Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

Studies eligible for this review were determined by searching MEDLINE on the PubMed platform (1946-present), Elsevier EMBASE.com (1974-present), EBSCOhost CINAHL (Cumulative Index to Nursing and Allied Health Literature), and Cochrane Library's (John Wiley & Sons) Central Register of Controlled Trials (CENTRAL).

The controlled vocabularies of the databases furnished subject headings for the strategies that were combined with title/abstract words and keywords. Using each database platform's command language and search fields, the librarian searched for various relevant combinations of the following Subject Headings (MeSH, EMTREE, etc.) and word groupings: palliative care, supportive care, caregivers, symptom management, terminal and/or life-limiting illness, cancer, pain, cost, quality of life, and satisfaction. Boolean operators (AND, OR, NOT) were applied to combine the topic hedges. The randomized trial string was adapted from the Cochrane Strategy and used to narrow the retrieval. The "similar articles" link, grant numbers, and reference lists of retrieved articles were used to identify additional eligible records.

PubMed/MEDLINE Search strategy

((((((((("Palliative Care"[Mesh] OR "Terminal Care"[Mesh] OR "Terminally Ill"[Mesh] OR "Hospices"[Mesh] OR "Hospice Care"[Mesh] OR "Hospice and Palliative Care Nursing"[Mesh] OR palliat* OR "End of life" OR EOL[tiab] OR "terminal care" OR "terminal illness" OR "terminally ill" OR "Terminal phase" OR "terminal stage" OR hospice*[tiab] OR hospice*[ot] OR "Stage IV cancer" OR "Life-limiting"[tiab] OR "Actively dying" OR "terminal stage" OR "limited survival" OR terminal patient* OR "Advance Care Planning"[Mesh] OR "Advance Care Planning"[ot] OR "Advance care planning"[tiab] OR "life-threatening illness" OR life-threatening diagnos* OR "Bereavement"[Majr] OR bereavement[ot] OR bereave*[title])) OR ((((("Caregivers"[Mesh]) OR "supportive care")) AND ("life-threatening illness" OR "life-threatening diagnoses" OR "progressive lung cancer" OR "Last year of life" OR "advanced illness" OR "advanced cancer" OR "advanced cancer"[ot] OR "advanced disease" OR "advanced lung cancer" OR "advanced dementia" OR "advanced transitional cell carcinoma" OR "advanced stages" OR "advanced heart" OR "limited survival"[tiab] OR Inoperable OR Incurable OR unresectable))) OR ((("symptom control"[tiab] OR "symptom management"[title] OR "symptom control"[ot] OR "symptom burden" OR "end stage")) AND ("life-threatening illness" OR "life-threatening diagnoses" OR "progressive lung cancer" OR "Last year of life" OR "advanced illness" OR "advanced cancer" OR "advanced cancer"[ot] OR "advanced disease" OR "advanced lung cancer" OR "advanced dementia" OR "advanced transitional cell carcinoma" OR "advanced stages" OR "advanced heart" OR Inoperable OR Incurable OR unresectable)))))) AND ("Randomized Controlled Trials as Topic"[Mesh] OR "Pragmatic Clinical Trials as Topic"[Mesh] OR (Randomised Clinical Trial* OR Randomized Controlled Trial* OR randomised controlled trial OR RCT OR RCTs OR RCT's OR randomized clinical trial* OR Quasi-random* OR "randomized trial" OR "Randomised controlled" OR cluster random* OR randomised fast-track OR "randomised trial" OR "Randomized controlled" OR randomized fast-track OR "randomized trial" OR randomised[ot] OR randomized[ot] OR Randomized Controlled Trial[ptyp]) OR randomized interventions[tiab] OR random*[title] OR cluster randomized trial OR pilot randomized OR (Random* AND clinical AND trial[title])))) OR (((((((((("Pain/drug therapy"[Mesh:NoExp] OR "Pain/etiology"[Mesh:NoExp] OR "Pain/prevention and control"[Mesh:NoExp] OR "Pain/psychology"[Mesh:NoExp] OR "Pain/radiation effects"[Mesh:NoExp] OR "Pain/surgery"[Mesh:NoExp])) OR ("Pain, Intractable/drug therapy"[Mesh] OR "Pain, Intractable/prevention and control"[Mesh] OR "Pain, Intractable/radiotherapy"[Mesh] OR "Pain, Intractable/surgery"[Mesh] OR "Pain, Intractable/therapy"[Mesh])) OR ("Neuralgia/drug therapy"[Mesh:NoExp] OR "Neuralgia/prevention and control"[Mesh:NoExp] OR "Neuralgia/radiotherapy"[Mesh:NoExp] OR "Neuralgia/surgery"[Mesh:NoExp] OR "Neuralgia/therapy"[Mesh:NoExp])) OR ("Neuralgia, Postherpetic/drug therapy"[Mesh] OR "Neuralgia, Postherpetic/prevention and control"[Mesh] OR "Neuralgia, Postherpetic/surgery"[Mesh] OR "Neuralgia, Postherpetic/therapy"[Mesh])) OR ("Nociceptive Pain/drug therapy"[Mesh] OR "Nociceptive Pain/prevention and control"[Mesh] OR "Nociceptive Pain/radiotherapy"[Mesh] OR "Nociceptive

eText 1. Methodological Details Regarding Search Strategy

Pain/surgery"[Mesh] OR "Nociceptive Pain/therapy"[Mesh])) OR ("Acute Pain/drug therapy"[Mesh] OR "Acute Pain/prevention and control"[Mesh] OR "Acute Pain/radiotherapy"[Mesh] OR "Acute Pain/surgery"[Mesh] OR "Acute Pain/therapy"[Mesh])) AND "Pain"[Majr:NoExp]) OR "Pain Management"[Mesh] OR "Breakthrough Pain"[Mesh] OR "Pain Clinics"[Mesh] OR "Pain Measurement"[Mesh] OR breakthrough pain[tiab] OR breakthrough pain[ot] OR cancer pain[ot] OR pain flare[ot] AND (("Costs and Cost Analysis"[Mesh] OR "Patient Satisfaction"[Mesh] OR "Quality of Life"[Mesh] OR "Survival Rate"[Mesh] OR "Communication"[Mesh] OR "Fatigue"[Mesh] OR "Dyspnea"[Mesh] OR "quality of life" OR QOL[tiab] OR satisfaction[tiab] OR clinical outcome*)) AND ((neoplasms OR cancer[tiab] OR cancer[ot])) AND ("Randomized Controlled Trials as Topic"[Mesh] OR "Pragmatic Clinical Trials as Topic"[Mesh] OR Randomised Clinical Trial* OR Randomized Controlled Trial* OR randomised controlled trial OR RCT OR RCTs OR RCT's OR randomized clinical trial* OR Randomized Controlled Trial[ptyp]))) OR (SurvivorCare[tiab] OR "family meetings"[title] OR “CONNECT intervention”[tiab] OR "transitional care bridge”[title] OR "supportive care interventions”[title]) AND English[lang] NOT ((infant[MeSH] OR infant*[tiab] OR newborn*[tiab] OR neonat*[tiab] OR child*[ot] OR infant*[ot] OR teen*[tiab] OR teen*[ot] OR pediatric*[ot] OR pediatric*[title] OR child[MeSH]))

