

Special Article

A Systematic Review in Support of the National Consensus Project Clinical Practice Guidelines for Quality Palliative Care, Fourth Edition



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Abstract

Context. Palliative care continues to be a rapidly growing field aimed at improving quality of life for patients and their caregivers.

Objectives. The purpose of this review was to provide a synthesis of the evidence in palliative care to inform the fourth edition of the National Consensus Project Clinical Practice Guidelines for Quality Palliative Care.

Methods. Ten key review questions addressing eight content domains guided a systematic review focused on palliative care interventions. We searched eight databases in February 2018 for systematic reviews published in English from 2013, after the last edition of National Consensus Project guidelines was published, to present. Experienced literature reviewers screened, abstracted, and appraised data per a detailed protocol registered in PROSPERO. The quality of evidence was evaluated using the Grading of Recommendations, Assessment, Development and Evaluations criteria. The review was supported by a technical expert panel.

Results. We identified 139 systematic reviews meeting inclusion criteria. Reviews addressed the structure and process of care (interdisciplinary team care, 13 reviews; care coordination, 18 reviews); physical aspects (48 reviews); psychological aspects (26 reviews); social aspects (two reviews); spiritual, religious, and existential aspects (11 reviews); cultural aspects (three reviews); care of the patient nearing the end of life (grief/bereavement programs, six reviews; final days of life, two reviews); ethical and legal aspects (36 reviews).

Conclusion. A substantial body of evidence exists to support clinical practice guidelines for quality palliative care, but the quality of evidence is limited. *J Pain Symptom Manage* 2018;56:831–870. © 2018 National Coalition for Hospice and Palliative Care.

Key Words

Palliative care, clinical guidelines, quality

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Introduction

Palliative care continues to be a rapidly growing field aimed at improving quality of life for patients with serious illness and their caregivers. Inpatient palliative care programs have increased their penetration by 85% from 2008 to 2015.¹ In 2015, 67% of hospitals with 50 or more beds in the U.S. reported having an interdisciplinary palliative care team, up from 53% in 2008.² Recent data showing a decrease in length of stay before a palliative care consult and an increase in hospital discharges after a palliative care consult indicate that patients are being referred to palliative care earlier and thus better able to maximize the benefit of these services.³ A rapidly aging population with complex care needs, growing fiscal pressures, and increasing attention on value-based payment will likely accelerate emphasis on palliative care services in the U.S.

Concurrently, research in palliative care has significantly expanded. Several important and well-designed studies have demonstrated that hospice and palliative services can improve patient and caregiver quality of life, satisfaction with care, and end-of-life care communication and care planning, as well as reduce costs and unwanted care among a range of conditions and settings.^{4–14} There is a growing body of research on the use and effectiveness of symptom management approaches, palliative care delivery models, and psychosocial, spiritual, and grief support services that can help to guide clinical practice and improve quality. As our understanding of what works in palliative and end-of-life care is growing, there is a need to usefully synthesize evidence across key areas about which interventions work, for whom, and under what conditions, to more directly guide clinical practice, quality measurement, and training/education, and to help make evidence-based policy decisions.

Clinical practice guidelines for palliative care provide a foundation for improving the quality and delivery of palliative care in the context of the rapid expansion of the field. The National Consensus Project (NCP) Clinical Practice Guidelines for Quality Palliative Care have played a critical role in advancing palliative care practice and providing guidance and support for providers. These guidelines informed the National Quality Forum palliative care framework endorsed in 2006 in addition to 38 preferred practices that provided a foundation for palliative care quality measurement and reporting.¹⁵

The NCP Guidelines are consensus-based guidelines, informed by expert knowledge and current research. In response to an increasing need to develop evidence-based guidelines to inform policymakers, payors, and practitioners, the fourth edition of the guidelines will include and be informed by a robust systematic review

of current evidence in palliative care. Palliative care clinical practice guidelines grounded in research evidence will help to ensure adoption and adherence by health care providers, health plans, accrediting agencies, and regulatory agencies and will assure they remain as the gold standard for informing practice and policy within the field.

We therefore undertook a systematic review of current evidence in palliative care to inform the fourth version of the NCP guidelines. In this study, we describe the review methods, key findings, and implications for the field.

Methods

Overview

This systematic review synthesizes the best current evidence for palliative care interventions across eight domains that structure the NCP clinical practice guidelines. The systematic review was supported by a technical expert panel. The review is registered in PROSPERO (CRD42018100065) and followed PRISMA guidelines.¹⁶ Palliative care is defined as care, services, or programs with the primary intent of relieving suffering and improving health-related quality of life, including dimensions of physical, psychological/emotional, social, and spiritual well-being. Ten key questions (KQs) were selected to guide the review ([Supplemental File: Key Questions Search and Eligibility Criteria Table](#)).

Search Strategy

An experienced evidence-based practice center librarian designed and executed all searches. We searched the Cochrane Database of Systematic Reviews (health research), the database of systematic reviews by the Campbell Collaboration (health and social work research), PubMed (biomedical literature), PsycINFO (psychological literature), EMBASE (pharmacology research), CINAHL (nursing research), Academic Search Complete (social science and education), and the Web of Science (general science literature). We used search terms to reflect palliative, hospice, supportive, terminal, or end-of-life care for all KQs ([Supplemental File: Search Strategy](#)), combined with search terms relevant to each KQ. All searches were limited to English-language publications from 2013 (i.e., after the third edition of the NCP Guidelines was published) to February 2018. In addition, we reference-mined systematic reviews, used existing literature collections, and consulted with content experts.

Study Selection

To select studies for inclusion in the review, we applied eligibility criteria determined a priori following a PICOTSS (population, intervention, comparator, outcome, timing, setting, and study design) framework. Population: Eligible populations included patients of all ages with advanced illness and/or if relevant to the KQ, their family members and informal caregivers. Disease-specific (e.g., cancer, heart failure and other cardiac conditions, chronic pulmonary disease, dementia and other neurological conditions, liver disease, or renal disease) and nonspecific studies of advanced, late- or end-stage, or metastatic illness were eligible for inclusion. Identified reviews had to target patients with advanced, late- or end-stage, or metastatic illness and/or describe subgroup analyses of this population to be eligible for inclusion. Intervention: Studies had to report the effects of palliative care interventions on relevant patient and family/caregiver outcomes. Eligibility criteria for types of interventions varied by KQ ([Supplemental File](#)). Comparator: Studies had to include a comparator (usual care, waiting list, or other intervention) to be eligible but no other study design criterion for primary research was imposed. Outcome: Eligibility criteria for outcomes varied by KQ ([Supplemental File](#)). Timing: Studies could be of any duration and follow-up period. Setting: Reviews had to include studies conducted in U.S. settings to be eligible, although reviews could report on multiple geographic locations. All practice settings (e.g., inpatient, outpatient, home, community) were eligible. Study design: Systematic reviews were eligible for inclusion. Systematic reviews use a resource-intensive approach to identify relevant studies, searching multiple sources with comprehensive search strategies. The reviews appraise the risk of bias of individual studies and assess the study results independently from the original study authors. Systematic reviews often include a meta-analysis that aggregates data across studies to increase statistical power and to obtain an objective effect summary.

Screening Procedures

Experienced literature reviewers screened citations identified in the literature searches and trained a machine learning algorithm to identify relevant citations. One reviewer screened all citations; citations identified by the algorithm as potentially relevant were screened by two independent literature reviewers. Titles and abstracts deemed relevant by at least one reviewer were obtained as full-text publications to ensure that no relevant study was missed. Full-text publications were reviewed by two independent

reviewers against the explicit eligibility criteria to minimize reviewer errors and bias. Discrepancies were resolved through discussion with the review team.

Data Abstraction and Critical Appraisal

From each included review, we abstracted review details (e.g., search dates, settings, number of included studies), participant characteristics, intervention descriptions, relevant results, and authors' conclusions. Where provided (e.g., meta-analyses), we abstracted pooled effect estimates. Data were abstracted in an online database for systematic reviews, using a pilot-tested form with detailed reviewer instructions to ensure standardized and accurate data extraction. Data were abstracted by one literature reviewer and checked for accuracy by an experienced second reviewer. Discrepancies were resolved by team discussion. We used an explicit and transparent approach to assess the methodological quality of included systematic reviews across 11 critical appraisal dimensions: 1) explicitly stated review questions; 2) appropriate inclusion criteria; 3) appropriate search strategy; 4) adequate sources and multiple databases searched; 5) appropriate appraisal criteria; 6) dual appraisal; 7) data abstraction process minimizing errors; 8) appropriate synthesis; 9) publication bias assessment; 10) recommendations supported by data; and 11) appropriate research suggestions. In addition, we considered context-specific criteria such as the applicability of the results to a palliative care review question.

Synthesis and Quality of Evidence Assessment

Evidence tables were created to allow a transparent and accessible overview and structure the available study details and results for all included studies. We summarized findings organized by KQ, intervention type, study population/age group (e.g., pediatric vs. adult), setting (e.g., inpatient vs. outpatient), and outcome in a Summary of Findings table. We assessed the quality of evidence using the Grading of Recommendations, Assessment, Development and Evaluations framework. The Grading of Recommendations, Assessment, Development and Evaluations framework¹⁷ allows for a transparent overview using internationally accepted criteria to differentiate high, moderate, low, and very low quality of evidence to describe confidence in the findings among studies. We downgraded for study limitations (e.g., no randomized controlled trials contributing to the evidence), inconsistency in results across studies or lack of replication, imprecision (e.g., due to lack of reported effect estimates or imprecise estimates). We used the assessment of the systematic reviews evaluating the evidence base regarding indirectness, publication bias, or other criteria where applicable.

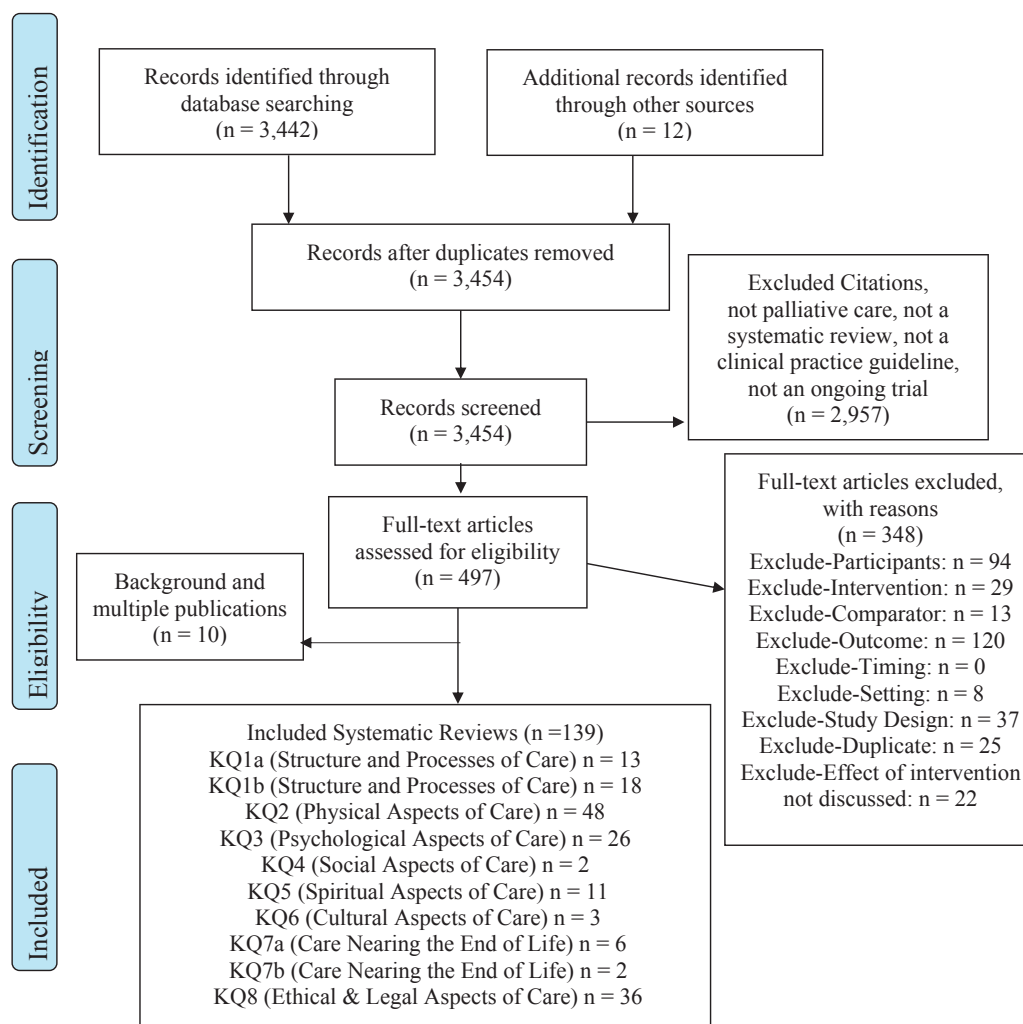


Fig. 1. Systematic review flow diagram. KQ = key question.

Results

Our search identified 3454 citations and we obtained 497 publications as full text (Fig. 1). We identified 139 systematic reviews meeting the inclusion criteria (18–156) and contributing to one or more KQ. All included reviews and their findings are documented in detail in an evidence table in Supplemental File. The methodological quality of the systematic reviews is summarized in a critical appraisal figure in Supplemental File. Key findings are summarized in Summary of Findings Tables 1–8.

Domain 1: Structure and Processes of Care

KQ 1a: What Is the Effect of Interdisciplinary Team Care on Patient Outcomes and Family/Caregiver Satisfaction With Care? Thirteen reviews met inclusion criteria for evaluating the effect of an interdisciplinary team on patient and family outcomes. There was moderate-quality evidence for the impact of interdisciplinary

teams on quality of life (Summary of Findings Table 1). Seven reviews reported on quality of life outcomes and consistently concluded that interdisciplinary care teams improved quality of life for patients with advanced illness.^{18–20,22,23,26,27} A 2017 review noted growing support for the utilization of palliative care teams for improving quality of life in advanced illness (SMD 0.16; CI 0.01–0.31; six RCTs).²⁰ Another review found an association between the number of disciplines included on the interdisciplinary care team and improved quality of life.²⁶ Two reviews focused on cancer and heart failure patients also showed positive impacts.^{23,27}

There was moderate-quality evidence for a positive impact of interdisciplinary teams on advance care planning (ACP) decisions, death at home, and patient and family satisfaction with care but low-quality evidence for a positive impact of interdisciplinary palliative care teams on patient physical symptoms and patient and family psychological

