR 1; Risk of bias: High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: Serious indirectness - Actual outcome for Adults (aged 18 years or over): Inpatient hospice death (males); Group 1: OR 2.02 (1.13-3.60), Group 2: OR 1; Risk of bias: High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: Serious indirectness - Actual outcome for Adults (aged 18 years or over): Inpatient hospice death (females); Group 1: OR 2.69 (1.55-4.66), Group 2: OR 1; Risk of bias: High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: Serious indirectness	
Protocol outcomes not reported by the study	Quality of life; Number of hospital visits; Number of visits to accident and emergency; Number of unscheduled admissions; Use of community services; Length of survival; Staff satisfaction; Avoidable/inappropriate admissions to ICU; Inappropriate resuscitation; Patient/carer reported outcomes (satisfaction); Length of stay

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Appendix E: Forest plots

E.1 Early referral to (or provision of) palliative care services versus late referral to (or provision of) palliative care services in people in their last year of life

E.1.1 Early (> 3 months between first palliative care consultation and death) versus late (< 3 months between first palliative care consultation and death) referral to palliative care services

Figure 3: Number of unscheduled admissions (inpatient hospice utilisation) up to death

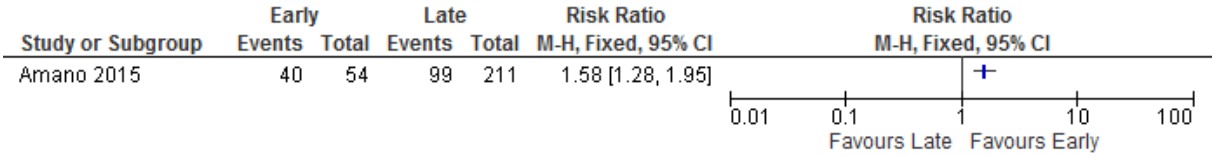

Figure 4: Preferred and actual place of death (Hospital deaths)

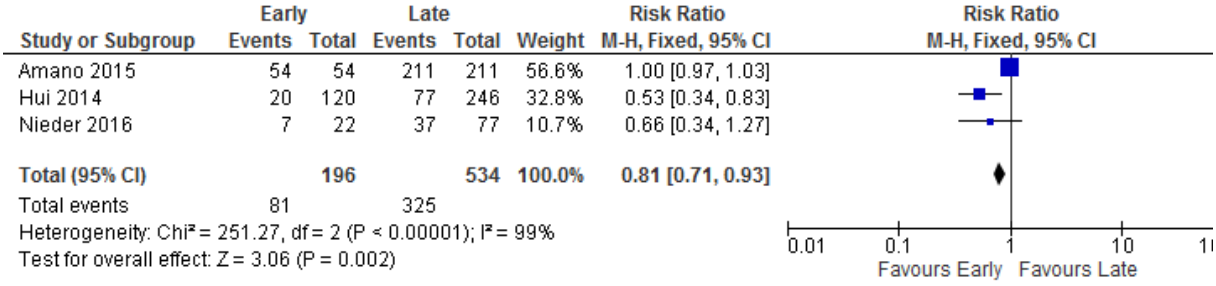

Figure 5: Number of visits to accident and emergency (People with ≥2 emergency room visits) within last 30 days of life

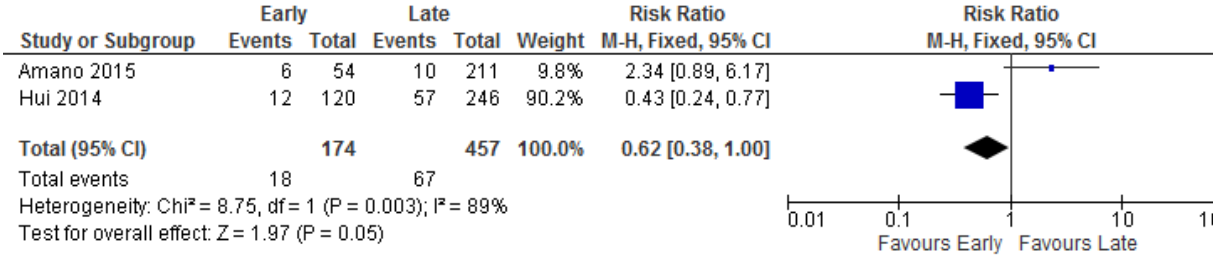

Figure 6: Number of unscheduled admissions at hospital (People with ≥2 hospital admissions) within last 30 days of life

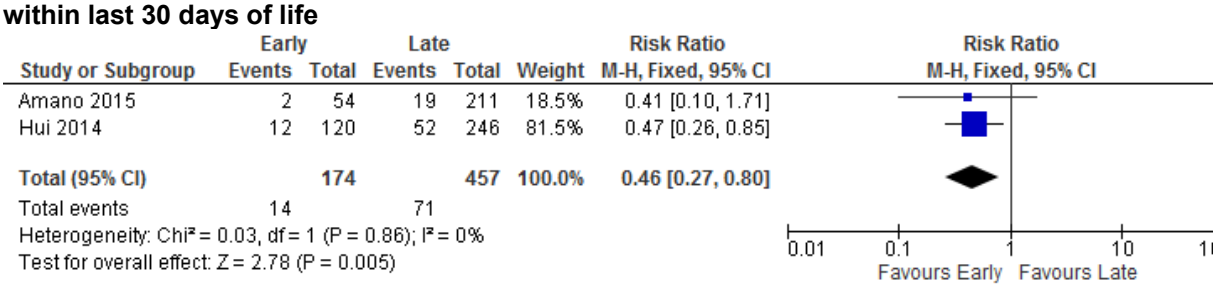

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Figure 7: Hospitalisation (People with >14 days of hospital admission) within last 30 days of life