eTable 1. Study Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
• Sample: Life-limiting illness (defined by classifications of disease severity, such as tumor stage or New York Heart Association class) • Sample: Ages 18 and older • Intervention: Self-described as "palliative care" and/or comprises at least two domains of palliative care, as defined by the National Consensus Project for Quality Palliative Care[1] • Study design: randomization • Comparators: usual care, enhanced usual care, attention control • Outcomes: study reports on at least one of pre-specified review outcomes (i.e., patient quality of life, symptom burden, mood, advance care planning, survival, resource utilization, satisfaction with care, healthcare expenditures, site of death)	• Sample: Indication for palliative care is not related to life-limiting illness (e.g., chronic, non-malignant pain) • Intervention: single-focus intervention (e.g., advance care planning only, opioid therapy only), or study does not otherwise meet our definition of "palliative care" based on National Consensus Project for Quality Palliative Care[1] • Intervention: patient is not the target of intervention • Intervention: caregiver is the exclusive or primary target of intervention • Study design: non-randomized

eText 2. Methodological Details Regarding Risk of Bias Assessment

Outcome-level risk of bias was assessed using the Cochrane Collaboration's Risk of Bias tool. This tool comprises seven domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other bias. Per recommendations from the Cochrane Collaboration, we modified the tool to assess risk of bias by categories of outcomes, as certain outcomes may be more or less susceptible to bias. As such, the risk of detection bias (blinding of outcome assessors) was evaluated separately for subjective (e.g., patient-reported outcomes) and objective (e.g., survival) outcomes. Within each domain, two reviewers independently judged each trial as having "low," "high," or "unclear" risk of bias. In the event that articles did not contain adequate information to render a conclusive judgment, study authors were contacted using open-ended questions as recommended by the Cochrane Collaboration (Section 8.3.4).

Although we assessed risk of performance bias (blinding of participants and personnel), this domain was excluded when generating summary judgments, as it is impracticable to blind patient participants in a behavioral intervention such as palliative care.

Each trial has two overall summary risk of bias judgments based on outcome type. If a trial was found to be of low risk of bias on all of the following domains, it was deemed to have low summary risk of bias for subjective outcomes: sequence generation, allocation concealment, incomplete outcome data, selective outcome reporting, and other sources of bias. If a trial was found to be of high risk of bias on any of the aforementioned domains, it was deemed to be of high summary risk of bias; similarly, if a trial was found to be of unclear risk of bias on any of the aforementioned domains, it was deemed to be of unclear summary risk of bias. Summary judgments for objective outcomes were generated similarly, except that "blinding of objective outcomes" was included in the summary determination.

We further modified the tool to assess risk of bias in cluster-randomized trials, adding the following domains per recommendations from the Cochrane Collaboration (Chapter 8.14.1.1): recruitment bias, baseline imbalance, and clustering-adjusted analysis. We excluded the domain of "recruitment bias" from summary judgments due to similar concerns regarding the impracticality of recruiting participants before cluster allocation in a seriously ill population.

eText 3. Translation of Standardized Mean Differences to Clinical Values

For QOL (Quality of Life), we translated the SMD (standardized mean difference) to the FACIT-Pal (Functional Assessment of Chronic Illness Therapy – Palliative), a disease-agnostic measure of QOL developed to be sensitive to the burdens of individuals with serious illness. The SD (Standard Deviation) of the FACIT-Pal used in our calculations (SD: 24.7) is from a cross-sectional analysis of patients with advanced cancer (n=256).[2] Regarding symptom burden, we re-expressed SMDs using the ESAS (Edmonton Symptom Assessment Scale), a disease-agnostic symptom assessment measure commonly used in palliative populations. For our calculations, we calculated the pooled SD of baseline ESAS scores from an oncology palliative care trial (n= 461, SD: 15.6).[3]

eTable 2. Trial Characteristics and Outcomes of 6 Palliative Care Interventions at Low Risk of Bias

Trials with patient-level randomization

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
Trials with patient-level randomization										
Bakitas et al, 2009[4,5] (USA)	Parallel	Recent GI, lung, GU, or breast cancer diagnosis; Prognosis approx. 1 year; Mean age: 65	Structure, Physical, Psychological, Social, Legal	Manualized, nurse-led telephone intervention focusing on: problem solving, activation, education, symptom management, and advance care planning	161	Usual care	161	**QOL** • [FACIT-Pal]: Mean difference [SE], 4.6[2]; P=0.02 **Symptom burden** • [ESAS]: mean difference [SE], -27.8[15]; P=0.06 **Survival**: • Median, 14 months [95% CI, 10.6-18.4] vs. 8.5 [7.0-11.1]; P=0.14 **Mood** • [CES-D]: Mean difference [SE], -1.8[0.81]; P=0.02 **Utilization**: • Days in hospital, 6.6 vs. 6.5; P=0.14 • Days in ICU, 0.06 vs. 0.06; P>0.99 • ED visits, 0.86 vs. 0.63; P=0.53 **Caregiver burden** • [MBCB]: NS, data not reported	Low	Low
Higginson et al, 2014[6] (UK)	Parallel	COPD (54%), cancer (lung, breast,	Physical, Psychological, Spiritual	Multi-professional integrated service	53	Usual care	52	**QOL** • [Chronic Respiratory Disease	Low	Low