Summary of Findings Table 1
Structure and Process of Care

Intervention and Comparator Age Group Setting Outcome	N	Effect Estimate and Direction of Effects	GRADE ^a
Interdisciplinary team care Pediatric	0	NA	NA
Interdisciplinary team care Adults or mixed samples Multiple settings Patient outcome: quality of life	7 SRs ^{18–20,22,23,26,27}	Seven reviews reported on quality of life outcomes and effects were positive; for example, a 2017 review noted growing support for the utilization of specialist palliative care teams for improving quality of life in advanced illness (SMD 0.16; CI 0.01–0.31; six RCTs) but highlighted important study limitations of included studies. ²⁰ One review found moderate-quality evidence that the use of a comprehensive early (initiated up to 24 months before death) team-based contact model improved patient quality of life. In another review, specialist palliative care was associated with a small effect on QoL. One review found an association between the number of disciplines included on the interdisciplinary care team and improved quality of life. Another review found that 40% of interventions with a significant effect of quality of life involved a multidisciplinary team. Another review found that interdisciplinary palliative care teams improved quality of life among cancer patients at the end of life. In another review, patient quality of life significantly improved in five of six included studies examining palliative care team interventions for patients with heart failure.	M (S)
Interdisciplinary team care Adults or mixed samples Multiple settings Patient outcome: ACP decisions	4 SRs ^{19,23,25,28}	Four reviews reported on ACP decisions using different measures but finding positive effects; including a Canadian HTA review that reported that a hospital team-based model has been shown to increase the odds of completing ACPs compared to usual care (OR 1.6; no CI; low-moderate QoE). ¹⁹ One review concluded that review by specialist teams at the point of acute deterioration serves as a useful trigger for ACP decisions. Another review found that five of seven included studies examining palliative care team interventions for patients with heart failure showed increased documentation of preferences for care, advance directives, and DNR and end-of-life orders. One review found 12 pre-post studies demonstrating that palliative care team consultation was associated with code status changes and improved disease and prognosis awareness of patients.	M (Im)
Interdisciplinary team care Adults or mixed samples Multiple settings Patient outcome: death at home	4 SRs ^{19,22,23,29}	Four reviews examined the likelihood of dying at home and effects were positive. Two reviews found evidence that the use of a home team-based model increased the odds of having a home death; the Canadian HTA estimated an 89% or more increase based on two RCTs (no CI). ¹⁹ Another review also identified a single RCT demonstrating that the use of an interdisciplinary palliative care team increased odds of having a home death. One review found that two of four included studies showed that palliative care team interventions were associated with an increase in death at home compared to in a hospital.	M (Im)
Interdisciplinary team care Adults or mixed samples Multiple settings Patient outcome: satisfaction with care	3 SRs ^{19,23,29}	Three reviews found that interdisciplinary team care was associated with statistically significant improvements in patient satisfaction compared to usual care (no effect estimate reported).	M (Im)
Interdisciplinary team care Adults or mixed samples Multiple settings Patient outcome: physical symptoms	4 SRs ^{19,22,25,29}	Four reviews found evidence that the use of an interdisciplinary palliative care team was associated with improvements in symptom management and physical comfort and reduced physical symptoms but effect estimates were not reported and effects varied by study and outcome.	L (Im, In)
Interdisciplinary team care Adults or mixed samples	4 SRs ^{18,21,22,29}	Four reviews found mostly positive effects but reported on different psychological outcomes and none reported an	L (Im, In)

(Continued)

Summary of Findings Table 1
Continued

Intervention and Comparator Age Group Setting Outcome	N	Effect Estimate and Direction of Effects	GRADE ^a
Multiple settings Patient outcome: psychological symptoms		effect estimate. One review found that case management, palliative care teams, hospice, skills training, and other interventions were all effective on patient depressive symptoms, indicated by 12 studies. Another review noted moderate evidence that specialist palliative care teams reduce psychological symptoms. A third review found that use of an interdisciplinary palliative care team was associated with reduced anxiety and depression. One review identified one RCT showing no difference in emotional burden associated with interdisciplinary care teams.	
Interdisciplinary team care Adults or mixed samples Multiple settings Family/caregiver outcome: satisfaction with care	1 SR ¹⁹	A Canadian HTA review reported moderate-quality evidence that the use of a comprehensive, direct, and early team-based contact model initiated up to nine months before death improved informal caregiver satisfaction but provided no effect estimate.	M (Im)
Interdisciplinary team care Adults or mixed samples Multiple settings Family/caregiver outcome: psychological symptoms	1 SR ¹⁸	One review found that interventions with a significant effect on caregiver depressive symptoms (12 studies) often involved a home component, did not use multidisciplinary teams, were long-term, and often involved caregiver skills training or counseling and therapy but did not report effect estimates.	L (Im, In)
Interdisciplinary team care Adults or mixed samples ICU Patient outcome: mortality	2 SRs ^{24,30}	Two reviews came to different conclusions: one review found that ICU-based palliative care team interventions did not change hospital mortality; however, another review found that the introduction of palliative care teams can reduce mortality rates in the ICU.	V (S, In, Im)
Interdisciplinary team care Adults or mixed samples ICU Family/caregiver outcome: satisfaction with care	1 SR ³⁰	One review found that ICU-based palliative care team interventions did not change family/caregiver satisfaction with care.	V (S, Im, In)
Interdisciplinary team care Adults or mixed samples ICU Family/caregiver outcome: ACP	1 SR ³⁰	One review found that ICU-based palliative care team interventions statistically significantly decreased nonconsensus between family members and providers but did not report an effect estimate.	L (Im)
Interdisciplinary team care Adults or mixed samples ICU Family/caregiver: psychological symptoms	1 SR ³⁰	One review found that ICU-based palliative care team interventions statistically significantly decreased family member PTSD and anxiety but the result was based on a single study.	L (Im, In)
Telehealth Adults and pediatrics Setting: home/outpatient Patient outcome: quality of life	2 SRs ^{44,47}	Two reviews found that quality of life and well-being may be affected positively by telehealth interventions but neither reported an effect estimate, study results varied, and no summary was reported.	L (Im, In)
Telehealth Adults Setting: home/outpatient Patient outcome: quality of life	2 SRs ^{39,46,47}	Two reviews reported quality of life outcomes and reported mixed evidence. One review identified a single RCT demonstrating a significant improvement in quality of life compared to usual care. Another review found that although overall evidence for palliative telehealth is weak, there is potential for some telehealth interventions to support patients' quality of life but the review reported no effect estimate.	L (Im, In)
Telehealth Adults Setting: home/outpatient Patient outcome: physical symptoms	2 SRs ^{46,47}	Two reviews addressed physical symptoms and found mixed evidence but did not report effect estimates. One review identified observable but nonsignificant reductions in physical symptoms associated with telehealth but did not report an effect estimate. One review found that although overall evidence for palliative telehealth is weak, some telehealth interventions can aid in physical symptom control.	L (Im, In)
Telehealth Adults and pediatrics Setting: home/outpatient Patient outcome: psychological health	4 SRs ^{39,44,46,47}	Four reviews addressed psychological health including anxiety and reported positive results but none provided an effect estimate. One review concluded that anxiety may be affected positively by telehealth interventions,	M (Im)

(Continued)

Summary of Findings Table 1
Continued

Intervention and Comparator Age Group Setting Outcome	N	Effect Estimate and Direction of Effects	GRADE ^a
Telehealth Adults and pediatrics Setting: home/outpatient Patient outcome: resource use	1 SR ⁴⁴	while another review identified improvements in emotional symptoms including anxiety, depression, PTSD, and negative affect. One more review identified improvements in anxiety, depression, and distress. Another review identified two RCTs demonstrating significant improvements in depression. One review included a study demonstrating a 60% reduction in hospital admissions was associated with telehealth.	V (S, Im, In)
Telehealth Adults Setting: home/outpatient Patient outcome: resource use	1 SR ⁴⁶	One review found that telehealth interventions can reduce unnecessary/avoidable utilization but the review reported no effect estimate.	L (Im)
Telehealth Adults Setting: home/outpatient Patient outcome: satisfaction with care	2 SRs ^{46,47}	Two reviews identified positive impacts of telehealth on increasing satisfaction with the telehealth intervention but reported no effect estimate.	L (Im, In)
Telehealth Adults and pediatrics Setting: home/outpatient Family/caregiver outcome: quality of life	1 SR ⁴⁴	One review found that family/caregiver quality of life may be affected positively by telehealth interventions but the review reported no effect estimate.	L (Im, In)
Early/integrated palliative care Adults or mixed samples Setting: mixed Patient outcome: quality of life	2 SRs ^{38,40}	Two reviews addressed quality of life but conclusions varied. One review concluded on the basis of three RCTs and one quasi-experimental study all demonstrating significant improvements in quality of life that there is robust evidence that early palliative care integrated into standard oncology care significantly improves quality of life. Another review noted that two of seven RCTs reported improved quality of life while the remaining four RCTs and one prospective cohort study reported no difference.	L (Im, In)
Early/integrated palliative care Adults or mixed samples Setting: home/outpatient Patient outcome: quality of life	3 SRs ^{35,41}	Three reviews addressed early/integrated care in home/outpatient settings and reported mixed evidence, including a Cochrane review that reported a positive effect (SMD 0.27; CI 0.15, 0.38; low QoE) compared to usual care. ³⁵ A second review concluded that early/integrated palliative care may be slightly better than usual care at improving quality of life and another review reported mixed evidence on the impact of early/integrated palliative care (no effect estimates).	L (S, In)
Early/integrated palliative care Adults or mixed samples Setting: mixed Patient outcome: physical symptoms	4 SRs ^{32,36,38,40}	Four systematic reviews addressed physical symptoms and identified mixed evidence but none reported an effect estimate. One review concluded that integrated palliative care could help maintain functional status; another review identified a single study demonstrating improvements in physical symptoms. Another review identified mixed evidence regarding the impact of integrated care on symptom management. One review found one RCT reporting partially improved symptoms control and four RCTs reporting no difference.	L (Im, In)
Early/integrated palliative care Adults or mixed samples Setting: home/outpatient Patient outcome: physical symptoms	3 SRs ^{35,41}	Three reviews addressed physical symptoms in home/outpatient settings and reported mixed evidence, including a Cochrane review that reported a statistically significant reduction (SMD -0.23; CI -0.35, -0.10; seven studies; low QoE). ³⁵ Two reviews reported mixed evidence on the impact of early/integrated palliative care on physical symptoms and did not report effect estimates.	L (S, In)
Early/integrated palliative care Adults or mixed samples Setting: mixed Patient outcome: depression	1 SR ³⁸	One review reported there is robust evidence that early palliative care reduces depression but did not report an effect estimate.	L (Im)
Early/integrated palliative care Adults or mixed samples	3 SRs ^{35,41}	Three reviews reported on home/outpatient settings and identified mixed evidence, including a Cochrane review	V (S, In)

(Continued)

Summary of Findings Table 1
Continued

Intervention and Comparator Age Group Setting Outcome	N	Effect Estimate and Direction of Effects	GRADE ^a
Setting: home/outpatient Patient outcome: psychological health		that reported no statistically significant difference for depression (SMD -0.11; CI -0.26, 0.03; five RCTs; very low QoE) ³⁵ and another review that reported some evidence that early/integrated palliative care is associated with improvements in depression. Another review reported mixed evidence on the impact of early/integrated care on depression and anxiety.	
Early/integrated palliative care Adults or mixed samples Setting: mixed Patient outcome: mortality	2 SRs ^{32,38}	Two reviews addressed mortality but the effect of early/integrated palliative care is unclear. One review found mixed evidence on the impact of early/integrated palliative care on survival, with some studies reporting improvements in survival associated with integrated care, and other studies reporting nonsignificant or no improvements in survival. Another review included a study that found integrated primary care for patients with cancer provided no advantage over cancer care alone.	V (Im, In)
Early/integrated palliative care Adults or mixed samples Setting: home/outpatient Patient outcome: mortality	2 SRs ^{35,45}	Two reviews reported on mortality in outpatient settings and found unclear evidence on the effect of early/integrated palliative care. A 2017 Cochrane review reported no difference across treatment arms (HR 0.85; CI 0.56, 1.28; four RCTs; very low QoE) ³⁵ and another review reported mixed evidence but did not report an effect estimate.	V (S, In)
Early/integrated palliative care Adults or mixed samples Setting: mixed Patient outcome: rehospitalization	2 SRs ^{23,37}	Two reviews addressed integrated care and rehospitalizations and found mixed evidence. One review (based on a search in one database only) reported a positive effect estimate for heart failure patients (RR 0.58; CI 0.44, 0.77; three RCTs) ²³ but a second review noted mixed results regarding associations of outpatient palliative care with a reduction in hospital admissions and rehospitalization.	L (S, In)
Early/integrated palliative care Adults or mixed samples Setting: mixed Patient outcome: resource use	5 SRs ^{34,36,38,42}	Several reviews addressed resource use but results varied across and within reviews and measures and only one review reported effect estimates (appropriate use of care SMD 0.37; CI 0.29, 0.45; six studies; utilization reduced SMD 0.22; CI -0.05, 0.49; four studies). ³⁴ One review concluded that integrated palliative care can reduce hospitalizations. One review found that integrated care leads to reduced ED, hospital and acute care visits, and decreased hospital length of stay. Another review found that integrated care was associated with increased hospice referrals. However, two reviews found no difference between integrated and usual care in terms of health care use and hospital length of stay.	V (Im, In)
Early/integrated palliative care Adults or mixed samples Setting: home/outpatient Patient outcome: resource use	2 SRs ^{41,45}	Two reviews reported mixed evidence on the impact of early/integrated palliative care on resource utilization including ED admissions, hospital length of stay, and use of aggressive care at the end of life.	L (Im, In)
Early/integrated palliative care Adults or mixed samples Setting: home/outpatient Patient outcome: satisfaction with care	1 SR ⁴⁵	One review noted that early/integrated palliative care was found to be associated with increased satisfaction with care in a majority of studies but did not report an effect estimate.	L (Im, In)
Early/integrative palliative care Adults or mixed samples Setting: mixed Patient outcome: ACP	1 SR ⁴²	One review found early palliative care improved goals of care discussion and advance care planning.	L (S, Im)
Early/integrative palliative care Adults or mixed samples Setting: home/outpatient Patient outcome: ACP	2 SRs ^{41,45}	Two reviews reported mixed evidence on the impact of early palliative care on advance care planning. One review reported increased advanced directives associated with early/integrated palliative care while another review found no significant impact of early/integrated care on advance care planning.	L (Im, In)
Early/integrative palliative care Adults or mixed samples	4 SRs ^{34,38,41,45}	Four reviews reported on family quality of life but results varied across and within reviews. One review found	L (Im, In)

(Continued)

Summary of Findings Table 1
Continued

Intervention and Comparator Age Group Setting Outcome	N	Effect Estimate and Direction of Effects	GRADE ^a
Setting: mixed Family/caregiver: quality of life		mixed evidence while another review found no difference between groups on the impact of early/integrated care on family/caregiver quality of life (none provided an effect estimate). One review reported that some RCTs testing early palliative care in various settings and populations found improved caregiver burden and better maintenance of caregiver quality of life. One review found no evidence on significant impact of early/integrated palliative care on family/caregiver quality of life.	
Early/integrative palliative care Adults or mixed samples Setting: mixed Family/caregiver: psychological health	1 SR ³⁸	One review found mixed evidence for the impact of early/integrated care on family/caregiver psychological symptoms and well-being.	V (S, Im, In)
Early/integrative palliative care Adults or mixed samples Setting: home/outpatient Family/caregiver: psychological health	1 SR ⁴⁵	One review noted that early/integrated palliative care was associated with reductions in depressive symptoms in one study but did not report an effect estimate.	L (Im, In)
Early/integrative palliative care Adults or mixed samples Setting: mixed Family/caregiver: satisfaction with care	1 SR ³⁴	One review found no difference in satisfaction with care after the implementation of an early/integrated care intervention.	V (S, Im)
Early/integrative palliative care Adults or mixed samples Setting: home/outpatient Family/caregiver: satisfaction with care	1 SR ⁴¹	One review reported that some RCTs testing early palliative care in various settings and populations found improved family satisfaction.	L (Im, In)
Early/integrative palliative care Adults or mixed samples Setting: mixed Family/caregiver: ACP	1 SR ³⁷	One review concluded that continuous palliative care after discharge may result in greater advance care planning communication, based on findings from a pilot study.	V (S, Im, In)
Home-based palliative care Adults or mixed samples Setting: home/outpatient Patient outcome: death at home	2 SRs ^{31,33}	Two reviews reported on dying at home as an outcome of home-based palliative care and both were positive. One review found that patients in home-based palliative care were more likely to die at home compared to usual care (OR 2.21; CI 1.31, 3.71; five RCTs, two CCTs). ³³ Another review found a similar significant association (RR 1.33; CI 1.14, 1.55; three RCTs). ³¹	H
Home-based palliative care Adults or mixed samples Setting: home/outpatient Patient outcome: physical symptoms	1 SR ³³	One review found three RCTs reporting a strong positive effect of home palliative care on symptom burden; nine RCTs reporting mixed evidence regarding the effect of home palliative care on pain improvement; and five RCTs reporting mixed evidence on the effect of home palliative care on physical function; concluding that evidence for home-based palliative care for improving pain and physical function is inconclusive but that evidence for reducing symptom burden is reliable and clear.	L (In, Im)
Home-based palliative care Adults or mixed samples Setting: home/outpatient Patient outcome: quality of life	1 SR ³³	One review concluded that evidence is inconclusive regarding the effect of home palliative care on patient quality of life, on the basis of three RCTs reporting no significant effects and two RCTs reporting significant effects.	L (In, Im)
Home-based palliative care Adults or mixed samples Setting: home/outpatient Patient outcome: satisfaction	2 SRs ^{31,33}	Two reviews examined the effect of home palliative care on patient satisfaction and reported mixed results. One review noted that evidence regarding satisfaction with care is conflicting; three RCTs found significant positive effects but two RCTs reported no significant between-group differences. Another review found two RCTs demonstrating small increases in satisfaction for patients receiving end-of-life care at home reported at one month.	L (Im, In)
Home-based palliative care Adults or mixed samples Setting: home/outpatient Patient outcome: resource use	1 SR ³³	One review found six RCTs showing moderate evidence on no significant effect of home-based palliative care on ED visits.	M (Im)