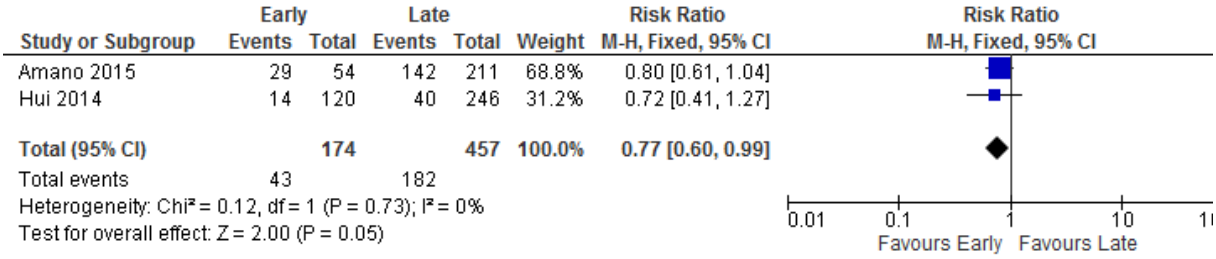


Figure 8: Avoidable/inappropriate admissions to ICU (People with any ICU admissions)

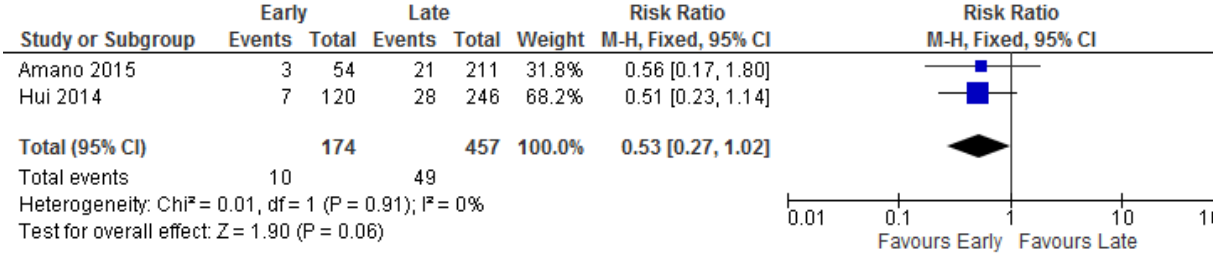


Figure 9: Number of visits to accident and emergency (people with any number of emergency room visits) within last 30 days of life

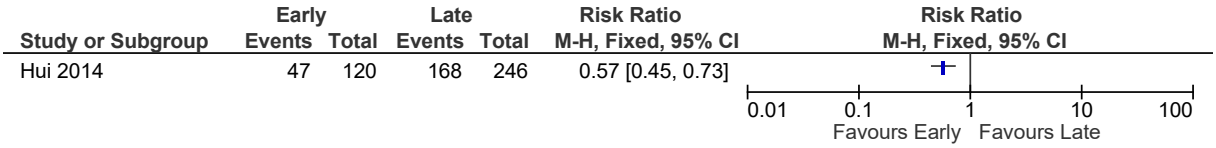


Figure 10: Number of unscheduled admissions at hospital (People with any number of hospital admissions) within last 30 days of life

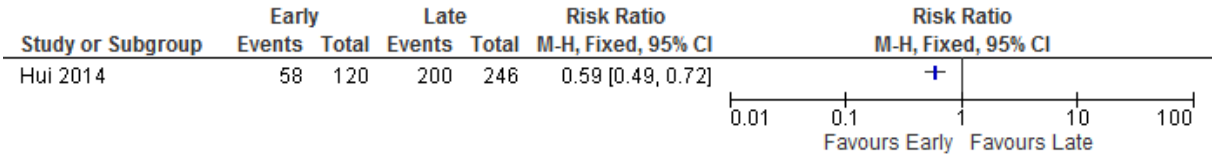


Figure 11: Preferred and actual place of death (ICU deaths)

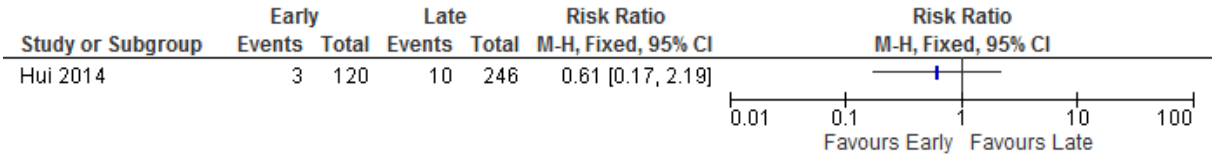
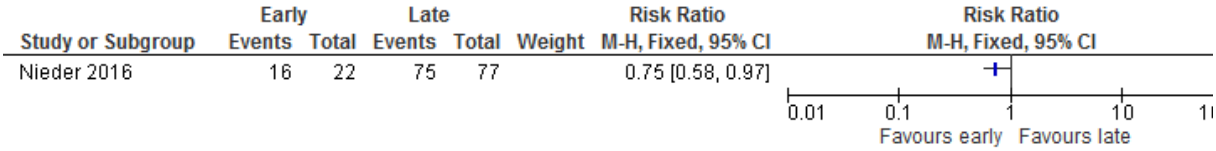