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Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
		urethral, colon, prostate, hematological) (20%), interstitial lung disease (18%), CHF (5%); Mean age: 67		combining respiratory medicine, physiotherapy, occupational therapy, and palliative care assessment and management				Questionnaire] Difference, 4.21 (95% CI, -4.52 to 12.94); P=0.34 • [EQ-5D] Difference, 0.092 (95% CI, -0.23 to 0.04); P=0.18 **Symptom burden** • [NRS: dyspnea 24hr. mean]: Difference, -0.33 (95% CI, -1.28 to 0.62); P=0.49 • [Chronic Respiratory Disease Questionnaire - dyspnea]: Difference, 0.08 (95% CI, -0.38 to 0.52); P=0.75 • [Chronic Respiratory Disease Questionnaire - fatigue]: Difference, 0.02 (95% CI, -0.56 to 0.2); P=0.93 **Survival** • Overall 6-month (94% vs. 75% alive; P=0.048); Survival benefit among cancer subgroup (P=0.97)		

eTable 2. Trial Characteristics and Outcomes of 6 Palliative Care Interventions at Low Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
								Mood • [HADS - anxiety] Difference, 0.1 (95% CI, -0.93 to 1.24); P=0.78 • [HADS - depression] Difference, -1 (95% CI, -1.82 to 0.30); P=0.16 **Utilization** • [Days in hospital] Difference, -0.52 (95% CI, -0.14 to 1.91); P=0.58 **Expenditures** • [6-week mean costs] £1422 (95% CI, £897 to £2101) vs. £1408 (95% CI, £899 to £2023) **Other** • [Chronic Respiratory Disease Questionnaire – breathlessness mastery subscale][a] ES, 0.44 (P=0.048)		
Lowther et al, 2015[7] (Kenya)	Parallel	HIV with pain/symptom burden; Mean age: 39	Physical, Psychological, Social, Spiritual, Legal	Primary palliative care (pain management, symptom management, nutrition,	60	Usual care	60	**QOL** • [MOS-HIV Physical subscale] coefficient, 0.44 (95% CI, -0.02 to 0.91); P=0.06	Low	N/A

eTable 2. Trial Characteristics and Outcomes of 6 Palliative Care Interventions at Low Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
				psychosocial and spiritual support, ethical and legal issues) provided in an outpatient HIV clinic setting by HIV nurses without palliative care specialization				• [MOS-HIV Mental subscale] coefficient, 0.61 (95% Cl, 0.13 to 1.10); P=0.01 **Symptom burden** • [African Palliative Outcomes Scale - Pain][a] coefficient, -0.01 (95% CI, -0.36 to 0.34); P=0.95 • [African Palliative Outcomes Scale -Other symptoms composite] coefficient, -0.05 (95% CI, -0.39 to 0.29); P=0.78 **Mood** • [GHQ-12] coefficient, -0.50 (95% CI, -0.97 to -0.03); P=0.04 **Other** • [African Palliative Outcome Scale]: Palliative care needs, coefficient, 0.69 (95% CI, 0.26 to 1.12); P=0.002		
Northouse et al, 2007[8] (USA)	Parallel	Prostate cancer; Prognosis: ≥ 12 months; Mean age: 63	Physical, Psychological, Social	Northouse et al, 2005 intervention adapted for prostate	129 patients, 129 caregivers	Usual care	134 patients, 134 caregivers	**QOL** • [FACT-G]: 4 months (ES=0.16; P=0.10), 8 months	Low	N/A

eTable 2. Trial Characteristics and Outcomes of 6 Palliative Care Interventions at Low Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
								(ES=0.01; p=0.89), 12 months (ES=0.03; P=0.77) • [SF-12 Physical]: 4 months (ES= -0.02; P=0.96), 8 months (ES=-0.05; p=0.80), 12 months (ES= 0.03; P=0.88); • [SF-12 Mental]: 4 months (ES=0.08; P=0.53), 8 months (ES=-0.06; p=0.69), at 12 months (ES= -0.07; P=0.96) **Symptom burden** • [Omega Screening Questionnaire symptom distress]: 4 months (ES= -0.06; P=0.60), 8 months (ES=0.08; p=0.45), 12 months (ES=0.06; P=0.59) **Caregiver QOL** • [SF-12: Physical] 4 months (ES=-0.04; P=0.67), 8		

eTable 2. Trial Characteristics and Outcomes of 6 Palliative Care Interventions at Low Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
								months (ES = 0.28; P=0.02), 12 months (ES = 0.32; P=0.005) • [SF-12: Mental] 4 months (ES=0.25; P=0.03), 8 months (ES = -0.12; P=0.40), 12 months (ES = -0.07; P=0.76) • [FACT-G] 4 months (ES = 0.26; P=0.004), 8 months (ES = 0.19; P=0.06), 12 months (ES = 0.14; P=0.18) **Caregiver burden** • [Appraisal of Caregiving Scale]: Negative appraisal at 4 months (ES = -0.32; P=0.002), 8 months (ES = 0.16; P=0.17), 12 months (ES = -0.08; P=0.51)		
Rummans et al, 2006[9,10] (USA)	Parallel	Advanced cancer (brain, head and neck, lung, ovarian, GI, other) undergoing	Structure, Physical, Psychological, Social, Spiritual	Structured, multidisciplinary, patient intervention to address physical, mental, social,	49 patients, 43 caregivers	Usual care	54 patients, 40 caregivers	**QOL** • [Spitzer Uniscale] [a]: Improved at week 4 (72.8 vs. 64.1; P=0.047); NS at week 8 (71.9 vs 68.4,	Low	N/A

eTable 2. Trial Characteristics and Outcomes of 6 Palliative Care Interventions at Low Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
		radiation treatment; Prognosis: estimated 5 year survival of 0-50%; Mean age: 60		emotional, and spiritual				p=0.4229); NS at week 27 (72.1 vs 72.1, p=0.9922) **Symptom burden** • [Linear Analog Scale Assessment (LASA): physical symptoms composite] 0.4 vs -10.0,; P =0.022 • [Symptom Distress Scale] NS (data not reported) **Mood** • [Profile of Mood States] Improved tension/anxiety (not reported; P=0.042) and improved confusion/bewilderment (not reported; P=0.014) subscales at week 4 • [LASA] Emotional well-being Improved (2.8 vs. -5.4; P=0.046) at week 4 **Caregiver QOL** • [LASA]: NS at week 4 (mean,		

eTable 2. Trial Characteristics and Outcomes of 6 Palliative Care Interventions at Low Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
								77.4 vs. 75.9; P=0.68); NS at week 8 (mean, 77.6 vs. 76.3; P=0.75); NS at week 27 (mean, 72.2 vs. 78.9; P=0.10) **Caregiver burden** • [Zarit]: NS at week 4 (mean, 76.9 vs. 76.2; P=0.81); NS at week 8 (mean, 75.1 vs. 75.8; P=0.80); NS at week 27 (mean, 75.1 vs. 77.2; P=0.55)		
Trials with cluster randomization										
Zimmermann et al, 2014[3] (Canada)	Cluster, parallel	Advanced cancer (lung, gastrointestinal, genitourinary, breast, gynecological); Prognosis: 6-24 months; Mean age: 61	Structure, Physical, Psychological, Social, Spiritual, EOL, Legal	Specialist palliative care focusing on: comprehensive assessment of symptoms, psychosocial concerns, and home services; routine contact with palliative care nurse; monthly outpatient palliative care follow-up	228	Usual care	233	**QOL** • [FACIT-Sp][a] 3-month primary endpoint (ES, 0.26; P=0.07); 4 months (ES, 0.44; P=0.006); • [QUAL-E] 3 months (ES, 0.28; P=0.05); 4 months (ES, 0.45; P=0.003) **Symptom burden** • [ESAS] 3 months (ES, -0.13; P=0.33); 4 months (ES, -0.31; P=0.05)	Low	Low