(Continued)

Summary of Findings Table 1
Continued

Intervention and Comparator Age Group Setting Outcome	N	Effect Estimate and Direction of Effects	GRADE ^a
Home-based palliative care Adults or mixed samples Setting: home/outpatient Family/caregiver outcome: caregiver burden	2 SRs ^{31,33}	Two reviews found conflicting evidence on the positive impact of home palliative care on caregiver burden.	L (Im, In)
Home-based palliative care Adults or mixed samples Setting: home/outpatient Family/caregiver outcome: satisfaction	1 SR ³³	One review found one controlled before-after study found significantly higher satisfaction with care among caregivers in the hospital-based intervention versus home care.	V (S, Im, In)
Case management Adults or mixed samples Setting: mixed Patient outcome: resource use	1 SR ⁴³	One review found mixed low-quality evidence on the impact of case management on hospital utilization at the end of life.	V (S, Im, In)
Case management Adults or mixed samples Setting: mixed Patient outcome: physical symptoms	1 SR ⁴³	One review found evidence on the positive impact of case management on reducing symptom distress, including one RCT, but no effect estimates were reported.	L (Im)
Care coordination/coordinators Adults or mixed samples Setting: mixed Patient outcome: quality of life	1 SR ³⁴	One review found no statistically significant effects of care coordination/coordinators on quality of life in cancer patients (g = 0.12; CI -0.01, 0.26; five studies). ³⁴	L (S)

N = number of systematic reviews; NA = not applicable; SR = systematic review; SMD = standardized mean difference; CCT = controlled clinical trial(s); RCT(s) = randomized controlled trial(s); QoL = quality of life; M = moderate quality of evidence; S = study limitation; ACP = advance care planning; HTA = health technology assessment; OR = odds ratio; QoE = quality of evidence; DNR = do-not-resuscitate; Im = imprecision; L = low quality of evidence; In = inconsistency; ICU = intensive care unit; V = very low quality of evidence; PTSD = post-traumatic stress disorder; RR = risk ratio; ED = emergency department; H = high quality of evidence.

^aThe GRADE category is based on identified systematic reviews published between 2013 and February 2018. We used the following reasons for downgrading confidence in the evidence (downgraded by 1 or 2): Study limitation (observational studies start with a low GRADE value), Inconsistency (individual studies do not come to the same conclusions or there is only one study so inconsistency cannot be evaluated), Imprecision (there is no effect estimate, there is no measure of dispersion, or the CI is very broad); we used the systematic review authors' evaluation for other GRADE criteria if there was a formal quality of evidence assessment (see text).

outcomes. The quality of the evidence for the impact of teams on these outcomes was downgraded because of inconsistent conclusions and lack of pooled effect estimates. There was very low-quality evidence from two reviews of a positive impact of interdisciplinary team care in the ICU on mortality and family satisfaction with care, due to an absence of randomized controlled trials studying these outcomes, inconsistency in conclusions, and lack of pooled effect estimates.^{24,30}

KQ 1b: What Is the Impact of Palliative Care Interventions to Improve Continuity and Coordination of Care on Patient and Family/Caregiver Outcomes? Eighteen reviews met inclusion criteria for evaluating the impact of palliative care interventions to improve continuity and coordination of care on patient and family/caregiver outcomes. Interventions included telehealth, early/integrated palliative care, home-based palliative care, case management, and care coordinators.

Telehealth: There was moderate-quality evidence on a positive impact of telehealth for adults and children in the home/outpatient setting on psychological health (i.e., improvements in anxiety, depression,

distress, PTSD; however, no effect estimates were provided),^{39,44,46,47} but low- to very low-quality evidence for all other outcomes including resource use, patient quality of life, physical symptoms, satisfaction with care, and family/caregiver quality of life, due to inconsistent findings, lack of pooled effect estimates, and study limitations described in included reviews.

Early/integrated care: There was low-quality evidence on the impact of early/integrated palliative care (i.e., palliative care provided early in the trajectory of an illness and/or integrated with standard treatment) on most patient outcomes including quality of life, physical symptoms, rehospitalization, patient satisfaction with care, and ACP, mainly due to individual study limitations and inconsistent findings. There was very low-quality evidence for early/integrated palliative care on patient psychological health and mortality and family psychological health, satisfaction with care, and ACP.

Home-based care: There was high-quality evidence from two reviews for the impact of home-based palliative care on the likelihood of a patient dying at home.^{31,33} One review found that patients in home-based palliative care were more likely to die at home

Summary of Findings Table 2
Physical Aspects of Care

Intervention and Comparator Age Group Setting Outcome	N	Effect Estimate and Direction of Effects	GRADE ^a
Pharmacological interventions for pain Pediatrics only Outcome: pain management	1 SR ⁷⁸	One review found mixed evidence on the impact of pharmacological interventions for pain in pediatric populations. The review identified two RCTs where intrathecal baclofen was significantly associated with an improvement in pain among children with cerebral palsy, two RCTs where botulinum was not associated with improvements in pain in the same population, and three trials with mixed evidence on the positive impact of alendronate/risedronate for pain in osteogenesis imperfecta. The review did not report effect estimates.	L (Im, In)
Comprehensive palliative care Adults and mixed samples Outcome: symptom burden	1 SR ⁴⁸	One review found that comprehensive palliative care was associated with a statistically and clinically significant reduction in symptom burden in adults with advanced illness at one- to three-month follow-up (SMD -0.66; CI -1.25, -0.07; 10 RCTs) and at four- to six-month follow-up (SMD -0.31; CI -0.05, -0.07; six RCTs; ⁴⁸ however, the review noted extremely high heterogeneity across identified studies.	M (S)
Pharmacological interventions Adults and mixed samples Outcome: pain management	8 SRs ^{54,56,60,65,66,68,70}	Eight reviews reported pain management outcomes associated with various pharmacological interventions but effects varied by study and outcome. Transdermal buprenorphine and transdermal fentanyl demonstrate equivalent analgesic efficacy in patients with cancer pain. There is limited evidence for the efficacy of metamizole in treating cancer pain. One review concluded that levomepromazine is completely or partially effective at managing pain. One review reported a lack of data to support a net conclusion but noted that methadone is a first-choice opioid for treating cancer pain. There is limited evidence as to the effect of using paracetamol and morphine to treat pain among people with dementia. Among adult patients with glioma, dexamethasone once a day is the preferred corticosteroid for pain control, though one review noted that nonsteroidal anti-inflammatory drugs (NSAIDs), analgesics, and coanalgesics should also be considered in the treatment of headache in patients with primary brain tumors. Among adult patients with metastatic bone pain, one review concluded that the use of bisphosphonates and denosumab for direct pain relief is weak. Similarly, another review concluded that there is no or very low-quality evidence to support the use of adjuvant analgesics in patients with metastatic bone pain. None of the reviews reported effect estimates.	L (Im, In)
Pharmacological interventions Adults and mixed samples Outcome: nausea/vomiting	4 SRs ^{59,73,86,89}	Four reviews reported nausea/vomiting outcomes, with mixed evidence on the benefits of pharmacological interventions. A 2017 Cochrane review found very low-quality evidence that neither supported nor refuted corticosteroid use for nausea/vomiting among patients with advanced cancer (SMD 0.48; CI -1.53, 0.57; two RCTs). ⁵⁹ Another review concluded that levomepromazine is completely or partially effective at managing nausea/vomiting. Two reviews concluded there is insufficient direct evidence to definitively support the use of haloperidol for the management of nausea and vomiting.	V (S, Im, In)
Pharmacological interventions Adults and mixed samples Outcome: dyspnea management	5 SRs ^{67,70,74,91,93}	Five reviews reported on dyspnea outcomes with mixed evidence on the benefits of pharmacological interventions. A 2016 Cochrane review concluded there is some low-quality evidence that shows the ability for oral or parenteral opioids to palliate breathlessness although the number of included participants was small (change from baseline SMD -0.09; CI -0.36, 0.19; $P = 0.54$; seven studies; post-treatment SMD 0.28; CI	L (S)

(Continued)

Summary of Findings Table 2
Continued

Intervention and Comparator Age Group Setting Outcome	N	Effect Estimate and Direction of Effects	GRADE ^a
Pharmacological interventions Adults and mixed samples Outcome: constipation	2 SRs ^{92,95}	<p>–0.50, –0.05; $P = 0.02$; 11 studies).⁶⁷ Another review found evidence for opioids for improving breathlessness among patients with advanced cancer. One review reported evidence that some opioids are effective at treating dyspnea in advanced cancer patients and that benzodiazepines showed no significant benefit at treating dyspnea. One review concluded there is evidence from weak study designs for improvements in dyspnea after administration of diamorphine. Another review reported potential benefits for using nebulized furosemide, hydromorphone, and fentanyl to treat dyspnea, but mixed evidence for nebulized morphine.</p> <p>Two reviews reported constipation-related outcomes of pharmacological interventions but did not report effect estimates and found mixed evidence. One review found several RCTs supporting the use of dietetic interventions with probiotics and prebiotics for relieving symptoms of constipation, and mixed evidence supporting the use of lubiprostone, macrogol, and injections of botulinum neurotoxin A for outlet obstruction constipation. Another review found six RCTs and concluded that evidence supporting the use of laxatives such as lactulose and senna for management of constipation was uncertain but that subcutaneous methylnaltrexone is effective in inducing laxation in palliative care patients with opioid-induced constipation.</p>	L (Im, In)
Cannabinoids Adults and mixed samples Outcome: pain management	1 SR ⁵²	One review found two trials reporting trends toward improvements in cancer-related pain associated with cannabinoids (SMD 0.07; CI –0.01, 0.16; two RCTs). ⁵²	L (In)
Cannabinoids Adults and mixed samples Outcome: nausea/vomiting	1 SR ⁵²	A single review found one trial reporting nonsignificant improvements in cancer-related nausea and vomiting, while another trial found no effects (SMD 0.21; CI 0.10, 0.52; two RCTs). ⁵²	L (In)
Radiation/chemotherapy Adults and mixed samples Outcome: pain management	12 SRs ^{50,55,61–64,75,79,82–84,90}	Twelve reviews reported pain management outcomes related to radiation and/or chemotherapy intervention; effects varied by study and outcome. One review concluded that palliative RT was effective at improving pain and that low regimens appear to be adequate for symptom palliation. Two reviews concluded that single-fraction and multifraction schedules held equivalent effectiveness for pain relief, while another review found greater use of shorter or single-fraction regimens may be beneficial, especially in patients with poor performance status. One review concluded that there was no difference in pain response across multiple fraction radiotherapy doses. One review concluded there was no significant difference in palliation of chest pain between higher and lower RT doses (combined OR 1.83; CI 0.76, 4.38; $P = 0.176$; three RCTs). ⁷⁹ One review found that 10 and 6 Gy may produce superior pain response compared to 8 Gy, and 6 Gy may result in better partial response than 8 Gy, but noted that only a few studies documented doses other than 8 Gy. Similarly, another review concluded that 8 Gy should be the standard dose against which future treatments are compared due to its reproducible pain response rate and its established safe profile. Another review concluded that the efficacy of re-irradiation is comparable to initial radiation treatment. One review concluded that palliative pelvic RT was effective at relieving pain in rectal cancer (pooled positive response across 23 studies: 78%) but noted there is considerable heterogeneity in treatments and outcomes across studies. ⁸² One review found positive impact of radionuclides on pain relief.	L (In, Im)

(Continued)

Summary of Findings Table 2
Continued

Intervention and Comparator Age Group Setting Outcome	N	Effect Estimate and Direction of Effects	GRADE ^a
Cementoplasty/ kyphoplasty/ vertebroplasty Adults and mixed samples Outcome: pain management	2 SRs ^{54,77}	Two reviews reported largely positive pain outcomes related to cementoplasty and related interventions but neither review provided effect estimates. One review concluded that percutaneous long bone cementoplasty is safe and offers good pain relief based on data from 10 non-RCT studies; another review found one RCT supporting the use of kyphoplasty for pain relief in patients with vertebral tumors or metastases.	L (S, Im)
Education/self-management Adults and mixed samples Outcome: pain management	2 SRs ^{81,88}	Two reviews reported pain outcomes and found uncertain evidence on the effect of education and self-management interventions. One review found mixed moderate-quality evidence on the effectiveness of combining multiple educational modalities to improve patient pain; however, another review found two studies that reported no significant improvements in pain control after provider educational interventions. Neither review provided effect estimates.	L (Im, In)
Physical therapy/exercise Adults and mixed samples Outcome: pain management	1 SR ⁷¹	One review concluded that physical therapy in palliative care can decrease musculoskeletal pain.	L (S, Im)
Physical therapy/exercise Adults and mixed samples Outcome: physical function	2 SRs ^{57,71}	Two reviews examined physical function outcomes; evidence suggests that physical therapy in palliative care and other exercise-based interventions can improve physical function in patients with advanced illness, though outcome measures varied widely across studies where physical function was the primary outcome.	L (Im, In)
Exercise Adults and mixed samples Outcome: dyspnea management	1 SR ⁵⁷	A single review found one RCT and two non-RCTs that showed exercise interventions improved dyspnea but did not provide effect estimates.	L (Im, In)
Music/art therapy Adults and mixed samples Outcome: pain management	3 SRs ^{51,69,94}	Three reviews reported pain management outcomes related to music/art therapies and all reported positive effects on pain management, while acknowledging differences across studies in control groups and pain assessment tools. One review found that exposure to creative arts and music therapies is shown to reduce pain postintervention compared to no treatment, waiting list, usual care, or placebo controls (SMD 0.54; CI 0.33, 0.75; 18 RCTs) and at follow-up (SMD 0.59; CI 0.41, 0.77; seven RCTs). ⁹⁴ Another review found that music therapy was associated with a significant reduction in pain compared to comfort measures, a volunteer visit, or standard care only but noted a high risk of bias among included studies (SMD -0.42; CI -0.68, -0.17; three non-RCT studies). ⁶⁹ Another review found that five of seven studies reported a significant decrease in pain associated with music therapy compared to standard care or extra interventions such as volunteer visits and verbal relaxation exercises.	Moderate
Nonpharmacological physical (oxygen, cool air, yoga) Adults and mixed samples Outcome: pain management	1 SR ⁸⁰	One review examining different modalities such as massage, aromatherapy, TENS, acupuncture, and warm footbaths found mixed evidence regarding benefits and thus could not draw conclusions about the effects of these nonpharmacological interventions in reducing cancer pain.	V (Im, In)
Nonpharmacological physical (oxygen, cool air, ventilation) Adults and mixed samples Outcome: dyspnea management	2 SRs ^{49,70}	Two reviews reported dyspnea management outcomes related to nonpharmacological physical interventions. One review reported moderate efficacy of a stream of cool air on the face in reducing breathlessness and also reported high-quality evidence that oxygen is not effective for relief of breathlessness in nonhypoxemic patients (SMD -0.09; CI -0.22, 0.04). ⁷⁰ Another review found only a single RCT showing that noninvasive	L (In)