Figure 12: Hospitalisation (Hospitalised in the last 3 months of life)



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E.1.2 Early (within 30 days of diagnosis of advanced cancer) versus late (> 3 months of diagnosis of advanced cancer) referral to palliative care services

Figure 13: Quality of life at 3 months (FACET-Pal, 0-184)

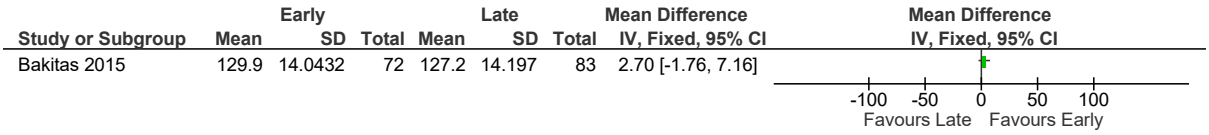


Figure 14: Quality of life at 6 months (FACET-Pal, 0-184)

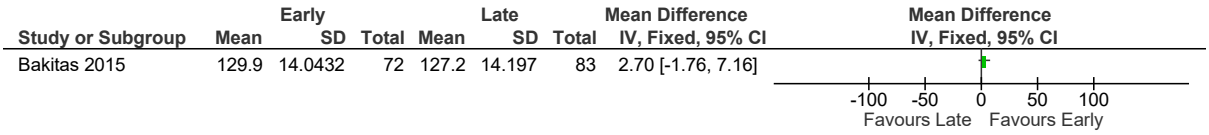


Figure 15: Quality of life at 12 months (FACET-Pal, 0-184)

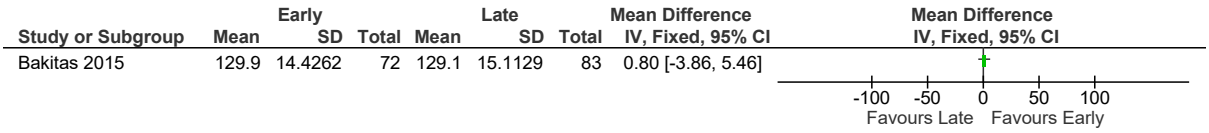
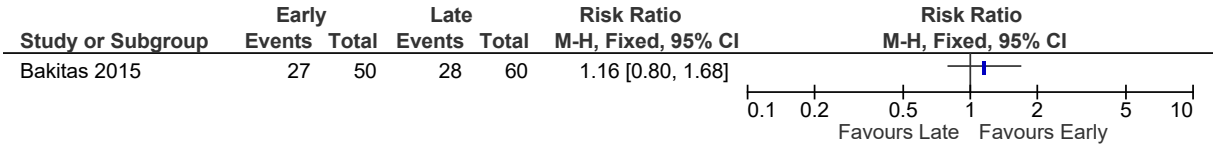


Figure 16: Place of death (participants who died at home)



E.1.4 Early (> 6 months between first palliative care consultation and death) versus late (< 6 months between first palliative care consultation and death) referral to palliative care services

Figure 17: Number of visits to accident and emergency (People with any number of emergency room visits) within last 30 days of life

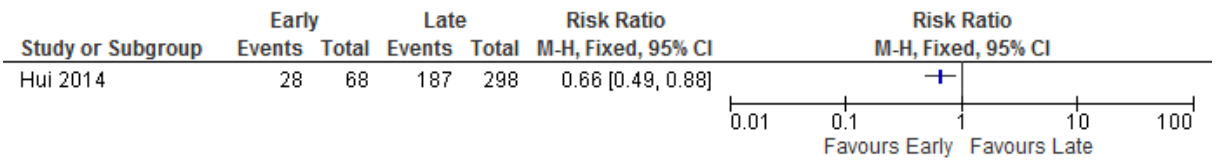


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Figure 18: Number of visits to accident and emergency (People with ≥2 emergency room visits) within last 30 days of life

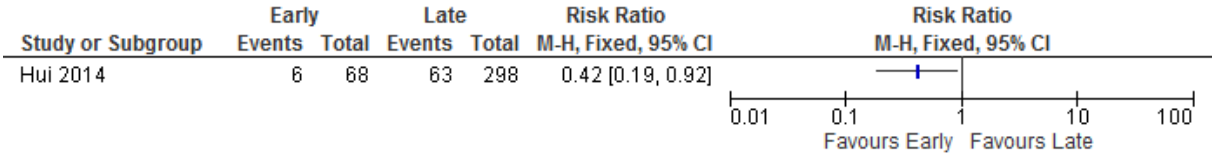


Figure 19: Number of unscheduled admissions at hospital (People with any number of hospital admissions) within last 30 days of life

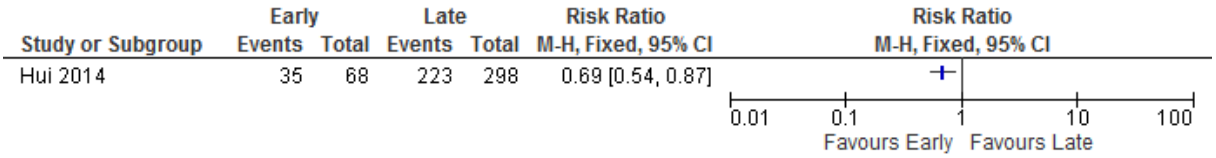


Figure 20: Number of unscheduled admissions at hospital (People with ≥2 hospital admissions) within last 30 days of life