eTable 2. Trial Characteristics and Outcomes of 6 Palliative Care Interventions at Low Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
				visits; and, 24-hour on-call service. Ancillary services included: home care nursing, home palliative care, or inpatient admission for urgent needs or terminal care				**Satisfaction** • [FAMCARE-P16] 3 months (ES, 0.47; P=0.0003); 4 months (ES, 0.73; P<0.0001); • [CARES-MIS] 3 months (ES, -0.21; P=0.40); 4 months (ES, -0.24; P=0.11)		

Legend:
[a] Primary outcome measure; otherwise, not defined in article.
ES, effect size. NS, not significant. d, Hedges' d. g, Hedges' g. h, Hedges' h. OR, odds ratio. CI, confidence interval. GI, gastrointestinal. GU, genitourinary. FACIT-Pal, Functional Assessment of Chronic Illness Therapy- Palliative Care. ESAS, Edmonton Symptom Assessment Scale. CESD, Center for Epidemiologic Studies Depression Scale. SE, Standard Error. ICU, Intensive Care Unit. ED, Emergency Department. MBCB, Montgomery Borgatta Caregiver Burden scale. COPD, Chronic Obstructive Pulmonary Disease. QOL, Quality of Life. CHF, Congestive Heart Failure. EQ-5D, EuroQOL Five Dimensions Scale. NRS, Numerical Rating Scale. HADS, Hospital Anxiety and Depression Scale. HIV, Human immunodeficiency virus. MOS-HIV, Medical Outcomes Study HIV Health Survey. GHQ-12, 12 Item General Health Questionnaire. FACT-G, Functional Assessment of Cancer Therapy – General. SF-12, 12-Item Short Form Survey. EOL, end of life. FACIT-SP Functional Assessment of Chronic Illness Therapy – Spiritual Well-being. QUAL-E, Quality of Life at the End of Life. CARES-MIS, Cancer Rehabilitation Evaluation System Medical Interaction Subscale.

Structure, Structure and processes of care. Psychological, Psychological and psychiatric aspects of care. Social, Social aspects of care. Cultural, Cultural aspects of care. Spiritual, Spiritual, religious, and existential aspects of care. EOL, Care of the imminently dying patient. Legal, Ethical and legal aspects of care.

Note: Primary outcome reported, regardless of whether it is one of our pre-specified outcomes of interest. If no primary outcome specified in paper, and the outcome is not one of our outcomes of interest, it is not reported here. All comparisons are intervention versus control, if not otherwise specified. Ambulatory interventions refer to those interventions where patients were required to travel to either an outpatient clinic or an intervention delivery site. Subjective outcomes include all patient-reported outcomes (e.g., QOL, symptoms, mood), whereas objective outcomes include those outcomes which are not subject to detection bias (e.g., survival, healthcare utilization and expenditures abstracted from clinical or administrative records).

eTable 3. Trial Characteristics and Outcomes of 26 Palliative Care Interventions at High Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
Trials with patient-level randomization										
Aiken et al, 2006[11] (USA)	Parallel	Class IIIB-IV HF (68%) or COPD (32%); Prognosis: < 2 years; Mean age: 69	Structure, Physical, Psychological, Social, Spiritual, Legal	Home-based, nurse-led care management	101	Usual care	91	**Symptoms** • [MSAS] Lower distress from most troublesome symptom among COPD patients at 6 months (g=0.60; P=0.07) • [MSAS] Distress from most troublesome symptom among CHF patients in intervention at 6 months (g=0.60; P<0.05) **Utilization** • ED visits, NS (data not reported) **Advance care planning** • Possession of living will or advance directive (71% vs. 65%; P<0.05)	High	High

eTable 3. Trial Characteristics and Outcomes of 26 Palliative Care Interventions at High Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
Bakitas et al, 2015[12] (USA)	Waitlist parallel	Advanced solid or hematologic cancer (lung, GI tract, breast, other solid tumor, genitourinary tract, hematologic malignancy); Prognosis: 6-24 months; Mean age: 64	Structure, Physical, Psychological, Social, Spiritual, Legal	Early delivery (30-60 days post diagnosis) of Bakitas et al, 2009 intervention plus life-review and caregiver components	104 patients, 61 caregivers	Delayed intervention, 3 months post diagnosis	103 patients, 61 caregivers	**QOL** • [FACIT-Pal]: 3 months, mean, 129.9 (95% CI, 126.6 to 133.3) vs. 127.2 (95% CI, 124.1 to 130.3); overall P=0.34 • [TOI]: 3 months, mean, 99.5 (95% CI, 96.5 to 102.4) vs. 97.7 (95% CI, 94.9 to 100.5); overall P=0.24 **Symptom burden** • [QUAL-E]: 3 months, mean, 11.4 (95% CI, 10.8 to 12.1) vs. 12.2 (95% CI, 11.6 to 12.8); overall P=0.09 **Survival** • 1-year survival	High	High

eTable 3. Trial Characteristics and Outcomes of 26 Palliative Care Interventions at High Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
								among early vs. delayed groups (63% vs. 48%; P=0.038);Overall median survival, 18.3 months vs. 11.8 months (P=0.18) **Mood** • [CES-D]: 3 months, 11.2 (95% CI, 9.7 to 12.7) vs. 10.8 (95% CI, 9.5 to 12.1); overall P=0.33 **Utilization** • Hospital days, RR, 0.73 (95% CI, 0.41 to 1.27); P=0.26; • ICU days, RR, 0.68 (95% CI, 0.23 to 2.02); P=0.49; • ED visits, RR, 0.73 (95% CI, 0.45 to 1.19); P=0.21; • Chemotherapy in last 2		