(Continued)

Summary of Findings Table 2
Continued

Intervention and Comparator Age Group Setting Outcome	N	Effect Estimate and Direction of Effects	GRADE ^a
Nonpharmacological physical (oxygen, cool air, yoga) Adults and mixed samples Outcome: function	1 SR ⁸⁵	ventilation was associated with mild improvements in dyspnea, but this was only significant for a subgroup of patients with hypercapnia. One review identified a single RCT demonstrating that yoga significantly improved physical functioning, and two RCTs demonstrating that taichi significantly improved functional capacity among adult cancer patients.	L (Im)
Psychosocial Adults and mixed samples Outcome: physical function	1 SR ⁵⁸	One review concluded that very low-quality evidence indicates that psychological therapies may improve physical functioning directly after the intervention (SMD 0.32; CI 0.01, 0.63, seven RCTs), and at first follow-up, psychosocial interventions were not associated with statistically significant improvement in physical functioning (SMD 0.37, CI -0.20, 0.94; two RCTs). ⁵⁸	V (S, In)
Nonpharmacological cognitive (relaxation, imagery) Adults and mixed samples Outcome: pain management	1 SR ⁸⁰	One review examining cognitive modalities such as relaxation, distraction, and imagery exercises found mixed evidence regarding benefits and thus could not draw conclusions about the effects and safety of the nonpharmacological interventions in reducing cancer pain.	V (Im, In)
Nonpharmacological cognitive (relaxation, imagery, hypnosis) Adults and mixed samples Outcome: dyspnea management	1 SR ⁵³	One review concluded that mindfulness meditation schemes did not show a statistically significant benefit at improving dyspnea management, based on a single RCT.	V (Im, In)
Information and communication tools (telehealth, web sites) Adults and mixed samples Outcome: pain	1 SR ⁷²	One review found two RCTs and one time-series study demonstrating improvements in pain and symptom control associated with telephone, Web-based, and video tools, but studies used various measures and the review did not report effect estimates.	L (Im)
Organizational quality improvement Adults and mixed samples Outcome: symptom improvement	1 SR ⁸⁷	One review examining various quality improvement interventions and outcomes found five RCTs; three RCTs reported nonsignificant improvements in symptoms with patient education and self-management; two RCTs reported significant improvements in symptoms.	V (Im, In)

N = number of systematic reviews; RT = radiotherapy; SR = systematic review; RCT(s) = randomized controlled trial(s); L = low quality of evidence; Im = imprecision; In = inconsistency; SMD = standardized mean difference; M = moderate quality of evidence; S = study limitation; MD = mean difference; V = very low quality of evidence; OR = odds ratio.

^aThe GRADE category is based on identified systematic reviews published between 2013 and February 2018. We used the following reasons for downgrading confidence in the evidence (downgraded by 1 or 2): Study limitation (observational studies start with a low GRADE value), Inconsistency (individual studies do not come to the same conclusions or there is only one study so inconsistency cannot be evaluated), Imprecision (there is no effect estimate, there is no measure of dispersion, or the CI is very broad); we used the systematic review authors' evaluation for other GRADE criteria if there was a formal quality of evidence assessment (see text).

compared to usual care (odds ratio [OR] 2.21; CI 1.31–3.71; five RCTs and two controlled clinical trials).³³ Another review found a similar significant association (RR 1.33; CI 1.14–1.55; three RCTs).³¹ However, there was low- to very low-quality evidence for home-based palliative care on other outcomes including physical symptoms, quality of life, and family/caregiver burden and satisfaction.

Case management: There was low- to very low-quality evidence for the impact of case management on physical symptoms and resource use at the end of life. One review found evidence on the positive impact of case management on reducing symptom distress, including one RCT.⁴³

Domain 2: Physical Aspects of Care

KQ 2: What Is the Impact of Palliative Care Interventions on Physical Symptom Screening, Assessment, and Management of Patients? Forty-eight reviews met inclusion criteria for evaluating the impact of palliative care interventions on physical symptom screening, assessment, and management of patients. Much of the evidence in this domain is low quality largely due to inconsistent findings regarding the impact of interventions on symptoms (Summary of Findings Table 2).

Music/art therapy: However, there was moderate-quality evidence from three reviews^{51,69,94} demonstrating the positive impact of music/art therapy on

Summary of Findings Table 3
Psychological and Psychiatric Aspects of Care

Intervention and Comparator Age Group Setting Outcome	N	Effect Estimate and Direction of Effects	GRADE ^a
Pediatric interventions	0	NA	NA
Comprehensive palliative care Adults and mixed samples Outcome: mood	1 SR ⁴⁸	One review concluded there is mixed evidence from 23 trials of associations of palliative care with improved patient mood.	L (Im, In)
Social support Adults Outcome: mood	1 SR ¹⁰⁶	One review concluded that social support interventions may have a positive impact on mood disturbance but noted that outcome measures and study designs were heterogeneous.	L (S, Im)
Psychosocial interventions Adults Outcome: depression	2 SRs ^{99,108}	Two reviews reported depression outcomes related to psychosocial and psychotherapeutic interventions. One review found that psychotherapy was associated with moderate decrease in depression score (SMD -0.67; CI -1.06, -0.29; 12 studies). ¹⁰⁸ Another review identified a single RCT demonstrating no significant impact of a psycho-educational intervention on patient depression but also found a prospective study reporting improvements in depression after palliative care consultation with a psychosocial component.	L (In)
Psychosocial interventions Adults Outcome: quality of life	1 SR ⁹⁹	One review found one RCT and one prospective study demonstrating that a palliative care consultation with a psychosocial component improves quality of life.	L (Im)
Psycho/spiritual (life review, dignity therapy) Adults Outcome: depression	5 SRs ^{100,101,103,104,107}	Five systematic reviews reported depression outcomes related to psychospiritual interventions and found mixed evidence. One review reported evidence that life review interventions can improve depressive symptoms (SMD -0.78; CI -1.46, -0.11; five RCTs) but noted considerable heterogeneity across studies. ¹⁰⁷ One review found mixed evidence on the effects of dignity therapy on depression and concluded that effects of dignity therapy on depression are still controversial, requiring further evidence on greater impact. Similarly, another review also concluded that additional research is needed to determine the efficacy of dignity therapy. One review identified a single nonrandomized study reporting decreases in depression after a manualized psychospiritual therapy intervention. One review found a single RCT of dignity therapy among patients with high levels of psychological distress and demonstrated significant improvements in depression scores; however, another RCT demonstrated no significant improvement in depression related to dignity therapy.	V (S, In)
Psycho/spiritual (life review, dignity therapy) Adults Outcome: anxiety	7 SRs ^{97,98,100,101,103,104,107}	Seven reviews reported anxiety outcomes related to psychospiritual interventions and found mixed evidence. Two reviews reported evidence that life review interventions can improve anxiety among patients with life-threatening illnesses. One review found mixed evidence on the effects of dignity therapy on anxiety and concluded that effects of dignity therapy on anxiety are still controversial, requiring further evidence on greater impact. Similarly, another review also concluded that additional research is needed to determine the efficacy of dignity therapy for anxiety. One review of various psychospiritual interventions reported that meaning-centered couples therapy, dignity therapy, and a brief psychotherapy intervention to relieve distress were all associated with decreased death anxiety. One review identified a single study reporting decreases in anxiety after a manualized psychospiritual therapy intervention. One review found a single RCT of dignity therapy among patients with high levels of psychological	V (Im, In)

(Continued)

Summary of Findings Table 3
Continued

Intervention and Comparator Age Group Setting Outcome	N	Effect Estimate and Direction of Effects	GRADE ^a
Psychospiritual (life review, dignity) Adults Outcome: distress	1 SR ⁹⁸	distress and demonstrated significant improvements in anxiety scores; however, another RCT demonstrated no significant improvement in anxiety related to dignity therapy. One review concluded that life review interventions may be effective in alleviating general distress (SMD -0.32; CI -0.55, -0.09; five RCTs) but no significant results were reported for psychological distress. ⁹⁸	L (In)
Pharmacological interventions Adults Outcome: depression	3 SRs ^{105,109}	Three reviews reported depression outcomes related to pharmacological interventions; none reported effect estimates. One review found a single RCT demonstrating that methylphenidate reduced symptoms of depression compared to placebo. One review found limited evidence from uncontrolled cohort studies in favor of methylphenidate, oxcarbazepine, bupropion SR, ginkgo biloba, and donepezil compared with placebo for treatment of depression in adult patients with glioma and concluded that it remains unknown whether any of these treatments are effective for depressive disorder. A third review concluded on the basis of four recent clinical trials that the use of serotonergic hallucinogens may improve depressive symptoms among patients with life-threatening illness.	V (S, Im)
Cannabinoids Adults Outcome: depression	1 SR ⁵²	One review found two RCTs reporting no significant differences between cannabinoids and placebo in the treatment of depression.	M (Im)
Cannabinoids Adults Outcome: well-being (negative effect)	1 SR ⁵²	One review reported very low quality of evidence suggesting the effect of cannabinoids for reduction of negative effect compared with placebo, on the basis of a single RCT.	V (Im, In)
Nonpharmacological cognitive (meditation, relaxation, imagery, hypnosis) Adults and mixed samples Outcome: depression	2 SRs ^{60,96}	Two reviews reported depression outcomes but neither review reported effect estimates. One review identified a single RCT of a multimodal psychosocial intervention demonstrating clinically significant benefit on depressive symptoms. Another review found a large and medium of mindfulness-based interventions on depression.	L (Im, In)
Nonpharmacological cognitive (meditation, relaxation, imagery, hypnosis) Adults and mixed samples Outcome: quality of life	3 SRs ^{53,85,96}	Three reviews reported mixed evidence regarding quality of life outcomes but none reported effect estimates. One review found a single RCT reporting no significant differences between mindfulness meditation and controls in quality of life—physical and mental aspects for adult cancer patients. Another review found a large and medium effect of mindfulness-based interventions on cancer-specific quality of life. One review found a single RCT demonstrating improvements in quality of life associated with transcendental meditation.	L (Im, In)
Non-pharmacological cognitive (meditation, relaxation, imagery, hypnosis) Adults and mixed samples Outcome: well-being (stress)	3 SRs ^{53,85,96}	Three reviews reported mixed evidence regarding quality of life outcomes but none reported effect estimates. One review found a single RCT reported low-level evidence suggesting mindfulness meditation improves perceived stress for adult cancer patients. Another review found a medium effect of mindfulness-based interventions on reducing negative emotions, increasing general well-being and relaxation and overall mood. One review found a single RCT demonstrating improvements in emotional well-being associated with transcendental meditation.	L (Im, In)
Nonpharmacological physical (acupuncture, massage, noninvasive ventilation, yoga) Adults and mixed samples	4 SRs ^{49,60,85,105}	Four reviews reported mixed evidence anxiety outcomes of nonpharmacological physical interventions but none reported effect estimates. One review identified a single RCT reporting that	V (S, Im, In)

(Continued)

Summary of Findings Table 3
Continued

Intervention and Comparator Age Group Setting Outcome	N	Effect Estimate and Direction of Effects	GRADE ^a
Outcome: anxiety		acupuncture had transient effects on anxiety. One review concluded that there is limited evidence suggesting a possible beneficial role of massage therapy for anxiety. Another review found no significant association between noninvasive ventilation and improvements in anxiety. Another review studying yoga found a single RCT reporting significant improvements in anxiety.	
Nonpharmacological physical (acupuncture, noninvasive ventilation, yoga) Adults and mixed samples Outcome: depression	3 SR ^{49,85,105}	Three reviews reported depression outcomes of nonpharmacological physical interventions but none reported effect estimates. One review identified a single RCT reporting that acupuncture had transient effects on depression. One review reported no significant association between noninvasive ventilation and improvements in depression.	V (S, Im, In)
Nonpharmacological nurse-led interventions (telemonitoring, education, complementary care) Adults and mixed samples Outcome: anxiety	1 SR ¹⁰²	One review found seven RCTs examining the role of nurses in addressing anxiety in patients with advanced cancer; two demonstrated significant improvements in anxiety associated with a psychoeducational intervention and a telemonitoring program. However, another RCT of a telemonitoring program and an RCT of a complementary care program found no significant changes in anxiety associated with the interventions.	V (S, Im, In)
Music/art therapy Adults Outcome: anxiety	3 SRs ^{51,69,94}	Three reviews reported anxiety outcomes for music/art therapies. One review reported that creative art therapies significantly reduced anxiety compared to controls (SMD 0.28; CI 0.11–0.44; 25 RCTs) after intervention. ⁹⁴ Another review found four studies (one RCT and three pre-post) demonstrating positive effects of music therapy on anxiety. Finally, a third review found two studies examining the effect of music therapy; both found significant reductions in anxiety associated with the intervention.	M (Im)
Music/art therapy Adults Outcome: depression	2 SRs ^{51,94}	Two reviews reported depression outcomes for music/art therapies and the effects were positive. One review reported that creative arts therapies significantly reduced depression compared to no treatment, waiting list, usual care, or placebo controls (SMD 0.23; CI 0.05, 0.40; 11 RCTs) after intervention. ⁹⁴ Another review found three studies (one RCT and two pre-post) demonstrating mixed effects of music therapy on depression.	M (In)
Information and communication tools (telehealth, web sites) Adults and mixed samples Outcome: emotional well-being	1 SR ⁷²	One review found one pre-post study showing videoconferencing significantly improved anxiety for patients at rural health care sites, and one RCT showing that palliative care telephone support significantly improved mood and emotional bother but did not report effect estimates.	L (Im)
Education Adults Outcome: depression	1 SR ⁸¹	One review identified a single RCT of an educational intervention for health care professionals that reported a significant improvement in depressive symptoms among patients nearing the end of life.	V (Im, In)
Exercise Adults Outcome: anxiety	1 SR ⁵⁷	One review found a single pre-post single-arm study demonstrating positive effect of exercise on anxiety.	V (S, Im, In)
Exercise Adults Outcome: depression	1 SR ⁵⁷	One review concluded that based on two pre-post single-arm studies and one program evaluation study, exercise does not improve depression.	V (S, Im)

N = number of systematic reviews; NA = not applicable; SR = systematic review; L = low quality of evidence; Im = imprecision; In = inconsistency; S = study limitation; SMD = standardized mean difference; RCT(s) = randomized controlled trial(s); V = very low quality of evidence; M = moderate quality of evidence. ^aThe GRADE category is based on identified systematic reviews published between 2013 and February 2018. We used the following reasons for downgrading confidence in the evidence (downgraded by 1 or 2): Study limitation (observational studies start with a low GRADE value), Inconsistency (individual studies do not come to the same conclusions or there is only one study so inconsistency cannot be evaluated), Imprecision (there is no effect estimate, there is no measure of dispersion, or the CI is very broad); we used the systematic review authors' evaluation for other GRADE criteria if there was a formal quality of evidence assessment (see text).

Summary of Findings Table 4
Social Aspects of Care

Intervention and Comparator			
Age Group			
Setting			
Outcome	N	Effect Estimate and Direction of Effects	GRADE ^a
Pediatrics	0	NA	NA
Social work interventions	1 SR ¹¹⁰	One review found that various caregiver support services helped to identify caregivers' direct support service needs, decreased caregiver role overload, and led to a nonsignificant increase in social support and benefits finding; however, the review reported no effect estimate across studies.	L (Im)
Adults			
Outcome: identification of and access to social services			
Social support	1 SR ¹⁰⁶	One review reported findings from a single RCT of group therapy for patients with life-limiting illness that showed no demonstrable difference in social support; the review did not report effect estimates.	V (Im, In)
Adults			
Outcome: social support			

N = number of systematic reviews; NA = not applicable; SR = systematic review; L = low quality of evidence; Im = imprecision; RCT(s) = randomized controlled trial(s); V = very low quality of evidence; In = inconsistency.