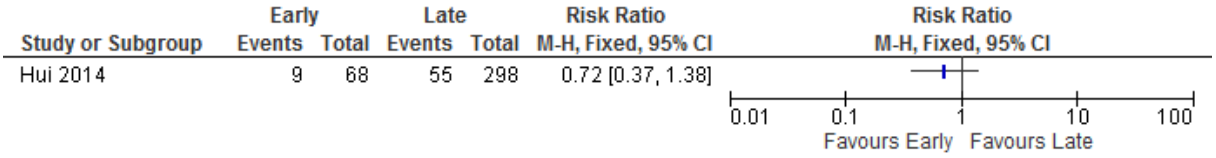


Figure 21: Hospitalisation (People with >14 days of hospital admission) within last 30 days of life

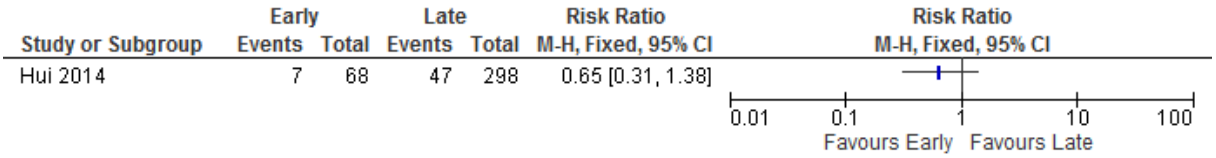


Figure 22: Preferred and actual place of death (Hospital deaths)

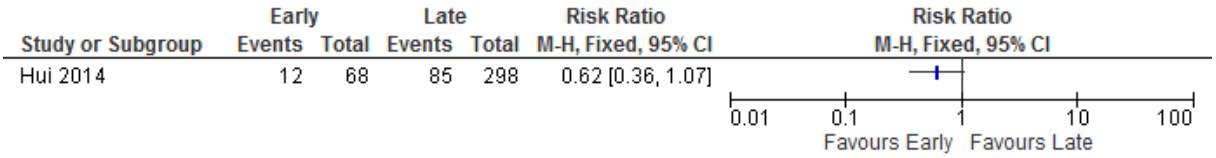


Figure 23: Preferred and actual place of death (ICU deaths)

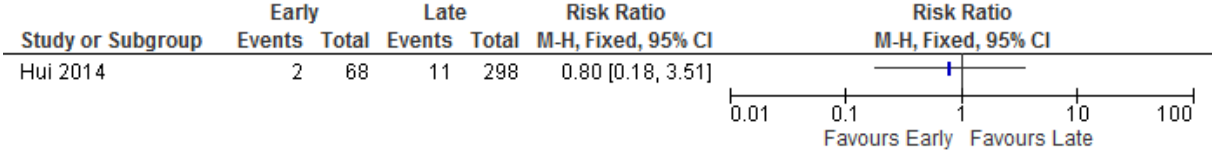
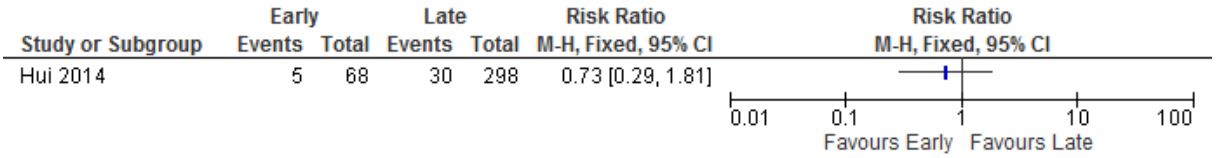


Figure 24: Avoidable/inappropriate admissions to ICU (People with any ICU admissions) within last 30 days of life



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E.1.6 Early (palliative care >30 days before death) versus late (palliative care <30 days before death)

Figure 25: Preferred and actual place of death (home deaths – male patients)

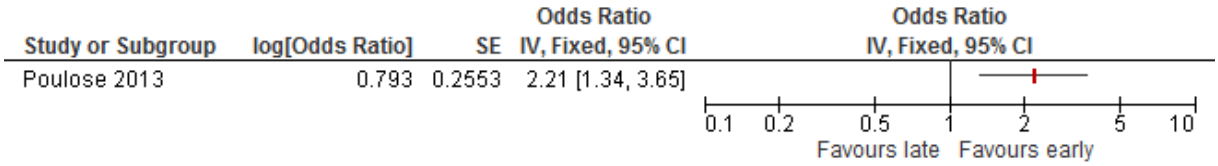


Figure 26: Preferred and actual place of death (home deaths – female patients)

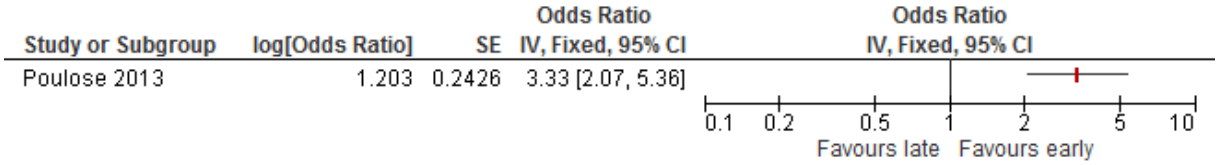


Figure 27: Preferred and actual place of death (inpatient hospice deaths – male patients)