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Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
								weeks of life, RR, 1.57 (95% CI, 0.37 to 6.7); P=0.54 • Hospice use, RR, 1.08 (95% CI, 0.8 to 1.45); P=0.62. **Site of death** • At-home death, 54% vs. 47% (P=0.60) **Caregiver QOL** • [CQOL-C]: 3 months, *d*=-0.13 (P=0.37) **Caregiver burden** • [MBCB]: Objective burden (*d*=0.09; P=0.62); Demand burden (*d*=0; P=0.99); Stress burden 36 weeks prior to patient death (*d*=0.44, P=0.01)		

eTable 3. Trial Characteristics and Outcomes of 26 Palliative Care Interventions at High Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
								Caregiver mood[13] • [CES-D]: Depressive symptoms at 3 months, d=-0.32 (P=0.02); 36 weeks prior to patient death, *d*=-0.39 (P=.02); 8-12 weeks among caregivers of decedents, *d*=0.07 (P=0.07) • [PG13]: Complicated grief at 8-12 weeks post patient death, *d*=-0.21 (P=0.51).		
Brännström et al, 2014[14] (Sweden)	Parallel	NYHA Class III-IV HF; Mean age: 79	Structure, Physical, Psychological, Social, Spiritual	Multidisciplinary, home-based collaborative care to provide HF disease management and palliative care services	36	Usual care	36	**QOL** • [EQ5D] [a] Improved (57.6 ± 19.2 vs. 48.5 ± 24.4; *P*=0.05) • [KCCQ][a] NS, data not reported **Symptom burden**	High	High

eTable 3. Trial Characteristics and Outcomes of 26 Palliative Care Interventions at High Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
								• [ESAS][a] NS, data not reported **Survival** • Six-month mortality NS, *P*=0.34 **Utilization** • Fewer hospitalizations, mean (SD)=0.42 (0.60) vs. 1.47 (1.81); *P*=0.009 **Expenditures**[15] • Total costs NS, €4078 vs. €5727 (*P* not reported) **Other** • [NYHA class][a]: Increased proportion of patients with improved NYHA class (39% vs. 9%; *P*=0.015)		
Chapman et al, 2007[16] (USA)	Partial crossover	Advanced dementia nursing home residents; Mean age: 86	Structure, Physical, Psychological	Multidisciplinary Advanced Illness Care Teams (AICT) that focused on medical issues, meaningful activity,	57	Delayed intervention (8 weeks)	61	**Symptom burden** • [Faces Legs Activity Cry Consolability Behavioral Pain Scale] Pain NS,	High	N/A

eTable 3. Trial Characteristics and Outcomes of 26 Palliative Care Interventions at High Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
				psychosocial problems, and behavioral concerns				mean 0.24 vs 0.30, *P* not reported • [Pain in Advanced Dementia] Pain NS, mean 1.29 vs. 1.55, *P* not reported **Mood** • [Cornell Scale for Depression in Dementia] Depression NS, mean 0.09 vs. 0.07, *P* not reported		
Cheung et al, 2010[17] (Australia)[b]	Parallel	ICU inpatients (e.g. cardiovascular, gastroenterology, neurology, respiratory, sepsis, trauma and other); Prognosis: ≥ 6 months; Mean age: 77	Structure, Physical, Psychological, Social, EOL	Inpatient specialist palliative care consultation and management in the ICU	10	Usual care	10	**Utilization** [a] • Median ICU LOS, days, 3 [IQR, 7] vs. 5 [8]; P=0.97 • Median hospital LOS, days, 5[8] vs. 11[27]; P=0.44 **Site of death** • ICU mortality, 50% vs. 60%; P>0.99 Hospital mortality, 90%	High	High

eTable 3. Trial Characteristics and Outcomes of 26 Palliative Care Interventions at High Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
								vs. 70%; P=0.58 **Satisfaction** [a c] • Family, P=0.56		
Clark et al, 2013[18] (USA)	Parallel	Advanced cancer (brain, gastrointestinal, head and neck, lung, other) undergoing radiation treatment; Prognosis: 0-50% @ 5 years; Mean age: 59	Structure, Physical, Psychological, Social, Spiritual	Structured, multidisciplinary nurse-led patient/caregiver intervention to address physical, mental, social, emotional, and spiritual QOL, plus 10 brief individual telephone counseling sessions	65 patients, 65 caregivers	Usual care	66 patients, 66 caregivers	**QOL** • [FACT-G] [a]: Improved (mean, 74.2 vs. 68.7; P=0.02) at week 4; NS (mean, 77.6 vs. 77.7; P=0.88) at week 27 **Mood** • [POMS]: NS (data not reported) **Caregiver QOL** • [Caregiver QOL Index-Cancer]: NS at week 4 (58.0 vs. 57.7; P not reported); NS at week 27 (58.5 vs. 59.1; P not reported) **Caregiver mood** • [POMS]: NS (data not reported)	High	N/A

eTable 3. Trial Characteristics and Outcomes of 26 Palliative Care Interventions at High Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
Dyar et al, 2012[19] (USA)[d]	Parallel	Metastatic cancer (breast, lung, prostate, other) with expectation of hospice referral within upcoming year; Mean age: 66	Physical, Psychological, Social, Spiritual, EOL, Legal	Two consultations with an oncology advanced registered nurse practitioner to provide education regarding hospice, facilitate advance care planning, and conduct a comprehensive needs assessment	12	Usual care	14	**QOL** • [FACT-G Physical] 1 month (mean change, 0.3 vs. -0.4; P=0.93) • [FACT-G Family/social] 1 month (0.4 vs. 0.8; P=0.32) • [FACT-G Emotional] Improved at 1 month (1.2 vs. -4.5; P=0.01) • [FACT-G Functional] 1 month (-0.8 vs. 0.8; P=0.77) • [FACT-G Total] 1 month (1.2 vs. -3.9; P=0.31) • [LASA Overall QOL] 1 month (2.0 vs. -8.8; P=0.28) • [LASA Mental QOL] 1 month improved(19.0 vs. -10.0;	High	N/A

eTable 3. Trial Characteristics and Outcomes of 26 Palliative Care Interventions at High Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
								P=0.02) • [LASA physical] 1 month (7.0 vs. 3.8; P=0.89) **Symptom burden** • [LASA pain frequency] 1 month (-5.0 vs 7.5; P=0.38) • [LASA mean pain] 1 month (7.0 vs. 6.3; P=0.89) • [LASA mean fatigue] 1 month (0.0 vs -8.6; P=0.32)		
Engelhardt et al, 2006[20] (USA)	Parallel	Advanced cancer (esophagus, trachea, colon, liver, pancreas, lung, uterus, prostate, breast, melanoma, leukemia, lymphosarcoma, Hodgkin's disease, multiple myeloma) (65%), or COPD (19%) or CHF (16%) and either ICU	Structure, Psychological, Social, Spiritual, Legal	Six-session care coordination and education intervention to improve patient-provider communication regarding advanced illness, and to alleviate barriers to palliative/hospice care	133	Usual care	142	**Survival** • NS at 18 months, 43% vs. 42% (P not reported) **Advance care planning** • Median time to documentation (46 vs. 238 days; P=0.02) **Satisfaction** [e] • Improved	High	High