^aThe GRADE category is based on identified systematic reviews published between 2013 and February 2018. We used the following reasons for downgrading confidence in the evidence (downgraded by 1 or 2): Study limitation (observational studies start with a low GRADE value), Inconsistency (individual studies do not come to the same conclusions or there is only one study so inconsistency cannot be evaluated), Imprecision (there is no effect estimate, there is no measure of dispersion, or the CI is very broad); we used the systematic review authors' evaluation for other GRADE criteria if there was a formal quality of evidence assessment (see text).

pain management outcomes; one review found that exposure to creative arts and music therapies is shown to reduce pain postintervention (SMD 0.54; CI 0.33–0.75; 18 RCTs) and at follow-up (SMD 0.59; CI 0.41–0.77; seven RCTs).⁹⁴ Another review found that music therapy was associated with a significant reduction in pain (SMD –0.42; CI –0.68, –0.17; three non-RCT studies).⁶⁹

Comprehensive palliative care: There was also moderate-quality evidence for the impact of a comprehensive palliative care team for adults on symptom burden. One review found that comprehensive palliative care was associated with a statistically and clinically significant reduction in symptom burden in adults with advanced illness at 1- to 3-month follow-up (SMD –0.66; CI –1.25, –0.07; 10 RCTs) and at 4- to 6-month follow-up (SMD –0.31; CI –0.05, –0.07; six RCTs).⁴⁸

Pharmacotherapies: Fifteen reviews were found synthesizing evidence on pharmacological interventions for pain, dyspnea, nausea/vomiting, and constipation, but evidence was low- to very low-quality, due to inconsistent findings across studies and a lack of pooled effect estimates. Eight reviews addressed pharmacological interventions for pain management and concluded there is limited evidence for metamizole in cancer pain,⁷⁰ methadone as a first-choice opioid for cancer pain,⁷⁶ levomepromazine for pain among palliative care patients,⁸⁹ paracetamol and morphine for pain in dementia patients,⁶⁵ and the use of bisphosphonates⁶⁸ or adjuvant analgesics⁶⁶ for relief of metastatic bone pain. One review concluded that transdermal buprenorphine and transdermal fentanyl demonstrate equivalent analgesic efficacy in patients with cancer pain but noted that long-term data are lacking,⁵⁶ and another review concluded that once-a-day dexamethasone is the preferred corticosteroid for pain control among adult patients with glioma.⁶⁰

Three reviews reported dyspnea outcomes of pharmacological interventions; a 2016 Cochrane review

concluded that there is some low-quality evidence demonstrating the ability for oral or parenteral opioids to palliate breathlessness although the number of included participants was small (change from baseline SMD –0.09; CI –0.36, 0.19; $P = 0.54$; seven studies; post-treatment SMD –0.28; CI –0.50, –0.05; $P = 0.02$; 11 studies).⁶⁷

Evidence for pharmacological interventions for nausea and vomiting was of very low quality. A 2017 Cochrane review found very low-quality evidence that neither supported nor refuted corticosteroid use for nausea/vomiting among patients with advanced cancer (SMD 0.48; CI –1.53, 0.57; two RCTs).⁵⁹ Another review⁸⁹ concluded that levomepromazine is completely or partially effective at managing nausea/vomiting. Two reviews^{73,86} concluded that there is insufficient direct evidence to definitively support the use of haloperidol for the management of nausea and vomiting.

Two reviews reported constipation-related outcomes of pharmacological interventions but did not report effect estimates and found mixed evidence. One review found several RCTs supporting the use of dietetic interventions with probiotics and prebiotics for relieving symptoms of constipation, and mixed evidence supporting the use of lubiprostone, macrogol, and injections of botulinum neurotoxin A for outlet obstruction constipation.⁹² Another review found six RCTs and concluded that evidence supporting the use of laxatives such as lactulose and senna for management of constipation was uncertain but that subcutaneous methylaltrexone is effective in inducing laxation in palliative care patients with opioid-induced constipation.⁹⁵

Cannabinoids: Evidence for the impact of cannabinoids on pain and nausea/vomiting was also of low quality primarily due to the limited number of trials contributing to the evidence, and inconsistent findings among those trials.⁵² Evidence for nonpharmacological physical interventions (e.g., oxygen, cool air)

Summary of Findings Table 5
Spiritual, Religious, and Existential Aspects of Care

Intervention and Comparator Age Group Setting Outcome	N	Effect Estimate and Direction of Effects	GRADE ^a
Pediatric spiritual interventions	0	NA	NA
Spiritual interventions	0	NA	NA
Family/caregiver outcome Spiritual/religious interventions Adults and mixed samples Patient outcome: spiritual well-being	3 SRs ^{104,111,114}	Three reviews reported mixed evidence regarding spiritual well-being outcomes but none reported effect estimates. One review reported inconclusive evidence that interventions with spiritual or religious components for adults in the terminal phase of a disease may or may not enhance well-being. Similarly, a second review found only nonsignificant improvements in spiritual well-being associated with different spiritual interventions. However, one review found three studies of spiritual interventions with demonstrated improvements in spiritual well-being.	V (Im, In)
Life review/dignity therapy Adults and mixed samples Patient outcome: spiritual well-being	5 SRs ^{97,98,100,103,113}	Five reviews reported spiritual well-being outcomes of life review/dignity therapy interventions and found mixed evidence. A 2017 review reported beneficial effects of life review on spiritual well-being (SMD 0.33; CI 0.12, 0.53; four RCTs) ⁹⁸ but noted a high degree of heterogeneity. Another review also found that life review was associated with improvements in spiritual well-being. One review described evidence that dignity therapy was associated with decreased existential distress, enhanced interpersonal and transpersonal spirituality, and improved spiritual well-being. Another review also found that dignity therapy was associated with higher levels of spiritual well-being. A fifth review found that life review was associated with improved spiritual well-being and existential distress but that dignity therapy was not associated with significant improvement in existential domains.	M (In)
Life review/dignity therapy Adults and mixed samples Patient outcome: meaning and purpose	3 SRs ^{100,103,107}	In one review of life review interventions, two RCTs found no significant differences in purpose in life between life review and control groups. Owing to reported heterogeneity, pooled estimates were not calculated. One review reported that moderate to high level of evidence shows that dignity therapy increases sense of purpose and another review of dignity therapy interventions found two RCTs where the intervention was associated with higher levels of meaning in life.	L (Im, In)
Life review/dignity therapy Adults and mixed samples Patient outcome: will to live	1 SR ¹⁰⁰	Dignity therapy was associated with increased will to live in a single RCT described in the review.	L (Im, In)
Life review/dignity therapy Adults and mixed samples Patient outcome: acceptance of death	1 SR ¹⁰⁰	The review identified one quasi-experimental study reporting acceptance of death one month after dignity therapy.	V (S, Im, In)
Life review/dignity therapy Adults and mixed samples Patient outcome: emotional well-being	1 SR ¹⁰¹	One review found a single RCT of dignity therapy among patients with high levels of psychological distress and demonstrated significant improvements in anxiety and depression scores. However, another RCT demonstrated no significant improvement in anxiety or depression related to dignity therapy.	L (Im, In)
Meaning-centered interventions Adults and mixed samples Patient outcome: spiritual well-being	3 SRs ^{97,112,113}	In three reviews, meaning in life interventions was associated with improvements in spiritual well-being but effect estimates were not reported and effects varied by study and outcome.	L (Im, In)
Meaning-centered interventions Adults and mixed samples Patient outcome: emotional well-being	1 SR ¹¹²	In one review, meaning in life interventions was associated with clinical benefits on measures of hopelessness, anxiety, and depression but effect estimates were not reported and effects varied by study and outcome.	V (Im, In)

(Continued)

Summary of Findings Table 5
Continued

Intervention and Comparator Age Group Setting Outcome	N	Effect Estimate and Direction of Effects	GRADE ^a
Meaning-centered interventions Adults and mixed samples Patient outcome: meaning and purpose	1 SR ¹¹²	In one review, meaning in life interventions were associated with clinical benefits on measures of purpose in life but effect estimates were not reported and effects varied by study and outcome.	V (Im, In)
Meaning-centered interventions Adults and mixed samples Patient outcome: quality of life	1 SR ¹¹²	In one review, meaning in life interventions were associated with clinical benefits on measures of quality of life but effect estimates were not reported and effects varied by study and outcome.	V (Im, In)
Meaning-centered interventions Adults and mixed samples Patient outcome: will to live	1 SR ¹¹²	In one review, meaning in life interventions was associated with clinical benefits on measures of wish to hasten death but effect estimates were not reported and effects varied by study and outcome.	V (Im, In)

N = number of systematic reviews; NA = not applicable; SR = systematic review; V = very low quality of evidence; Im = imprecision; In = inconsistency; SMD = standardized mean difference; M = moderate quality of evidence; RCT(s) = randomized controlled trial(s); L = low quality of evidence; S = study limitation.

^aThe GRADE category is based on identified systematic reviews published between 2013 and February 2018. We used the following reasons for downgrading confidence in the evidence (downgraded by 1 or 2): Study limitation (observational studies start with a low GRADE value), Inconsistency (individual studies do not come to the same conclusions or there is only one study so inconsistency cannot be evaluated), Imprecision (there is no effect estimate, there is no measure of dispersion, or the CI is very broad); we used the systematic review authors' evaluation for other GRADE criteria if there was a formal quality of evidence assessment (see text).

and cognitive interventions (relaxation, imagery) was low- to very low-quality for pain, dyspnea, and physical function outcomes.^{49,53,70,80,85}

Domain 3: Psychological and Psychiatric Aspects of Care

KQ 3: What Is the Impact of Palliative Care Interventions on Psychological and Psychiatric Assessment and Management of Patients? Twenty-six reviews met inclusion criteria for evaluating the impact of palliative care interventions on psychological and psychiatric assessment and management of patients. There was moderate-quality evidence for the impact of music/art therapy on anxiety and depression (Summary of Findings Table 3). Three reviews reported anxiety outcomes for music/art therapies.^{51,69,94} One review reported that creative art therapies significantly reduced anxiety (SMD 0.28; CI 0.11–0.44; 25 RCTs) and depression (SMD 0.23; CI 0.05–0.40; 11 RCTs) compared to controls after intervention.⁹⁴ Another review found four studies (one RCT and three pre-post) demonstrating positive effects of music therapy on anxiety and three studies (one RCT and two pre-post) demonstrating reduced depression.⁵¹ A third review found two studies demonstrating significant reductions in anxiety associated with music therapy.⁵¹ There was moderate-quality evidence that cannabinoids did not have an impact on depression compared to placebo⁵² and very low-quality evidence indicating that nonpharmacological cognitive interventions such as relaxation, imagery, hypnosis, psychosocial interventions, and psychospiritual interventions can improve depressive symptoms. One review identified a single RCT of a multimodal psychosocial intervention demonstrating clinically significant benefit

on depressive symptoms.⁶⁰ There was also very low-quality evidence on the impact of education interventions and exercise interventions on depression and anxiety.^{57,81}

Domain 4: Social Aspects of Care

KQ 4: Does an Assessment of Environmental or Social Needs as Part of a Comprehensive Palliative Assessment Improve Needs Identification and Access to Relevant Services? Two reviews met inclusion criteria for evaluating an assessment of environmental or social needs as part of a comprehensive palliative assessment (Summary of Findings Table 4).^{106,110} There is low-quality evidence that social work interventions lead to the identification of and access to social services. One review found that various caregiver support services helped to identify caregivers' direct support service needs, decreased caregiver role overload, and led to a nonsignificant increase in social support and benefits finding; however, the review reported no effect estimate across studies.¹¹⁰ There is very low-quality evidence that social support interventions do not impact social support outcomes. A review reported findings from a single RCT of group therapy for patients with life-limiting illness that showed no demonstrable difference in social support; the review did not report effect estimates.¹⁰⁶

Domain 5: Spiritual, Religious, and Existential Aspects of Care

KQ 5: What Is the Effect of a Spiritual Assessment and/or Programs on Patient and Family/Caregiver Spiritual and Emotional Well-being? Eleven reviews met inclusion criteria for evaluating the effect of a spiritual assessment and/or program on patient and family/

Summary of Findings Table 6
Cultural Aspects of Care

Intervention and Comparator Age Group Setting Outcome	N	Effect Estimate and Direction of Effects	GRADE ^a
Pediatric interventions	0	NA	NA
Culturally relevant palliative care Adults and mixed samples Patient outcome: DNR	1 SR ¹¹⁵	One review found one study of a culturally tailored inpatient palliative care consultation services reporting a postintervention increase in DNR completion among Native American patients but did not report effect estimates.	V (S, Im, In)
Culturally relevant palliative care Adults and mixed samples Patient outcome: quality of death/dying	1 SR ¹¹⁷	One review found a single pilot study reporting significant increases in coping skills and significant decreases in depressive symptoms among patients but did not report effect estimates.	V (S, Im, In)
Culturally relevant palliative care Adults and mixed samples Family/caregiver outcome: quality of death/dying	1 SR ¹¹⁷	One review found a single pilot study reporting significant increases in coping skills and in self-efficacy among caregivers but did not report effect estimates.	V (S, Im, In)
Interpreters Adults and mixed samples Patient outcome: quality of care	1 SR ¹¹⁶	One review concluded that improving access to and/or standardizing utilization of professional interpreter services could improve the quality of care provided to patients at the end of life but did not report effect estimates.	V (S, Im, In)
Interpreters Adults and mixed samples Patient outcome: communication	1 SR ¹¹⁶	One review found a single pilot study reporting significant increases in coping skills and in self-efficacy among caregivers but did not report effect estimates.	V (S, Im, In)
Interpreters Adults and mixed samples Family/caregiver outcome: information sharing	1 SR ¹¹⁶	One review concluded that improving access to and/or standardizing utilization of professional interpreter services could improve the quality of care provided to patients at the end of life but did not report effect estimates.	V (S, Im, In)

N = number of systematic reviews; NA = not applicable; SR = systematic review; DNR = do-not-resuscitate; V = very low quality of evidence; S = study limitation; Im = imprecision; In = inconsistency.

^aThe GRADE category is based on identified systematic reviews published between 2013 and February 2018. We used the following reasons for downgrading confidence in the evidence (downgraded by 1 or 2): Study limitation (observational studies start with a low GRADE value), Inconsistency (individual studies do not come to the same conclusions or there is only one study so inconsistency cannot be evaluated), Imprecision (there is no effect estimate, there is no measure of dispersion, or the CI is very broad); we used the systematic review authors' evaluation for other GRADE criteria if there was a formal quality of evidence assessment (see text).

caregiver spiritual and emotional well-being (Summary of Findings Table 5).

Life review/dignity therapy: There is moderate-quality evidence for the positive impact of life review/dignity therapy on spiritual well-being. A 2017 review reported beneficial effects of life review on spiritual well-being (SMD 0.33; CI 0.12–0.53; four RCTs) but noted a high degree of heterogeneity.⁹⁸ Another review also reported that life review was associated with improvements in spiritual well-being.¹¹³ One review described evidence that dignity therapy was associated with decreased existential distress, enhanced interpersonal and transpersonal spirituality, and improved spiritual well-being.¹⁰⁰ Another review reported that dignity therapy was associated with higher levels of spiritual well-being.¹⁰³ A fifth review reported that life review was associated with improved spiritual well-being and existential distress but that dignity therapy was not associated with significant improvement in existential domains.⁹⁷ There was low to very low evidence for life review/dignity therapy's impact on other outcomes such as meaning and purpose, will to live, acceptance of death, and emotional well-being.