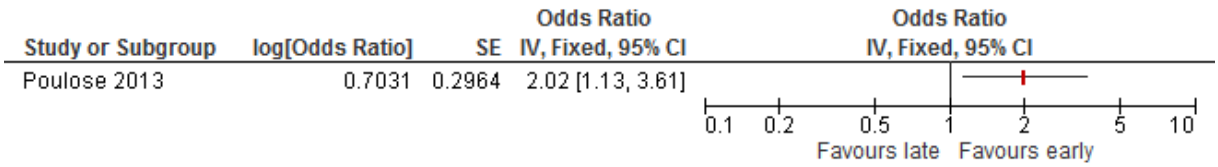
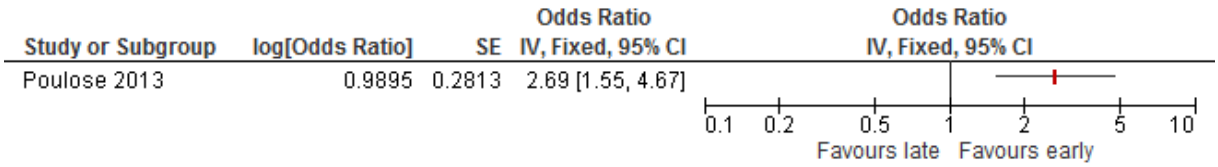


Figure 28: Preferred and actual place of death (inpatient hospice deaths – female patients)



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Appendix F: GRADE tables

Table 14: Clinical evidence profile: Early (> 3 months between first palliative care consultation and death) versus late (< 3 months between first palliative care consultation and death) referral to palliative care services

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	>3 months	<3 months	Relative (95% CI)	Absolute		
Number of unscheduled admissions (Inpatient hospice utilisation) (follow-up mean 1 year)												
1	observational studies[a]	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	40/54 (74.1%)	99/211 (46.9%)	RR 1.58 (1.28 to 1.95)	272 more per 1000 (from 131 more to 446 more)	⊕⊕OO LOW	IMPORTANT
Preferred and actual place of death (Hospital death) (follow-up mean 1 year)												
3	observational studies[a]	no serious risk of bias	no serious inconsistency	serious[b]	serious[c]	none	81/196 (41.3%)	325/534 (60.9%)	RR 0.81 (0.71 to 0.93)	116 fewer per 1000 (from 43 fewer to 176 fewer)	⊕OOO VERY LOW	CRITICAL
Number of visits to accident and emergency (People with ≥2 emergency room visits) (follow-up mean 1 year)												
2	observational studies[a]	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[c]	none	18/174 (10.3%)	67/457 (14.7%)	RR 0.62 (0.38 to 1)	56 fewer per 1000 (from 56 fewer to 0 more)	⊕OOO VERY LOW	IMPORTANT
Number of unscheduled admissions (People with ≥2 hospital admissions) (follow-up mean 1 year)												
2	observational studies[a]	no serious risk of bias	no serious inconsistency	serious[b]	serious[c]	None	14/174 (8%)	71/457 (15.5%)	RR 0.46 (0.27 to 0.8)	84 fewer per 1000 (from 31 fewer to 113 fewer)	⊕OOO VERY LOW	IMPORTANT
Hospitalisation (People with >14 days of hospitalisation) (follow-up mean 1 year)												

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2	observational studies[a]	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[c]	none	43/174 (24.7%)	182/457 (39.8%)	RR 0.77 (0.60 to 0.99)	92 fewer per 1000 (from 4 fewer to 159 fewer)	⊕OOO VERY LOW	IMPORTANT
Avoidable/inappropriate admissions to ICU (People with any ICU admission) (follow-up mean 1 year)												
2	observational studies[a]	no serious risk of bias	no serious inconsistency	serious[b]	very serious[c]	None	10/174 (5.7%)	49/457 (10.7%)	RR 0.53 (0.27 to 1.02)	50 fewer per 1000 (from 78 fewer to 2 more)	⊕OOO VERY LOW	IMPORTANT
Number of visits to accident and emergency (People with any number of emergency room visits)												
1	observational studies[a]	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	None	47/120 (39.2%)	168/246 (68.3%)	RR 0.57 (0.45 to 0.73)	294 fewer per 1000 (from 184 fewer to 376 fewer)	⊕⊕OO LOW	IMPORTANT
Number of unscheduled admissions (People with any hospital admission) (follow-up mean 1 year)												
1	observational studies[a]	no serious risk of bias	no serious inconsistency	serious[b]	no serious imprecision	None	58/120 (48.3%)	200/246 (81.3%)	RR 0.59 (0.49 to 0.72)	333 fewer per 1000 (from 228 fewer to 415 fewer)	⊕OOO VERY LOW	IMPORTANT
Preferred and actual place of death (ICU death) (follow-up mean 1 year)												
1	observational studies[a]	no serious risk of bias	no serious inconsistency	serious[b]	very serious[c]	none	3/120 (2.5%)	10/246 (4.1%)	RR 0.62 (0.17 to 2.19)	15 fewer per 1000 (from 34 fewer to 48 more)	⊕OOO VERY LOW	CRITICAL
Hospitalised in last 3 months of life (follow-up mean 1 year)												
1	observational studies[a]	very serious[1]	no serious inconsistency	no serious indirectness	serious[c]	none	16/22 (72.7%)	75/77 (97.4%)	RR 0.75 (0.58 to 0.97)	244 fewer per 1000 (from 29 fewer to 409 fewer)	⊕OOO VERY LOW	IMPORTANT