eTable 3. Trial Characteristics and Outcomes of 26 Palliative Care Interventions at High Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
		admission or 2+ hospital admissions in past 6 months; Mean age: 71						(ES, 0.18; P=0.03) **Expenditures** • Costs at 6-months NS, (ES, 0.18; P=0.29) **Caregiver satisfaction** • [Modified EOL Family Interview]: Improved (ES, 0.39; P=0.03)		
Farquhar et al, 2014[21] (UK)	Parallel, waitlist	Advanced cancer (lung, breast, rectal, prostate, lymphoma, mesothelioma, gastro-esophageal, renal, endometrial, hepatocellular, bladder, unknown) and symptomatic breathlessness; Mean age: 69	Structure, Physical, Psychological, Social	Multidisciplinary breathlessness support service	35	Usual care until two weeks, then intervention	32	**Symptom burden** • [NRS][a]: Decreased breathlessness distress (adjusted difference, -1.29; [95% CI: -2.57 to -0.005]; P=0.049) **Mood** • [HADS]: Anxiety NS (adjusted difference, 0.017; [95% CI: -1.52 to 1.56]; P=0.98) • Depression NS (adjusted	High	High

eTable 3. Trial Characteristics and Outcomes of 26 Palliative Care Interventions at High Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
								difference, -0.30; [95% CI: -1.79 to 1.20]; P=0.69) **Expenditures** • [total costs, including informal care]: NS (difference, -£354 [95% CI: -£1020 to £246])		
Farquhar et al, 2016[22] (UK)	Parallel, waitlist	Non-malignant disease and symptomatic breathlessness (83% COPD, 17% other not specified); Mean age: 72	Structure, Physical, Psychological, Social	Multidisciplinary breathlessness support service	44	Usual care until two weeks, then intervention	43	**Symptom burden** • [NRS]: Breathlessness distress, adjusted difference, -0.24; [95% CI: -1.30 to 0.82]; P=0.65 **Mood** • [HADS]: Anxiety (adjusted difference, -0.76 [95% CI: -1.95 to 0.44]; P=0.21) • [HADS] Depression (adjusted difference, -	High	High

eTable 3. Trial Characteristics and Outcomes of 26 Palliative Care Interventions at High Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
								0.61 [95% CI: -1.76 to 0.54]; P=0.29) **Expenditures** • Inpatient costs, difference, £799 [95% CI: -£237 to £1904])		
Given et al, 2002[20] (USA)	Parallel	Newly diagnosed cancer (breast, colon, lung, gynecologic, lymphoma); Mean age: 58	Physical, Social	Protocolized cognitive-behavioral pain and fatigue management intervention delivered by oncology nurses using computerized decision support tool	53	Usual care	60	**QOL** • [SF-36: physical]: 20 weeks (data not reported; P=0.05) • [SF-36: social function] 20 weeks (data not reported; P=0.07) **Symptom burden** • [Symptom Experience Scale] 20 weeks (data not reported; P=0.05)	High	N/A
Grande et al, 1999[23,24] (UK)	Parallel	Cancer (gastrointestinal, genitourinary, breast, lung) (82%), AIDS, motor neuron disease;	Structure, Physical, EOL	Hospital at home: Around-the-clock practical nursing care provided at the patient's home for up to 2 weeks	186	Usual care	43	**Utilization** • GP evening home visits in penultimate week, mean 0.17 vs. 0.61	High	High

eTable 3. Trial Characteristics and Outcomes of 26 Palliative Care Interventions at High Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
		Prognosis: < 2 weeks; Mean age:72						(P=0.022) • GP night visits (mean, 0.04 vs. 0.26; P=0.0003) • GP visits during the week (mean 2.18 vs. 2.32; p>0.05) • Daytime GP visits during the weekend (mean 0.35 vs 0.39; p>0.05) • GP evening home visits in final week (mean 0.59 vs. 1.11; P>0.05) • GP night visits (mean, 0.47 vs. 0.63; p>0.05) • Daytime GP visits during the week (mean 2.92 vs. 3.03; p>0.05) • GP daytime visits during the weekend (mean 0.95 vs 0.63;		

eTable 3. Trial Characteristics and Outcomes of 26 Palliative Care Interventions at High Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
								p>0.05) **Site of death** [a] • Likelihood of dying at home 58% vs. 67%; P=0.29		
Hopp et al, 2016[25] (USA)	Parallel	Inpatients with advanced HF (NYHA class III-IV) Prognosis: 1-year mortality risk ≥33%; Mean age: 68	Structure, Physical, Psychological, Social, Spiritual, Legal	Inpatient specialist palliative care consultation with physician and advance nurse practitioner (≥1 visit). Chaplaincy and social work involvement, as requested.	43	Usual care	42	**Utilization and/or advance care planning** • Composite outcome of hospice utilization or DNR order creation by 6 months, NS, difference 9.3% (95% CI, -11.8%, 30.0%); *P*=0.12	N/A	High
Hughes et al, 1992[26] (USA)	Parallel	Terminal illness (89% cancer (types not specified)); Prognosis: < 6 months; Mean age: 65	Structure, Physical, Social, EOL	Interdisciplinary home-based primary care team	86	Usual care	85	**Survival**: • NS (mean days [SD], 76.2 [67.1] vs. 83.1 [68.1]; P value not reported) **Utilization:** • Decreased VA hospital days (9.94 vs. 15.86, p=0.03) • Decreased	High	High

eTable 3. Trial Characteristics and Outcomes of 26 Palliative Care Interventions at High Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
								outpatient clinic visits (0.73 vs. 2.59; p=0.01) • Increased home nursing visits among intervention group (17.9 vs. 7.1; p=0.001) **Satisfaction** • [Greer Satisfaction with Care Survey]: Improved at one month (P=0.02) **Expenditures**: • Decreased VA hospital costs by 47% per capita (P=0.02) • Overall total per capita costs NS ($3,479.36USD vs. $4,248.68USD; P value not reported) **Caregiver satisfaction** • [Greer		