Other spiritual interventions: There is very low evidence for a positive impact of spiritual/religious

interventions on spiritual well-being. There was also very low-quality evidence for a positive impact of other meaning-centered interventions on spiritual well-being, emotional well-being, meaning and purpose, quality of life, and will to live.

Domain 6: Cultural Aspects of Care

KQ 6: What Is the Impact of Culturally and Linguistically Sensitive Care on Physical, Social, Emotional, and Spiritual Well-being of the Patient and Family/Caregiver? Three reviews met inclusion criteria for evaluating the impact of culturally and linguistically sensitive care on physical, social, emotional, and spiritual well-being of the patient and family/caregiver (Summary of Findings Table 6). Evidence is of very low-quality, owing to study limitations, inconsistency in findings, and lack of pooled effect estimates in the three identified reviews. There was very low-quality evidence that culturally relevant palliative care led to higher rates of do-not-resuscitate orders and improved quality of death from both the patient and family/caregiver perspectives. One review found one study of a culturally tailored inpatient palliative care consultation services reporting a postintervention increase in do-not-resuscitate completion among Native American patients but did not report effect estimates.¹¹⁵ Another

Summary of Findings Table 7
Care of the Patient Nearing the End of Life

Intervention and Comparator Age Group Setting Outcome	N	Effect Estimate and Direction of Effects	GRADE ^a
Grief/bereavement support services Pediatric Child outcome: grief	2 SRs ^{120,121}	Two reviews reported pediatric grief outcomes and found positive effects. One review identified five studies with strong evidence on medium to large effects of grief and bereavement support on parentally bereaved children's traumatic grief symptoms. Another review found some evidence that bereavement services for bereaved child siblings contributed positively to the grief experience. Neither review reported effect estimates across studies.	M (Im)
Grief/bereavement support services Pediatric Child outcome: emotional well-being	2 SRs ^{120,121}	Two reviews reported pediatric emotional well-being outcomes and found mixed evidence. One review identified some studies with strong evidence on small effects for parentally bereaved children's PTSD symptoms (one study), anxiety (two studies), and depression in girls (one study); one study identified in the same review did not show effects for boys on the anxiety and depression. Another review identified one study demonstrating a positive effect of group-based grief/bereavement services on bereaved child siblings' sense of isolation, development of healing friendships, and coping skills. Neither review reported effect estimates across studies.	L (Im, In)
Grief/bereavement support services Pediatric Adult family outcome: grief	2 SRs ^{120,121}	Two reviews reported bereaved parent grief outcomes and found mixed evidence. One review identified two studies with strong evidence on medium effects for grief discussions in the family; another study with strong evidence identified in the same review showed no effects of grief/bereavement services on bereaved parents' present grief. Another review found mixed evidence on the positive impact of grief/bereavement services for bereaved parents and concluded that bereavement services are most effective for parents experiencing more complex mourning. Neither review reported effect estimates.	L (Im, In)
Grief/bereavement support services Pediatric Adult family outcome: emotional well-being	2 SRs ^{120,121}	Two reviews reported emotional well-being outcomes related to parental grief/bereavement support interventions and found conflicting evidence. One review found evidence on the impact of grief/bereavement services on bereaved parents' feelings of being supported; parental depression; and mental health. However, two studies identified in the same review with strong evidence showed no effects on depression. Another review found qualitative evidence on improvements in bereaved parents' emotional status after a group-based grief/bereavement support group. Neither review reported effect estimates.	L (Im, In)
Grief/bereavement support services Adults Adult family outcome: grief	1 SR ¹²²	One review found that bereaved caregivers participating in predeath grief interventions had more favorable postdeath emotional health outcomes, including lower levels of grief, but did not report effect estimates.	L (Im)
Grief/bereavement support services Adults Adult family outcome: emotional well-being	2 SRs ^{117,122}	Two reviews reported family emotional well-being outcomes and found positive effects but neither reported effect estimates. One review identified a single RCT of family group therapy that demonstrated reductions in distress and depressive symptoms among informal caregivers for cancer patients. Another review found evidence showing that receiving affective support both before and after family members' death mediates negative bereavement outcomes such as depressive symptoms, anxiety, and guilt in bereaved caregivers.	L (Im)
Grief counseling/therapy Adults Adult family outcome: grief	2 SRs ^{118,119}	Two reviews reported grief outcomes related to grief counseling/therapy interventions and found mixed evidence on impact but neither reported effect estimates. In one review, complicated grief therapy was found to be more effective than interpersonal psychotherapy in reducing abnormal grief. Another review found that grief management and counseling interventions did not have a significant impact on caregiver anticipatory grief but did find a single RCT demonstrating small improvements in postdeath and complicated grief outcomes after a multicomponent grief counseling intervention.	V (S, Im, In)

(Continued)

Summary of Findings Table 7
Continued

Intervention and Comparator Age Group Setting Outcome	N	Effect Estimate and Direction of Effects	GRADE ^a
Grief counseling/therapy Adults Adult family outcome: emotional well-being	1 SR ¹¹⁹	In one review, complicated grief therapy was found to be more effective than interpersonal psychotherapy in improving work and social adjustment; however, the review did not report effect estimates.	V (S, Im)
End-of-life care Pediatric	0	NA	NA
End-of-life care—pharmacological sedation Adults Outcome: quality of care	1 SR ¹²⁴	One review found four nonrandomized studies comparing sedated and nonsedated groups and showed that despite sedation with the intent to control symptoms, delirium and dyspnea were still troublesome symptoms in these people in the last few days of life and were significantly worse in the sedated group. Control of other symptoms appeared to be similar in sedated and nonsedated groups. In addition, all studies identified in the review except one compared survival time in the sedated and nonsedated groups and concluded that there was no statistically significant difference between the groups. The review did not report effect estimates.	V (S, Im)
End-of-life care—pharmacological symptom control Adults Outcome: quality of care	1 SR ¹²³	One review examining a range of palliative interventions and outcomes concluded that there is a lack of evidence concerning the effectiveness and safety of palliative drug treatment in dying patients. No evidence was found for scopolamine hydrobromide and atropine for death rattle; some evidence was found supporting the use of morphine and midazolam for dyspnea, anxiety, or terminal restlessness; and some support was found for morphine, diamorphine, and fentanyl for pain. The review did not report effect estimates.	V (Im, In)

N = number of systematic reviews; SR = systematic review; M = moderate quality of evidence; Im = imprecision; PTSD = post-traumatic stress disorder; L = low quality of evidence; In = inconsistency; RCT(s) = randomized controlled trial(s); V = very low quality of evidence; S = study limitation; NA = not applicable. ^aThe GRADE category is based on identified systematic reviews published between 2013 and February 2018. We used the following reasons for downgrading confidence in the evidence (downgraded by 1 or 2): Study limitation (observational studies start with a low GRADE value), Inconsistency (individual studies do not come to the same conclusions or there is only one study so inconsistency cannot be evaluated), Imprecision (there is no effect estimate, there is no measure of dispersion, or the CI is very broad); we used the systematic review authors' evaluation for other GRADE criteria if there was a formal quality of evidence assessment (see text).

review found that a single pilot study reported significant increases in coping skills among patients and family/caregivers and decreases in depressive symptoms among patients but did not report effect estimates.¹¹⁷ There was also very low-quality evidence that interpreters have a positive impact on quality of care, communication, and information sharing.

Domain 7: Care of the Patient Nearing the End of Life
KQ 7a: What Is the Effect of Grief and Bereavement Programs on Family/Caregiver Outcomes? Six reviews met inclusion criteria for evaluating the effect of grief and bereavement interventions on family/caregiver outcomes. There is moderate-quality evidence for the positive impact of grief and bereavement support interventions on grief outcomes for children (Summary of Findings Table 7). Two reviews reported pediatric grief outcomes.^{120,121} One review identified five studies with strong evidence on medium to large effects of grief and bereavement support on parentally bereaved children's traumatic grief symptoms.¹²¹ Another review found some evidence that bereavement services for bereaved child siblings contributed positively to the grief experience.¹²⁰ Neither review

reported effect estimates across studies. There is low-quality evidence for these interventions on pediatric emotional well-being and adult grief and well-being outcomes due to imprecision and inconsistency of results. There is low-quality evidence for grief and bereavement support services on grief and emotional well-being outcomes among bereaved adult caregivers.^{117,122} There was also very low-quality evidence on the impact of grief counseling and therapy interventions on bereaved adult grief and emotional well-being outcomes. Results varied by type and style of counseling intervention and the specific outcomes measured; for example, complicated grief versus anticipatory grief.^{118,119}

KQ 7b: What Is the Impact of Hospice and Palliative Care in the Final Days of Life on Quality of Care and Quality of Death/Dying? Two reviews met inclusion criteria for the impact of hospice and palliative care in the final days of life on quality of care and quality of death/dying; one examined the effect of pharmacological sedation and the other examined pharmacological symptom control interventions at the end of life. There was very low-quality evidence to support that

Summary of Findings Table 8
Ethical and Legal Aspects of Care

Intervention and Comparator Age Group Setting Outcome	N	Effect Estimate and Direction of Effects	GRADE ^a
Advance directive implementation Pediatric Multiple settings Outcome: treatment decisions	1 SR ¹⁵²	One review concluded that pediatric ACP can facilitate treatment decision making, on the basis of a chart review study reporting that after the implementation of an advanced directive, ventilator support and catecholamines were withdrawn and narcotics added for most patients.	
Advance directive implementation Pediatric Multiple settings Outcome: death at home	1 SR ¹⁵²	One review found two qualitative studies suggesting that pediatric ACP sessions promote home deaths for children.	V (S, Im)
Advance directive implementation Pediatric Multiple settings Outcome: surrogate understanding	1 SR ¹⁵²	One review found evidence from a single RCT that pediatric ACP discussions improved surrogates' understanding of the patient's preferences.	V (Im, In)
Advance directive implementation Pediatric Multiple settings Outcome: quality of communication	1 SR ¹⁵²	One review found evidence from a single RCT that participants in pediatric ACP discussions report higher quality of communication than those who do not participate in ACP discussions.	V (Im, In)
Advance directive implementation Pediatric Multiple settings Outcome: caregiver well-being	1 SR ¹⁵²	One review found a single RCT indicating pediatric ACP triggers positive emotional experiences in surrogates of HIV-infected adolescent patients.	V (Im, In)
Family-centered ACP Pediatric Multiple settings Outcome: treatment decisions	2 SRs ^{141,147}	Two reviews concluded that family-centered ACP increases the likelihood of limiting the use of futile or expensive and invasive treatments at the end of life but did not report effect estimates.	L (S, Im)
Family-centered ACP Pediatric Multiple settings Outcome: decisional conflict	1 SR ¹⁵¹	One review identified a single RCT that reported that family-centered ACP leads to decreased decisional conflict.	V (Im, In)
Family-centered ACP Pediatric Multiple settings Outcome: preference-concordant care	1 SR ¹⁴¹	One review identified a single longitudinal cohort study reporting that family-centered ACP for children and adolescents with cancer increased the likelihood that patients were more likely to receive end-of-life care that was consistent with their preferences.	V (S, Im, In)
Family-centered ACP Pediatric Multiple settings Outcome: surrogate understanding	2 SRs ^{141,151}	Two reviews reported surrogate understanding of the outcomes and found positive effects but did not provide effect estimates. One review identified a longitudinal cohort study reporting that family-centered ACP for children and adolescents with cancer increased family's ability to honor the wishes of their children. Another review identified one RCT of a family-centered ACP intervention for children or adolescents with HIV that found the intervention increased congruence in adolescent/surrogate treatment preferences.	L (Im)
Family-centered ACP Pediatric Multiple settings Outcome: quality of communication	1 SR ¹⁵¹	One RCT of a family-centered ACP intervention for children or adolescents with HIV found that the intervention enhanced quality of communication.	V (Im, In)
Orders/advance directive Adults or mixed samples Multiple settings Outcome: treatment decisions	1 SR ^{125,127,148}	One review noted that most identified non-RCT studies of advance directive or physician order interventions led to decreased use of life-sustaining treatments, decrease in hospitalization, and increased use of hospice and palliative care.	L (S, Im)
Orders/advance directive Adults or mixed samples Multiple settings Outcome: preference-concordance	3 SRs ^{125,127,148}	Three reviews reported preference-concordance outcomes related to advance directive interventions and found positive effects. One review found that patients receiving advance directive interventions with communication had a significantly increased likelihood of receiving	M (S)

(Continued)

Summary of Findings Table 8
Continued

Intervention and Comparator Age Group Setting Outcome	N	Effect Estimate and Direction of Effects	GRADE ^a
Orders/advance directive Adults or mixed samples Multiple settings Outcome: documentation	2 SRs ^{125,148}	end-of-life care in concordance with their preferences compared with control groups (OR 4.66; CI 1.20, 18.08; three RCTs). ¹²⁵ Another review reported that chart-review and interview data from three studies showing orders documented on a structured advance directive form were largely consistent with patients' expressed preferences. A third review found that advance directive interventions were associated with an increase in compliance with patients' end-of-life wishes in three of four non-RCT studies investigating this effect. Two reviews found that advance directive—focused interventions increased documentation. One review showed an increased likelihood for the completion of advance directives compared to usual care (OR 3.26; CI 2.00, 5.32; 13 RCTs). ¹²⁵ Another review found two chart review studies indicating high rates of documentation of end-of-life conversations related to advance directive form completion.	M (S)
Orders/advance directive Adults or mixed samples Multiple settings Outcome: quality of communication	1 SR ¹²⁵	One review found two trials reporting significant results in favor of advance directive interventions for improving quality of communication between patients and health care providers but did not report effect estimates.	L (Im)
Orders/advance directive Adults or mixed samples Multiple settings Outcome: decisional conflict/consensus	1 SR ¹²⁵	One review found mixed evidence on the impact of advance directive interventions on decisional conflict and certainty; three identified intervention trials of advance directives demonstrated a decrease in decisional conflict but two other trials found no change in decisional conflict. The review did not report effect estimates.	L (Im, In)
Orders/advance directive Adults or mixed samples Multiple settings Outcome: quality of care/death	1 SR ¹²⁷	One review concluded that there is mixed evidence that advance directive interventions positively impact the quality of end-of-life care.	V (S, Im, In)
Decision tools Adults or mixed samples Multiple settings Outcome: treatment decisions	4 SRs ^{72,134,145,146}	Four reviews reported treatment decision outcomes related to the use of decision tools and found mixed evidence. One review reported low-quality evidence that patients receiving video decision tool interventions are less likely to prefer CPR than controls (RR 0.50; CI 0.27, 0.95; seven RCTs) but noted low-quality evidence due to considerable heterogeneity across studies. ¹⁴⁵ Three other reviews found that video decision tools were associated with significant increases in the selection of comfort care as primary goal, but none reported effect estimates.	L (S, In)
Decision tools Adults or mixed samples Multiple settings Outcome: concordance	2 SRs ^{72,146}	Two reviews reported patient-surrogate concordance outcomes related to the use of decision tools, but neither reported effect estimates. Both reviews identified the same single RCT of a video tool that significantly increased concordance of surrogate prediction and patient preference.	L (Im)
Decision tools Adults or mixed samples Multiple settings Outcome: documentation	3 SRs ^{72,145,146}	Three reviews reported on the impact of decision tools on documentation but found mixed evidence. One review concluded that there may be a small effect of decision aids on documentation of advance directives but with a wide CI including no effect (RR 1.1; CI 0.85,	L (S, In)

(Continued)