[a] Downgraded by 2 increments if the majority of the evidence was from studies with observational/non-randomised study design
[b] Downgraded by 1 increment because the majority of the evidence had indirect outcomes
[c] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

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Table 15: Clinical evidence profile: Early (> 30 days between diagnosis and referral) versus late (< 3 months between diagnosis and referral) referral to palliative care services

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Early	Late	Relative (95% CI)	Absolute		
Quality of life (FACIT-PAL) (follow-up mean 3 months; range of scores: 0-184; Better indicated by higher values)												
1	randomised trials	serious[a]	no serious inconsistency	no serious indirectness	serious[b]	none	72	83	-	MD 2.7 higher (1.76 lower to 7.16 higher)	⊕⊕OO LOW	CRITICAL
Quality of life (FACIT-PAL) (follow-up mean 6 months; range of scores: 0-184; Better indicated by higher values)												
1	randomised trials	serious[a]	no serious inconsistency	no serious indirectness	serious[b]	none	72	83	-	MD 2.7 higher (1.76 lower to 7.16 higher)	⊕⊕OO LOW	CRITICAL
Quality of life (FACIT-PAL) (follow-up mean 12 months; range of scores: 0-184; Better indicated by lower values)												
1	randomised trials	serious[a]	no serious inconsistency	no serious indirectness	serious[b]	none	72	83	-	MD 0.8 higher (3.86 lower to 5.46 higher)	⊕⊕OO LOW	CRITICAL
Preferred and actual place of death (participants who died at home) (follow-up until death)												
1	randomised trials	no serious risk of bias	no serious inconsistency	serious[c]	serious[b]	none	27/50 (54%)	28/60 (46.7%)	RR 1.16 (0.8 to 1.68)	75 more per 1000 (from 93 fewer to 317 more)	⊕⊕OO LOW	CRITICAL

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[b] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
[c] Downgraded by 1 increment because the majority of the evidence had indirect outcomes

Table 16: Clinical evidence profile: Early (> 6 months between first palliative care consultation and death) versus late (< 6months between first palliative care consultation and death) referral to palliative care services

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Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Early	Late	Relative (95% CI)	Absolute		
Number of visits to accident and emergency (People with any number of emergency room visits) (>6 months versus <6 months) (follow-up mean 1 years)												
1	observational studies[a]	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[b]	none	28/68 (41.2%)	187/298 (62.8%)	RR 0.66 (0.49 to 0.88)	213 fewer per 1000 (from 75 fewer to 320 fewer)	⊕OOO VERY LOW	IMPORTANT
Number of visits to accident and emergency (People with ≥2 emergency room visits) (>6 months versus <6 months) (follow-up mean 1 years)												
1	observational studies[a]	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[b]	none	6/68 (8.8%)	63/298 (21.1%)	RR 0.42 (0.19 to 0.92)	123 fewer per 1000 (from 17 fewer to 171 fewer)	⊕OOO VERY LOW	IMPORTANT
Number of unscheduled admissions (People with any hospital admission) (>6 months versus <6 months) (follow-up mean 1 years)												
1	observational studies[a]	no serious risk of bias	no serious inconsistency	serious[c]	serious[b]	none	35/68 (51.5%)	223/298 (74.8%)	RR 0.69 (0.54 to 0.87)	232 fewer per 1000 (from 97 fewer to 344 fewer)	⊕OOO VERY LOW	IMPORTANT
Number of unscheduled admissions (People with ≥2 hospital admissions) (>6 months versus <6 months) (follow-up mean 1 years)												
1	observational studies[a]	no serious risk of bias	no serious inconsistency	serious[c]	very serious[b]	none	9/68 (13.2%)	55/298 (18.5%)	RR 0.72 (0.37 to 1.38)	52 fewer per 1000 (from 116 fewer to 70 more)	⊕OOO VERY LOW	IMPORTANT
Hospitalisation (People with >14 days of hospitalisation) (>6 months versus <6 months) (follow-up mean 1 years)												
1	observational studies[a]	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[b]	none	7/68 (10.3%)	47/298 (15.8%)	RR 0.65 (0.31 to 1.38)	55 fewer per 1000 (from 109 fewer to 60 more)	⊕OOO VERY LOW	IMPORTANT
Preferred and actual place of death (Hospital death) (>6 months versus <6 months) (follow-up mean 1 years)												
1	observational studies[a]	no serious risk of bias	no serious inconsistency	serious[c]	serious[b]	none	12/68 (17.6%)	85/298 (28.5%)	RR 0.62 (0.36 to 1.07)	108 fewer per 1000 (from 183 fewer to 20 more)	⊕OOO VERY LOW	CRITICAL
Preferred and actual place of death (ICU death) (>6 months versus <6 months) (follow-up mean 1 years)												

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1	observational studies[a]	no serious risk of bias	no serious inconsistency	serious[c]	very serious[b]	none	2/68 (2.9%)	11/298 (3.7%)	RR 0.8 (0.18 to 3.51)	7 fewer per 1000 (from 30 fewer to 93 more)	⊕OOO VERY LOW	CRITICAL
Avoidable/inappropriate admissions to ICU (People with any ICU admission) (>6 months versus <6 months) (follow-up mean 1 years)												
1	observational studies[a]	no serious risk of bias	no serious inconsistency	serious[c]	very serious[b]	none	5/68 (7.4%)	30/298 (10.1%)	RR 0.73 (0.29 to 1.81)	27 fewer per 1000 (from 71 fewer to 82 more)	⊕OOO VERY LOW	IMPORTANT