eTable 3. Trial Characteristics and Outcomes of 26 Palliative Care Interventions at High Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
								Satisfaction with Care Survey]: Improved at one month (P=0.005)		
McCorkle et al, 1989[27] (USA)	Three-arm, parallel	Homebound patients with ≥ Stage 2 lung cancer; Mean age: 64	Structure, Physical, Psychological, Social	Intervention 1: Specialized oncology home care (OHC) program delivered by masters-prepared nurses with advanced training in symptom management, psychosocial assessment, and communication; Intervention 2: Standard home care (SHC) program delivered by interdisciplinary team of registered nurses, physical therapists, home health aides, social workers, occupational therapists, and speech pathologists	Overall=166 [f]	Usual care provided by patient's physicians without home nursing care	Overall=166 [f]	**Symptom burden** • [Symptom Distress Scale]: Improved in both intervention conditions, data not reported (P=0.03) **Mood** • [POMS]: NS, P not reported **Utilization**: • Hospitalizations NS, P not reported **Pain** • [McGill-Melzack Pain Questionnaire]: NS, data not reported	High	High
Northouse et al, 2005[28] (USA)	Parallel	Recurrent breast cancer; Prognosis: ≥ 6 months; Mean	Physical, Psychological, Social	Standardized, family-based intervention to provide in-home	94 patients, 94 caregi	Usual care	88 patients, 88	**QOL** • [FACT-B and SF-36 composite:	High	N/A

eTable 3. Trial Characteristics and Outcomes of 26 Palliative Care Interventions at High Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
		age: 54		and telephone support and education in five domains: Family involvement, Optimistic attitude, Coping effectiveness, Uncertainty reduction, and Symptom management	vers		care - give rs	physical]: change from baseline to 3 months (P=0.48); change from 3 months to 6 months (P=0.19) • [FACT-B and SF-36 composite mental]: change from baseline to 3 months (P=0.92);change from 3 months to 6 months (P=0.79); **Caregiver QOL** • [FACT-G and SF-36 composite: physical]: change from baseline to 3 months (P=0.91); change from 3 months to 6 months (P=0.48) • [FACT-G and SF-36 composite		

eTable 3. Trial Characteristics and Outcomes of 26 Palliative Care Interventions at High Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
								mental]: change from baseline to 3 months (P=0.81); change from 3 months to 6 months (P=0.57) **Caregiver burden** • [Negative Appraisal of Caregiving Scale]: change from baseline to 3 months (P=0.04); change from 3 months to 6 months (P=0.37)		
Pantilat et al, 2010[29] (USA)	Parallel	Hospitalized elderly with HF (51%), cancer (prostate, lung, bladder) (22%), COPD (20%), or cirrhosis (6%); Mean age: 76	Structure, Physical, Psychological, Spiritual, Legal	Palliative care physician consultation on enrollment and every weekday during hospitalization. Consultation focused on: symptom assessment, psychosocial and spiritual needs, and treatment preferences	54	Attention control, received brief visit from PC physician and a book on diet and exercise	53	**Symptom burden** • [NRS] Pain mean, 2.1 (95% CI, 1.1 to 3.1) vs. 2.4 (95% CI, 1.4 to 3.4) ; P=0.30 • [NRS] Dyspnea mean, 2.4 (95% CI, 1.5 to 3.3) vs. 1.6 (95% CI,	High	N/A

eTable 3. Trial Characteristics and Outcomes of 26 Palliative Care Interventions at High Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
								0.6 to 2.5); P=0.50 **Mood** • [NRS]: Anxiety mean, 2.5 (95% CI, 1.5 to 3.6) vs. 2.5 (95% CI, 1.3 to 3.6); P=0.08 **Satisfaction** • Felt heard by doctors, 81% vs. 77% (P>0.99)		
Radwany et al, 2014[30] (USA)[b]	Parallel	CHF, COPD, DM with complications, ESLD, active cancer (type not specified), renal disease, ALS, Parkinson's, or pulmonary hypertension; Mean age: 69	Structure, Physical, Psychological, Social, Spiritual, Legal	In-home geriatric/palliative care biopsychosocial needs assessments used to develop care plan implemented by an interdisciplinary team in consultation with patient's PC	40	Usual care	40	**QOL** • [QUAL-E] [a]: 6-month mean difference, -4.052 [95% CI, -11.487, 3.382]; 12-month mean difference, -3.889 [-10.722, 2.944] **Symptom burden** • [CMSAS] [a]: 6-month mean difference, -0.134 [95% CI, -0.439, 0.171]; 12-	High	High

eTable 3. Trial Characteristics and Outcomes of 26 Palliative Care Interventions at High Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
								month mean difference, -0.328 [-0.716, 0.061] **Survival** • Days from enrollment to death NS, 189 vs. 150; P not reported **Mood** • [HADS] [a]: 6-month mean difference, -2.919 [95% CI, -6.435, 0.598]; 12-month mean difference, -4.037 [-8.584, 0.51] **Utilization**: • Hospitalization, % of patients, 25 vs. 25; P=1.0 • ED visits, % of patients, 50 vs. 55; P=0.65 • Hospice utilization, % of patients, 7.5 vs. 7.5; P=1.0 • Nursing facility		

eTable 3. Trial Characteristics and Outcomes of 26 Palliative Care Interventions at High Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
								admissions, % of patients, 22.5 vs. 32.5; P=0.32 **ACP** • [POS] [a]: 6-month mean difference, -2.844 [95% CI, -5.633, -0.055]; 12-month mean difference, -4.546 [-7.853, -1.238]		
Sidebottom et al, 2015[31] (USA)	Parallel	Adult inpatient with acute HF; Mean age: 73	Structure, Physical, Psychological, Social, Spiritual, Legal	Inpatient specialist palliative care consultation. Content of visits included: symptom assessment; emotional, spiritual, and psychosocial aspects of care; care coordination; treatment recommendations; referral; and, advance care planning	116	Usual care	116	**QOL** • [Minnesota Living with Heart Failure Questionnaire] [a]: Improved (mean difference, 3.06; 95% CI, 2.75-3.37; P<0.001) **Symptom burden** • [ESAS] [a]: Improved total symptom burden (mean	High	High

eTable 3. Trial Characteristics and Outcomes of 26 Palliative Care Interventions at High Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
								difference, 4.31; 95% CI, 4.00-4.62; P<0.001); improvements in pain, fatigue, appetite, dyspnea at 3 mo. **Survival** • 6-month, HR, 1.90 (95% CI, 0.88, 4.09); P=0.10 **Mood** • [PHQ-9] [a]: Improved mean difference, 0.72 (95% CI, 0.41, 1.03); P<0.001 **Utilization** • 30-day readmission, HR, 1.43 (95% CI, 0.5, 4.1); P=0.50 • Hospice use within six months, HR, 1.60 (0.58, 4.38); P= 0.36		