Summary of Findings Table 8
Continued

Intervention and Comparator Age Group Setting Outcome	N	Effect Estimate and Direction of Effects	GRADE ^a
Decision tools Adults or mixed samples Multiple settings Outcome: quality of communication	2 SRs ^{72,146}	1.46; four RCTs). ¹⁴⁵ In another review, four studies were identified showing increased rates of ACP documentation, but two studies showed no change. Another review also found mixed evidence on the positive impact of decision aids on ACP documentation. Two reviews reported communication outcomes and found mixed evidence, but effect estimates were not reported. One review described three decision tools that were found to improve clinical communication. Another review found two studies demonstrating the positive effect of decision aids on quality and frequency of end-of-life communication, and one study where no change was detected.	L (Im, In)
Decision tools Adults or mixed samples Multiple settings Outcome: decisional conflict/consensus	5 SRs ^{72,134,135,145,146}	Five reviews reported decisional conflict outcomes and found mixed evidence on impact. None of the reviews reported effect estimates. One review found three studies reporting improved decisional conflict associated with multicomponent decision aid interventions. Another review reported a single RCT of a video decision aid that led to increased certainty about decision making. One review reported improvements in decisional conflict in eight studies but the reduction was only significant in four studies. Another review reported a single RCT reporting significantly lower decisional uncertainty associated with a video decision aid than control. Another review reported a single high-quality RCT that found no change in decisional conflict associated with a decision aid intervention.	L (Im, In)
Decision tools Adults or mixed samples Multiple settings Outcome: caregiver well-being	1 SR ¹⁴⁶	One review found a single RCT reporting the positive impact of a booklet assisting family members with the decision about disclosure of terminal status on caregiver depression.	L (Im, In)
Care planning discussion Adults or mixed samples Multiple settings Outcome: preference-concordance	1 SR ¹⁵⁰	A 2014 Health Quality Ontario systematic review found one RCT and two observational studies demonstrating that care planning discussions can increase preference-concordant care (OR: 2.28; CI 1.41, 3.70). ¹⁵⁰	M (In)
Care planning discussion Adults or mixed samples Multiple settings Outcome: concordance	1 SR ¹⁵⁰	A 2014 Health Quality Ontario systematic review found two RCTs and one observational study demonstrating that care planning discussions are associated with greater concordance between patient and family wishes but did not provide pooled effect estimates.	M (Im)
Care planning discussion Adults or mixed samples Multiple settings Outcome: documentation	1 SR ¹⁵⁰	A 2014 Health Quality Ontario systematic review found that based on evidence from one large cluster RCT and two large RCTs, single-provider care planning discussions were associated with a 13% to 77% (95% CIs ranged from 5% to 83%) increase in completion of ACP documents and processes, though results were not pooled because of heterogeneity. The review also reported a large RCT showing that team-based care planning discussions were associated with a 22% (95% CI: 15%, 30%) increase in the completion of ACP processes and documents.	M (Im)
Care planning discussion Adults or mixed samples Multiple settings Outcome: treatment decisions	1 SR ¹⁵⁰	One review noted that patients who had care planning discussions with a single provider were less likely to be resuscitated (two observational studies) and more likely to receive hospice care (one RCT) than those who did not participate in care planning discussions.	L (Im)

(Continued)

Summary of Findings Table 8
Continued

Intervention and Comparator Age Group Setting Outcome	N	Effect Estimate and Direction of Effects	GRADE ^a
Facilitated ACP Adults or mixed samples Multiple settings Outcome: documentation	2 SRs ^{130,155}	Two reviews examined the impact of facilitated ACP on documentation of ACP and reported mixed evidence. One review concluded on the basis of one RCT and seven non-RCT studies that a low level of evidence indicates that facilitated ACP models increase documentation of advance directives and physician orders; another review highlighted the lack of consistent patient outcome evidence to support the use of facilitated ACP models to improve documentation.	L (Im, In)
Facilitated ACP Adults or mixed samples Multiple settings Outcome: surrogate understanding	1 SR ¹³⁰	One review concluded on the basis of seven RCTs that a high level of evidence demonstrates facilitated ACP models positively impact patient-surrogate congruence but did not provide effect estimates.	M (Im)
Facilitated ACP Adults or mixed samples Multiple settings Outcome: preference concordance	2 SRs ^{130,155}	Two reviews concluded that evidence is mixed, inconclusive, and too poor in quality to determine whether facilitated ACP models change the consistency of treatment with wishes at the end of life.	L (Im, In)
Facilitated ACP Adults or mixed samples Multiple settings Outcome: treatment decisions	1 SR ¹³⁰	One review concluded on the basis of two identified implementation studies that evidence is mixed, inconclusive, and too poor in quality to determine whether facilitated ACP models change treatment decisions and health care use at the end of life.	V (S, Im, In)
Facilitated ACP Adults or mixed samples Multiple settings Outcome: decisional conflict/consensus	1 SR ¹⁵⁵	One review concluded that there is a lack of consistent patient outcome evidence to support any one facilitated ACP intervention as an approach to decreasing decisional conflict.	L (Im, In)
Facilitated ACP Adults or mixed samples Multiple settings Outcome: caregiver well-being	1 SR ¹⁵⁵	One review identified an RCT of a facilitated ACP model that demonstrated improvements in symptoms of anxiety and depression among bereaved family caregivers.	L (Im, In)
Statement of future care Adults or mixed samples Multiple settings Outcome: treatment decisions	1 SR ¹⁴³	One review concluded that there is mixed evidence on the effect of a statement about future care on types of treatment at the EOL.	V (S, Im, In)
Structured communication Adults or mixed samples Multiple settings Outcome: documentation	2 SRs ^{28,126}	One review concluded that standardized documentation may be helpful for improving the frequency and quality of documenting end-of-life decisions; another review concluded that low to very low-quality evidence suggests that structured communication tools may increase completion of advance directives.	L (S, Im)
Structured communication Adults or mixed samples Multiple settings Outcome: quality of communication	2 SRs ^{126,142}	Two reviews reported quality of communication outcomes related to the use of structured communication tools and found mixed evidence. One review found significant improvements in quality of communication between patients and health care providers (SMD 3.02; CI 1.26, 4.78; two RCTs) associated with structured communication tools, but no differences between intervention and controls in terms of quality of communication between patients and their surrogate decision makers (SMD 0.07; CI -0.28, 0.43). ¹²⁶ Another review identified two studies (one RCT) out of seven total studies measuring quality of communication showing significant improvements in quality of patient-provider communication associated with structured communication interventions but noted generally poor quality of included studies.	L (In)

(Continued)

Summary of Findings Table 8
Continued

Intervention and Comparator Age Group Setting Outcome	N	Effect Estimate and Direction of Effects	GRADE ^a
Structured communication Adults or mixed samples Multiple settings Outcome: preference-concordance	1 SR ²⁸ (Field, 2018)	One review found several studies that reported structured communication interventions moved preferences toward less invasive levels of care at life's end; however, a single study found no difference in the care received at the end of life.	V (S, In, Im)
Structured communication Adults or mixed samples Multiple settings Outcome: preference-concordance	2 SRs ^{28,126}	Two reviews reported preference-concordant care outcomes and found low-quality evidence on positive effects. One review found several studies that reported structured communication interventions increased compliance with participants' wishes (including DNR) and deaths at home; another review concluded that low to very low-quality evidence suggests that structured communication tools may increase concordance between the care desired and the care received by patients.	L (S, Im)
Electronic health record intervention Adults or mixed samples Multiple settings Outcome: documentation	1 SR ¹⁵⁶	One review found evidence, including from one RCT, that electronic health record interventions commonly demonstrated an improvement in documentation of advance care planning discussions, advance directives, and physician orders, in the medical record, but noted significant heterogeneity in study designs and intervention components.	L (S, Im)
Family meetings Adults or mixed samples Multiple settings Outcome: treatment decisions	1 SR ¹⁵⁴	One review found evidence from different studies that family meetings can result in earlier do-not-resuscitate decisions, shorter ICU lengths of stay, less use of resuscitation and mechanical ventilation, and earlier hospice admission.	L (S, Im)
Family meetings Adults or mixed samples Multiple settings Outcome: caregiver well-being	1 SR ¹⁵⁴	One review found evidence, including from a single multicenter RCT, that structured family meetings could improve psychological well-being and decrease posttraumatic stress symptoms in bereavement.	L (Im)
Comprehensive palliative care Adults or mixed samples Multiple settings Outcome: documentation	2 SRs ^{48,138}	Two reviews reported mixed evidence regarding ACP documentation associated with comprehensive palliative care interventions. One review reported that palliative care was associated with improvements in advance care planning. Another review of palliative care for homeless persons found some limited and mixed evidence on an association with documentation of advance directives and concluded that the effectiveness of ACP interventions for homeless persons is uncertain.	L (Im, In)
Comprehensive palliative care Adults or mixed samples Multiple settings Outcome: treatment decisions	1 SR ¹³³	A 2016 Cochrane review found no evidence that palliative care affected decisions to forgo CPR in the hospital in the single RCT where this was examined and concluded that there is insufficient evidence to assess the effect of palliative care interventions in advanced dementia.	L (Im, In)
Comprehensive palliative care Adults or mixed samples Multiple settings Outcome: decisional conflict/consensus	1 SR ¹³³	One review found limited evidence that palliative care may decrease decisional conflict and concluded that there is insufficient evidence to assess the effect of palliative care interventions in advanced dementia.	L (Im, In)
ACP (mixed) Adults or mixed samples Multiple settings Outcome: documentation	3 SRs ^{137,144,149}	Three reviews reported documentation outcomes noting positive effects, although none reported effect estimates. One review found three studies demonstrating increased advance directive completion as a result of ACP interventions; another review found one study demonstrating nurse-led facilitation of end-of-life communication led to significant increases in documentation of advance directives. One	L (S, Im)

(Continued)

Summary of Findings Table 8
Continued

Intervention and Comparator Age Group Setting Outcome	N	Effect Estimate and Direction of Effects	GRADE ^a
ACP (mixed) Adults or mixed samples Multiple settings Outcome: preference-concordance	2 SRs ^{60,137}	review found evidence in three of nine studies that ACP interventions led to an increase in the documentation of end-of-life care preferences compared to control. Two reviews concluded that there is limited and mixed evidence that multicomponent ACP interventions improve preference-concordant care.	V (S, Im, In)
ACP (mixed) Adults or mixed samples Multiple settings Outcome: treatment decisions	1 SR ¹⁴⁴	One review concluded that the evidence for multifocal ACP interventions leading to changes in end-of-life care treatment decisions and practices is unclear.	L (Im, In)
ACP (mixed) Adults or mixed samples Multiple settings Outcome: quality of communication	1 SR ¹⁴⁴	One review concluded that the evidence for multifocal ACP interventions improving quality of communication is unclear.	L (Im, In)
ACP (mixed) Adults or mixed samples Multiple settings Outcome: quality of care	1 SR ⁶⁰	One review found a single RCT showing that ACP in older patients with glioma admitted to the hospital improved the quality of end-of-life care.	L (Im, In)
ACP (mixed) Adults or mixed samples Multiple settings Outcome: concordance	1 SR ¹⁴⁹	One review found two RCTs demonstrating significant effects of advance care planning interventions on the congruence of patient wishes and surrogate knowledge.	M (Im)
ACP (mixed) Adults or mixed samples Multiple settings Outcome: decisional conflict/consensus	2 SRs ^{137,149}	Two reviews reported decisional conflict outcomes related to ACP interventions and found mixed evidence; none reported effect estimates. One review found two studies of ACP interventions and found no significant effects on decisional conflict; another review noted that there is very limited evidence (one of nine RCTs) that multicomponent ACP interventions result in reduced levels of decisional conflict.	L (Im, In)
ACP (mixed) Adults or mixed samples Multiple settings Outcome: end-of-life outcomes	1 SR ¹³¹	The single review found a positive effect but did not differentiate between observational and intervention studies.	L (S, Im)
ACP (mixed) Adults or mixed samples Multiple settings Outcome: surrogate understanding	1 SR ¹³⁷	One review noted there is very limited evidence (two of nine RCTs) that multicomponent ACP interventions result in improved understanding among surrogates of patient end-of-life preferences	L (Im)
ACP (mixed) Adults or mixed samples Multiple settings Outcome: caregiver well-being	3 SRs ^{60,137,144}	Three reviews reported caregiver well-being outcomes related to ACP interventions and reported mixed evidence. One review identified a single study of a structured end-of-life family conference that led to improvements in caregivers, caregiver psychological morbidity, and expressions of guilt. One review noted that there is very limited evidence that multicomponent ACP interventions lead to reduced levels of stress, anxiety, and depression among bereaved family members, but another review identified a single RCT demonstrating that ACP interventions reduced stress, anxiety, and depression in bereaved relatives.	L (Im, In)
Ethics consultation ICU/inpatient Adults Outcome: treatment decisions	2 SRs ^{129,153}	Two reviews reported treatment decisions related to ethics consultation and found mixed evidence. One review found that ethics consultation was associated with nonsignificant decreased use of mechanical ventilation (−3.18 d; CI −8.27, 1.90; <i>P</i> = 0.22, three RCTs) and artificial nutrition and hydration (−0.79 d; CI, −2.98, 1.41; <i>P</i> = 0.48). ¹²⁹ Another review found decreased use of mechanical ventilation associated with ethics consultation in one RCT.	M (Im)

(Continued)

Summary of Findings Table 8
Continued

Intervention and Comparator Age Group Setting Outcome	N	Effect Estimate and Direction of Effects	GRADE ^a
Ethics consultation ICU/inpatient Adults Outcome: decisional conflict/consensus	1 SR ¹²⁹	One 2018 systematic review concluded that ethics consultation facilitates consensus around clinical decisions (OR 4.09; CI 1.01, 16.55; two RCTs and one non-RCT). ¹²⁹	M (Im)
Ethics consultation ICU/inpatient Adults Outcome: quality of communication	1 SR ¹²⁹	One review described a single RCT that found patients receiving ethics consultation reported significantly higher quality of communication than those receiving usual care.	L (Im, In)
Ethics consultation ICU/inpatient Adults Outcome: caregiver well-being	1 SR ¹⁵³	One review found a single study showing that a structured family conference resulted in decreased symptoms of posttraumatic stress disorder, anxiety, and depression among family members.	V (S, Im, In)
Structured communication tools ICU/inpatient Adults Outcome: treatment decisions	2 SRs ^{128,140}	Two reviews reported treatment decision outcomes and reported conflicting evidence. One review found two RCTs demonstrating no significant difference between intervention and control groups in the withholding or withdrawal of life-sustaining treatments (RR 0.99, CI 0.89, 1.10; $P = 0.85$) but also found four observational studies demonstrating an increase in treatment withdrawal associated with the use of communication tools (RR 1.54; CI 1.2, 1.98, $P < 0.001$), though the authors noted large statistical heterogeneity across studies. ¹²⁸ Another review found limited mixed evidence to support the use of intensive communication structures and ethics consultations to decrease use of intensive intervention such as mechanical ventilation.	L (In)
Structured communication tools ICU/inpatient Adults Outcome: decisional conflict/consensus	1 SR ¹⁴⁰	One review identified multiple studies demonstrating that decision support and communication interventions led to decreased decision conflict, fewer nonconsensus days though the authors noted significant heterogeneity in the types of interventions evaluated.	L (Im, In)
Structured communication tools ICU/inpatient Adults Outcome: preference-concordant care	1 SR ¹²⁸	One review included a single RCT finding that communication tools led to a significant increase in family members expressing the patient's wishes and a reduction in expressing their own wishes.	L (Im)
Structured communication tools ICU/inpatient Adults Outcome: documentation	1 SR ¹²⁸	One review found mixed low- to very low-quality evidence on the impact of structured communication interventions on documentation. One RCT found a significant reduction in documented goals of care discussions (RR 0.82; CI 0.75, 0.90; $P < 0.001$) while four observational studies found an increase in documentation (RR 3.47; CI 1.55, 7.75; $P = 0.020$). Two RCTs (RR 1.04; CI 0.90, 1.20; $P = 0.57$) and four observational studies (RR 1.30; CI 0.95, 1.78; $P = 0.11$) found no significant difference between intervention and control on the documentation of DNR status.	L (In)
Structured communication tools ICU/inpatient Adults Outcome: quality of communication	2 SRs ^{128,140}	Two reviews reported quality of communication outcomes related to structured communication interventions and reported uncertain and mixed evidence. One review noted that low to very low-quality evidence suggests that structured communication tools may increase quality of communication between patients and health care providers (SMD 0.71; CI 0.32, 1.10; three observational studies), but that they have no effect on the quality of communication between	L (S, In)