[a] Downgraded by 2 increments if the majority of the evidence was from studies with observational/non-randomised study design.
[b] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
[c] Downgraded by 1 increment because the majority of the evidence had indirect outcomes

Table 17: Clinical evidence profile: Early (palliative care >30 days before death) versus late (palliative care <30 days before death)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Early**	**Late**	**Relative (95% CI)**	**Absolute**		
Place of death (males who died at home)												
1	observational studies	no serious risk of bias[a]	no serious inconsistency	serious[b]	no serious imprecision	none	824		OR 2.21 (1.34 to 3.65)	-	⊕OOO VERY LOW	CRITICAL
Place of death (females who died at home)												
1	observational studies	no serious risk of bias[a]	no serious inconsistency	serious[b]	no serious imprecision	none	824		OR 3.33 (2.07 to 5.36)	-	⊕OOO VERY LOW	CRITICAL
Place of death (males who died at inpatient hospice)												
1	observational studies	no serious risk of bias[a]	no serious inconsistency	serious[b]	serious[c]	none	824		OR 2.02 (1.13 to 3.61)	-	⊕OOO VERY LOW	CRITICAL
Place of death (females who died at inpatient hospice)												

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1	observational studies	no serious risk of bias[a]	no serious inconsistency	serious[b]	no serious imprecision	none	824	OR 2.69 (1.55 to 4.67)	-	⊕OOO VERY LOW	CRITICAL

[a] Downgraded by 2 increments if the majority of the evidence was from studies with observational/non-randomised study design
[b] Downgraded by 1 increment because the majority of the evidence had indirect outcomes
[c] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

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Appendix G: Excluded studies

G.1 Excluded clinical studies

Table 18: Studies excluded from the clinical review

Study	Exclusion reason
Adams 2009[1]	Inappropriate study design
Alsirafy 2010[2]	Inappropriate study design
Ansell 2007[4]	Inappropriate study design
Baek 2011[5]	Inappropriate study design
Bajwah 2015[6]	Inappropriate intervention (inappropriate definition of 'early' and 'late')
Bennett 2016[8]	Inappropriate study design
Blackhall 2016[9]	Inappropriate comparison
Broom 2012[10]	Inappropriate study design
Bruera 2012[11]	Inappropriate study design
Buchman 2016[12]	Inappropriate study design
Caissie 2014[13]	Incorrect interventions
Campbell 2004[14]	Incorrect interventions
Carpenter 2017[15]	Inappropriate outcome
Charalambous 2014[16]	Inappropriate study design
Christakis 1994[17]	Inappropriate study design
Costantini 1999[18]	Inappropriate study design. No relevant outcomes
Costantini 2018{Costantini, 2018 #3547}	Inappropriate study design . No comparison
Devi 2011[21]	Inappropriate study design
Diamond 2016[22]	Inappropriate comparison
Drieskens 2008[23]	Inappropriate study design
Fink 2015[24]	Inappropriate study design
Fukui 2011[25]	Inappropriate study design
Ghazali 2011[26]	Not review population
Glare 2013[27]	Inappropriate study design
Greer 2012[28]	Inappropriate comparison
Groenvold 2017[29]	Inappropriate comparison
Groenvold 2017 {Groenvold, 2017 #3107}	Inappropraite comparison and population
Gu 2016[30]	Unable to locate
Gunatilake 2014[31]	Inappropriate study design - study protocol
Haun 2017[32]	Inappropriate comparison
Hermans 2017[33]	Inappropriate intervention
Higginson 2008[34]	Not review population
Hui 2016[36]	Incorrect interventions
Humphreys 2014[37]	Inappropriate study design
Jacobsen 2011[38]	Inappropriate comparison
Johnsen 2013[39]	Not review population

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Study	Exclusion reason
Johnson 2011[40]	Inappropriate study design
King 2016[41]	Inappropriate comparison
Kozlov 2015[42]	Inappropriate study design
Lamba 2013[43]	Inappropriate study design
Lamont 2002[44]	Inappropriate study design
Le 2010[46]	Inappropriate study design
Le 2014[45]	Inappropriate study design
LeBlanc 2015[47]	Unable to locate
Ledoux 2015[48]	Inappropriate comparison
Lee 2015[49]	Inappropriate comparison
Lowery 2013[50]	No relevant outcome
Madden 2015[51]	Not review population
Maltoni 2017[52]	Inappropriate comparison
Maltoni 2016[53]	Inappropriate comparison
May 2017[54]	Inappropriate comparison
Mcdonald 2016[55]	Inappropriate comparison
Mcdonald 2016[56]	Inappropriate study design (abstract)
McNamara 2013[57]	Inappropriate comparison
Meffert 2015[58]	Inappropriate study design
Miller 2016[59]	Inappropriate comparison
Morita 2005[60]	Inappropriate study design
Morita 2009[61]	Inappropriate study design
Nakajima 2016[62]	Inappropriate comparison
Nipp 2016[65]	Incorrect interventions
Norton 2007[66]	Incorrect interventions
O'Leary 2014[67]	Inappropriate comparison
Reyes-Ortiz 2015[69]	Not review population
Rickerson 2005[70]	Inappropriate study design
Riedel 2017[71]	Unable to locate
Romano 2017[72]	Inappropriate comparison
Salins 2016[73]	No usable outcomes. Cross-referenced for included studies
Scarpi 2018{Scarpi, 2018 #3554}	Inappropriate comparison
Schockett 2005[74]	No relevant outcome
Seow 2010[75]	Incorrect interventions
Temel 2005[76]	Inappropriate study design (abstract)
Temel 2010[78]	Inappropriate comparison
Temel 2017[77]	Inappropriate comparison
Teno 2007[79]	No relevant outcome
Thoonsen 2011[80]	Inappropriate study design - study protocol
Vanbutsele 2015[81]	Inappropriate comparison
Vanbutsele 2018{Vanbutsele, 2018 #3543}	Inappropriate comparison
Von gunten 2011[82]	Inappropriate study design
Weber 2016[83]	Inappropriate comparison
Yamagishi 2015[84]	Incorrect interventions. Inappropriate study design