(Continued)

Summary of Findings Table 8
Continued

Intervention and Comparator Age Group Setting Outcome	N	Effect Estimate and Direction of Effects	GRADE ^a
Structured communication tools ICU/inpatient Adults Outcome: caregiver well-being	1 SR ¹⁴⁰	patients and substitute decision makers. ¹²⁸ Another review found that communication interventions including proactive communication techniques, designated family support personnel, use of conferences, and decision aids all had a significant impact on the quality of communication but noted that comparison of the differences in communication is limited by the inconsistent use of valid and reliable measures across studies. One review identified a single RCT showing that an ICU communication intervention was associated with statistically significant decreases in family member symptoms of post-traumatic stress disorder, anxiety, and depression.	L (S, Im)
Family meetings ICU/inpatient Adults Outcome: treatment decisions	2 SRs ^{136,153}	Two reviews reported mixed evidence regarding the effect of family meetings on treatment decisions. One review found that structured end-of-life conferences were associated with withdrawal of more life-support treatments than usual care controls. Another review found that family meeting interventions were associated with earlier withdrawal of life support measures, but the change was not significant.	L (Im, In)
Family meetings ICU/inpatient Adults Outcome: documentation	1 SR ¹³⁶	One review concluded that family meetings may increase documentation of DNR status and specified withdrawal of life support measures on the basis of a single pre-post study.	V (S, Im, In)
Family meetings ICU/inpatient Adults Outcome: quality of communication	1 SR ¹³⁶	One review found increased discussions about symptoms, palliative care, and goals of care associated with family meeting interventions although evidence was mixed.	V (S, Im, In)
Advance directive documentation ICU/inpatient Adults Outcome: quality of communication	1 SR ¹³⁹	One review found a single cohort study indicating that advanced care documents prompted end-of-life discussions and concluded that perceived effectiveness of advance care documentation in encouraging end-of-life discussions appears to be high but is mostly derived from low-level evidence studies.	V (S, Im, In)
Facilitated ACP with written or video information ICU/inpatient Adults Outcome: preference-concordant care	1 SR ¹³²	One review found mixed evidence on the impact of facilitated ACP on preference-concordant care; in some identified studies, ACP was associated with increased congruence between patients and proxies, while in other identified studies, no significant improvement was found in physician-patient agreement regarding preferences for withholding life-sustaining treatments.	V (S, Im, In)
Facilitated ACP with written or video information ICU/inpatient Adults Outcome: documentation	1 SR ¹³²	One review concluded that patients who participated in facilitated ACP interventions were more likely to clarify their preferences for treatment and create advanced care directives.	L (S, Im)
Facilitated ACP with written or video information ICU/inpatient Adults Outcome: caregiver well-being	1 SR ¹³²	One review noted that receiving facilitated ACP reduced stress, anxiety, and depression among caregivers.	L (S, Im)

N = number of systematic reviews; SR = systematic review; ACP = advance care planning; V = very low quality of evidence; S = study limitation; Im = imprecision; RCT(s) = randomized controlled trial(s); In = inconsistency; HIV = human immunodeficiency virus; L = low quality of evidence; OR = odds ratio; M = moderate quality of evidence; CPR = cardiopulmonary resuscitation; RR = risk ratio; EOL = end of life; SMD = standardized mean difference; DNR = do-not-resuscitate; ICU = intensive care unit.

^aThe GRADE category is based on identified systematic reviews published between 2013 and February 2018. We used the following reasons for downgrading confidence in the evidence (downgraded by 1 or 2): Study limitation (observational studies start with a low GRADE value), Inconsistency (individual studies do not come to the same conclusions or there is only one study so inconsistency cannot be evaluated), Imprecision (there is no effect estimate, there is no measure of dispersion, or the CI is very broad); we used the systematic review authors' evaluation for other GRADE criteria if there was a formal quality of evidence assessment (see text).

there was lower quality of care in patients receiving pharmacological sedation compared to nonsedated groups. One review found four nonrandomized studies comparing sedated and nonsedated groups and showed that despite sedation with the intent to control symptoms, delirium and dyspnea were still troublesome symptoms in these people in the last few days of life and were significantly worse in the sedated group. Control of other symptoms appeared to be similar in sedated and nonsedated groups. In addition, all studies identified in the review except one compared survival time in the sedated and nonsedated groups and concluded that there was no statistically significant difference between the groups. The review did not report effect estimates.¹²⁴ There was also very low-quality evidence supporting specific treatments for pharmacological symptom control at the end of life. One review examining a range of palliative interventions and outcomes concluded that there is a lack of evidence concerning the effectiveness and safety of palliative drug treatment in dying patients. No evidence was found for scopolamine hydrobromide and atropine for death rattle, some evidence was found supporting the use of morphine and midazolam for dyspnea, anxiety, or terminal restlessness, and some support was found for morphine, diamorphine, and fentanyl for pain. The review did not report effect estimates.¹²³

Domain 8: Ethical and Legal Aspects of Care

KQ 8: What Is the Impact of Advance Care Planning on Substituted Decision Making Regarding Life-Sustaining Treatments? Thirty-six reviews evaluating the impact of ACP on substituted decision making regarding life-sustaining treatments were included in the review. Interventions included ethics consultation; the use of advance directive documents and related interventions; care planning patient/caregiver-provider discussions; family meetings; decision aids, such as videos, web sites, printed materials, and telephone advice; and facilitator-led ACP approaches (Summary of Findings Table 8). Studies reported on a wide range of outcomes, commonly including preference documentation, decisional conflict/consensus, preference-concordant care, surrogate understanding, and communication quality.

Ethics consultation: There is moderate-quality evidence that ethics consultation in the ICU facilitates consensus around clinical decisions (OR 4.09; CI 1.01, 16.55; two RCTs and one non-RCT)¹²⁹ and moderate-quality evidence regarding the impact of ethics consultation on treatment decisions.^{129,153} One review found that ethics consultation was associated with nonsignificant decreased use of mechanical ventilation (-3.18 d; CI $-8.27, 1.90$; $P = 0.22$, three RCTs) and artificial nutrition and

hydration (-0.79 d; CI $-2.98, 1.41$; $P = 0.48$).¹²⁹ Another review found decreased use of mechanical ventilation associated with ethics consultation in one RCT.¹⁵³

Advance directives: There is moderate-quality evidence from three reviews that advance directive interventions lead to preference-concordant care (i.e., care provided consistent with expressed preferences) and to increased preference documentation.^{125,127,148} One review found that patients receiving advance directive interventions with communication had a significantly increased likelihood of receiving end-of-life care in concordance with their preferences compared with control groups (OR 4.66; CI 1.20, 18.08; three RCTs).¹²⁵ This review also showed an increased likelihood for the completion of advance directives compared to usual care (OR 3.26; CI 2.00, 5.32; 13 RCTs).¹²⁵ However there is low- to very low-quality evidence for advance directive interventions among pediatric populations, due to individual study limitations and lack of effect estimates and inconsistent findings.¹⁵²

Care planning discussions: There is also moderate-quality evidence synthesized in a 2014 Health Quality Ontario systematic review for the positive impact of care planning discussions on preference concordant care, concordance between patient and family wishes, and documentation of ACP processes and documents.¹⁵⁰ There is low-quality evidence for ACP decision aids. Mixed evidence suggests that decision aids may lead to lower intensity treatment decisions (RR 0.50; CI 0.27, 0.95; seven RCTs) but heterogeneity across studies tempers confidence in the evidence base.¹⁴⁵ One review concluded that there may be a small effect of decision aids on documentation of advance directives but with a wide CI including no effect estimate (RR 1.1; CI 0.85–1.46; four RCTs). There was inconsistency in findings related to the impact of decision aids on quality of communication, decisional conflict or consensus, concordance, and caregiver well-being, and no pooled effect estimates were reported.^{72,134,135,145,146}

Family meetings: There is low-quality evidence for family meetings improving caregiver well-being. One review found evidence, including from a single multicenter RCT, that structured family meetings could improve psychological well-being and decrease posttraumatic stress symptoms in bereavement.¹⁵⁴

Quality Assessment

The methodological quality of the included systematic reviews varied considerably. Most reviews stated explicit review questions, searched adequate sources, conducted an appropriate synthesis of the evidence, and made appropriate research suggestions (Supplemental File: Critical Appraisal Figure).

Discussion

This systematic review identified 139 systematic reviews addressing key research questions across the eight palliative care domains specified in the NCP Clinical Practice Guidelines, reflecting the growth in palliative care research over the past five years. Despite the major undertaking these reviews represent, much of the evidence for palliative care remains with low-quality, due to inconsistency in study findings, the lack of precise effect estimates to support the effectiveness of interventions, and large variation in study designs, with few RCTs that allow strong evidence statements contributing to the evidence base.

Palliative care is a relatively new specialty, with board certification by the American Board of Internal Medicine being offered for the first time in 2008. As palliative care as a specialty has matured over the last decade, so has the evidence supporting its practice. We identified 48 systematic reviews addressing palliative care interventions for physical symptoms, 36 reviews examining ACP interventions, and 26 reviews covering psychological/psychiatric management in palliative care, all published in the last five years. While it is impressive that as much research as exists is available to inform palliative care practice, more targeted efforts at strategically building the evidence base to conduct well-designed studies and provide high-quality support for specific palliative care interventions are needed. Moreover, despite the challenges of conducting RCTs in some areas of palliative care,¹⁵⁷ greater attention to the opportunities to do so combined with the use of other robust study designs examining key outcomes will increase the quality of the evidence.

We found high-quality evidence in only one area: the impact of home-based palliative care on home death. Home-based palliative care facilitates access to important services for the growing number of frail elderly persons who are homebound¹⁵⁸ and also allows patients to be cared for in their own home, as many express a preference for when asked about end-of-life care.¹⁵⁹ The robust evidence for this patient-centered intervention supports its continued growth in practice, with attention to adequate workforce expansion, quality assessment, and payment structure.

We found moderate-quality evidence for a few key palliative care interventions. There was moderate-quality evidence for the use of music and art therapies to improve anxiety and depression in patients with advanced illness. There has been growing interest in the use of complementary therapies at the end of life; data from a 2007 National Home and Hospice Care Survey showed that over 40% of hospice care providers offered these types of therapies and about 25% of patients received some form of

complementary therapy.¹⁶⁰ Music therapy was among the most commonly available therapies. Future research in this area will benefit from more rigorous and consistent methods to establish a high-quality evidence base and usefully guide clinical practice; trials should adequately characterize intervention characteristics, use well-validated assessments to measure symptom outcomes, and consider important mediating factors.⁹⁴

We also found moderate-quality evidence that ethics consultation improves decision-making consensus in the ICU and leads to decreased use of high-intensity and often futile life-sustaining treatments at the end of life in the ICU. The evidence suggests it may be beneficial to continue to use ethics consults to support the difficult decision-making process common to the ICU at the end of life and facilitate consensus. However, more research examining the effect of ethics consultation on outcomes such as family satisfaction and resource use (e.g., length of stay; use of LSTs) and identifying the specific components of the consult that is beneficial (e.g., communication, team coordination, ethical analysis) is warranted.¹⁶¹ In addition, improved partnership and coordination between the palliative care and ethics teams in clinical practice while communicating with patients and families may further support decisional certainty and consensus.

One key area with a moderate level of evidence is interdisciplinary team care. Findings across reviews consistently demonstrate that interdisciplinary care leads to positive outcomes related to quality of life, ACP, death at home, and patient/family satisfaction with care, though confidence is tempered by some study limitations and the absence of pooled effect estimates. Interdisciplinary team care is a central and unique aspect of palliative care delivery, which relies on the contributions of multiple disciplines to provide holistic, patient-centered services at the end of life. Despite the challenges associated with team care in practice, the evidence base indicates the need to prioritize and adequately resource interdisciplinary palliative care teams in practice.

Although important individual trials have demonstrated the beneficial impact of early/integrated palliative care in certain subpopulations such as patients with advanced cancer,^{4,6,162} we found low-quality evidence overall for early palliative care and outcomes such as quality of life and physical symptoms and very low-quality evidence for psychological health and mortality. The downgraded confidence reflects the variability in study designs as well as the variability in findings across studies, with different populations and the limited availability of pooled effect estimates to make strong conclusions about the impact of early palliative care broadly. Still, promising results from

these trials underscore the need to continue to investigate this area across populations and settings, to build the evidence base for a practice that has significant face validity and growing empirical support.

There are several areas with low- or very low-quality evidence where reviews show promising results, but confidence in the evidence base is limited by the lack of consistently structured studies with consistent outcomes. For example, grief and bereavement interventions evaluated in the systematic reviews included in this review showed wide variation in how these services are resourced and delivered across the health system, limiting the ability to make conclusions about their effectiveness. There are also some domains where there is simply a lack of evidence, underscoring the need to expand the palliative care research base. For example, there is little evidence regarding culturally sensitive palliative care, despite the importance of acknowledging and incorporating sociocultural norms and practices in end-of-life care. There were only two systematic reviews addressing the unique needs of patients in the last days of life, and these were focused on pharmacological interventions. Owing to the tenuous clinical condition and difficult emotional time for patients and their caregivers, it remains a challenge to our field to be able to practically recruit and retain patients at the end of life for studies that can inform clinical practice.

Our review has some limitations. Because our intent was to inform the fourth edition of the NCP clinical practice guidelines for palliative care, we limited our search to systematic reviews published since 2013, when the last edition of the guidelines was published. It is possible that we may have overlooked important evidence that was published before 2013 and that has not been replicated since. Furthermore, to support all domains of the guideline, we restricted our review to systematic reviews rather than primary studies which limited our analyses. Still, systematic reviews typically represent the best available evidence as they search multiple sources with robust and comprehensive search strategies, appraise the risk of bias of individual studies, assess the study results independently from the original study authors, and aggregate research results across all available studies. It is noteworthy though that despite a large number of systematic reviews, the primary research literature can be small and the number of systematic reviews is often not an indicator for the strength of the palliative care research evidence base. Our review was guided by 10 key review questions selected with the input of our technical expert panel and mapped to the eight domains of palliative care addressed by the NCP guidelines; there may be other key palliative care evidence not identified through these key questions

and thus not represented in this synthesis. We did not assess or stratify the evidence by individual interventions or conditions but instead grouped like interventions and combined advanced illness populations, which may mask important differences in the evidence. Overall, the conclusions of our review are limited by the amount and quality of available evidence. This review does not make any recommendations or state any implications for practice that go beyond an objective presentation of the evidence.

Conclusions

This systematic review highlights the large and varied body of research that exists in palliative care. Most promising areas in terms of structure and process of care are home-based palliative care, interdisciplinary team care, and telehealth approaches. There is documented evidence for comprehensive palliative care and music/art therapy addressing physical and psychological aspects of care. The existing evidence base for social needs assessments and culturally sensitive care remains very limited. There is documented evidence for life review/dignity therapy in the area of spiritual assessment approaches. Grief/bereavement support services appear to improve key outcomes for caregivers, but the evidence base for effective approaches for care in the last days of life is very limited. Evidence for ethics consults and advance directive/physician order interventions show the strongest evidence in the ethical and legal aspects of care domain. This comprehensive review underscores the importance of targeting future research toward building high-quality evidence in key areas of clinical practice and patient/caregiver needs.

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Supplementary Data

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