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Study	Exclusion reason
Zagonel 2016[85]	Not review population
Zambrano 2016[86]	Inappropriate study design
Zimmermann 2014[87]	Incorrect interventions
Zimmerman 2016[88]	Inappropriate study design

G.2 Excluded health economic studies

None.

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Appendix H: Research recommendations

H.1 RR1: Does early review of service provision and referral to additional specialist palliative care services improve outcomes for adults with progressive non-cancer disease thought to be entering their last year of life?

Why this is important:

There is a body of research into the optimal timing of referral to specialist palliative care (SPC) in cancer patients, which generally points to earlier referral leading to better patient-reported outcomes. The committee noted that similar evidence does not exist for patients with a non-cancer diagnosis, for example in patients with progressive organ failure, such as advanced heart failure or dementia. Such patients are typically referred very late to SPC, if at all. There is a need for further research in the latter group, which would compare outcomes from the combination of early identification and specialist palliative care input, versus usual care.

PICO question	There is a growing body of research into the benefits of introducing specialist palliative care earlier in the care of advanced cancer patients, but the committee noted that this was not the case for patients with a progressive non-cancer diagnosis who may be entering the last year of life. Population: A defined group of people with advanced progressive organ failure, or frailty, eg people with NYHA Stage IV heart failure under the care of cardiologists and heart failure nurse specialists. Intervention(s): Holistic needs assessment and advance care planning followed by immediate specialist palliative care review, in addition to any current cardiology support and specialist heart failure nurses. Comparison: People with end stage organ failure who are receiving usual care (which may include cardiology support and specialist heart failure nurses, or future SPC review). Outcome(s): quality of life, Patient and carer satisfaction;; other end of life specific PROMs; timing and number of referrals to specialist palliative care; service utilisation; achievement of preferred place of care/death; survival.
Importance to patients or the population	People in the last year of life may benefit from needs-based care plans and advance care planning taking into account preferences and wishes. These are done to a large extent in cancer patients, and specialist palliative care services are also heavily involved in

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	cancer patients in the last year of life. Studies have shown benefits to cancer patients from early review of needs, care planning and SPC involvement in terms of subjective outcomes - quality of life, symptoms, mood and reduced inappropriate resource utilisation. There may be a survival advantage for some. It would be useful to show if specific groups of people with non-cancer progressive disease could also benefit in these ways. Given that the majority of older people die from chronic non-cancer conditions, this would of great importance for health and social care planning and for resource allocation.
Relevance to NICE guidance	Relevant to future updates of NICE End of Life Care Service Delivery guideline, and NICE chronic disease guidelines, which have been hampered by lack of evidence on this question.
Relevance to the NHS	Clarification of role of NHS-funded SPC services for non-cancer conditions; optimal use of current resources and allocation of future resources; identification of future role for community and hospice services.
National priorities	Some non-cancer diseases have national service frameworks but lack of evidence on this question has prevented them from having a clear strategy on how best to plan and deliver SPC services in the last year of life.
Current evidence base	Most of the research in this area for cancer populations has been conducted in North America where the healthcare systems are very different from UK. Compared to the cancer population, the current evidence base for non-cancer conditions is limited with respect to this research question. Some studies have evaluated specialist palliative input along with conventional services or new interventions, eg in chronic lung disease, but usually focused on short-term or symptom-related outcomes.
Equality	Yes – people with chronic progressive non-cancer conditions such as lung or heart disease, MND and stroke have severe physical disabilities and may have cognitive impairment.
Study design	This should be a prospective study design, but different methodologies may be applicable. Possible approaches include: observational cohort studies; cluster or patient-level RCTs; point of care allocation studies. Both quantitative and qualitative designs are appropriate, ideally nested in the same study. There should be a preliminary feasibility study with clear criteria for progression to a larger study.
Feasibility	The embedded feasibility study should assess issues such as: the likelihood of SPC services being able to respond to increased referrals; functioning of new referral pathways including to hospices; ability to standardise the elements of SPC that can be offered; acceptability of HNA and ACP to non-cancer patients entering the last year of life; ability to conduct long-term follow-up of patients living in the community and care settings; ethical

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	constraints such as sharing of diagnostic and prognostic information to patients with longstanding conditions and limited cognition.
Other comments	As well as NIHR, disease-specific charities such as BHF, BLF, MNDA may be interested to fund a study in their populations.
Importance	High: the research is essential to inform future updates of key recommendations in this EOLC service delivery guideline and also of disease-specific NICE guidelines and national service frameworks.

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