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Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
								ACP • Improved (HR, 1.43; 95% CI, 1.09-7.59; P=0.03)		
Steel et al, 2016[32] (USA)	Parallel	Advanced gastrointestinal cancer, or other cancers with liver metastasis; Mean age: 61	Physical, Psychological	Web-based collaborative care intervention that included computerized cognitive behavioral therapy, as well as a care coordinator providing symptom management recommendations	144	Usual care	117	**QOL** • [FACT-G] QOL at 6 months, *d*=0.99 (*P*=0.05) **Symptom burden** • [BPI] Pain at 6 months, *d*=0.62 (*P*=0.11) • [FACT-Fatigue] Fatigue at 6 months, *d*=0.26 (*P*=0.09) **Mood** • [CESD] Depressive symptoms at 6 months, *d*=0.71 (*P*=0.18) **Caregiver mood** • [CESD] Depressive symptoms at 6 months, *d*=0.37	High	High

eTable 3. Trial Characteristics and Outcomes of 26 Palliative Care Interventions at High Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
								(*P*=0.10) **Caregiver QOL** • [Caregiver QOL Index-Cancer] Caregiver stress at 6 months, *d*=0.75 (*P*=0.05)		
Temel et al, 2010[33-35] (USA)	Parallel	Metastatic non-small cell lung cancer; Mean age: 65	Structure, Physical, Psychological, Spiritual, EOL, Legal	Specialist palliative care provided by physician/advance practice provider within 11 weeks of diagnosis and then monthly until death	77	Usual care	74	**QOL** • [TOI][a] 12 weeks (ES, 0.52; P=0.009) • [FACT-L] 12 weeks (ES, 0.42; P=0.03) **Symptom burden** • [LCS]12 weeks (ES, 0.41; P=0.04) **Survival** • Median, 11.6 vs. 8.9 months (P=0.02) **Mood** • [HADS] Patients meeting criteria for depression, 16% vs. 38%	Low	High for survival only; all others, Low

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Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
								(P=0.01) • [PHQ-9] Patients meeting criteria for depression, 4% vs. 17% (P=0.05) **Utilization** • Use of aggressive end-of-life care, 33% vs. 54% (P=0.05) **Advance care planning** • Documentation of resuscitation preferences, 53% vs. 28% (P=0.05)		
Wallen et al, 2012[36] (USA)	Parallel	Advanced cancer (types not specified) undergoing surgical procedures; Mean age: 53	Structure, Physical, Psychological, Social, Spiritual	Inpatient/outpatient palliative care consult service. Consults include comprehensive pain/symptom assessment, as well as emotional and spiritual distress	76	Usual care	76	**Symptom burden** • [Gracely Pain Scale][a] Pain unpleasantness at 9 months NS (mean difference, -2.31; *P*=0.23) • [Symptom Distress Scale] [a]	High	High

eTable 3. Trial Characteristics and Outcomes of 26 Palliative Care Interventions at High Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
								Symptom distress at 9 months NS (mean difference, -1.89; *P*=0.50)		
Wong et al, 2016[37] (Hong Kong)	Parallel	Advanced HF (e.g., NYHA stage III or IV); Mean age: 78	Structure, Physical, Psychological, Social, Legal	Transitional palliative care provided by palliative care home nurses via home visits and telephone	43	Usual care plus two attention control phone calls	41	**Symptom burden** • [ESAS] Clinically important improvement in total score, 73% vs. 41.4; P<0.05 **QOL** • [McGill] Better QOL at 4 weeks, 7.57 points vs. 6.46 points; P<0.001 • [Chronic HF Questionnaire] Better QOL at 4 weeks, 5.26 points vs. 4.47 points; P<0.001 **Satisfaction with care** • Higher satisfaction at 4 weeks,	High	High

eTable 3. Trial Characteristics and Outcomes of 26 Palliative Care Interventions at High Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
								48.84 points vs. 3.55 points, P<0.001 **Utilization** • Readmission at 4 weeks, 20.9% vs. 29.3%, P=0.38 • Readmission at 12 weeks, 33.6% vs. 61%, P=0.009		
Zimmer et al, 1984[38,39] (USA)	Parallel	Seriously ill homebound patients: cancer (type not specified) (19%), stroke (15%); Median age 77	Structure, Physical, Psychological, Social, EOL	Home health care team, plus 24-hour phone line. Initial consultation by physician, with additional home visits by nurse practitioner and social worker. Medical, nursing, social, emotional, and financial support services provided	85	Usual care	82	**Survival** • Six-month mortality, 36% vs. 29%; P>0.10 **Utilization** • Decreased per capita hospital admissions (mean, 0.35 vs. 0.41; P not reported) • Decreased nursing home admissions (mean, 0.06 vs. 0.11; P not reported) • Increased ED visits (mean	High	High

eTable 3. Trial Characteristics and Outcomes of 26 Palliative Care Interventions at High Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
								utilization rate per month, 0.26 vs. 0.05; P not reported) **Site of death** • Increased at-home death (71% vs. 47%; P not reported) **Satisfaction** • [McCusker scale]: NS at all time points; P not reported **Expenditures** • Lower mean total costs among decedents ($1,577 vs. $2,293, P not reported)[39] **Caregiver satisfaction** • [McCusker scale]: Improved at 3 months (96.9 vs. 82.1; P<0.0001) and at 6 months (99.8 vs. 88.8;		

eTable 3. Trial Characteristics and Outcomes of 26 Palliative Care Interventions at High Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
								P<0.002)		
Trials with cluster randomization										
McCorkle et al, 2015[40] (USA)	Cluster, parallel	Late-stage cancer (lung, head or neck, gastrointestinal, gynecological) diagnosis plus ≥1 chronic condition; Mean age:60	Structure, Physical, Psychological, Social, Legal	Multidisciplinary palliative collaborative care intervention led by advanced practice nurse, focusing on topics including symptom management, care coordination, and goals of care.	66	Enhanced usual care (usual care plus symptom management resource guide)	80	**Symptom burden** • [Symptom Distress Scale] NS at 1 month, (*P*=0.61) **QOL** • [FACT-G] NS at 1 month, (*P*=0.11); NS at 3 months, (*P*=0.37) **Mood** • [PHQ-9] Depression at 3 months, (*P*=0.93) • [HADS-Anxiety] Anxiety at 3 months, (*P*=0.12)	High	N/A
Rabow et al, 2004[41] (USA)	Cluster, parallel	Advanced CHF (34%), cancer (type not specified) (33%), or advanced COPD (32%); Prognosis: 1-5 years; Mean age: 69	Structure, Physical, Psychological, Social, Spiritual, Legal	Interdisciplinary PC team providing outpatient PC consultation, case management, psychological support, chaplaincy, caregiver training, medication review, and support groups	50	Usual care	40	**QOL** • [Multidimensional Quality of Life Scale-Cancer]: (F=1.02; P=0.32) **Symptom burden** • [UCSD Shortness of Breath	High	High

eTable 3. Trial Characteristics and Outcomes of 26 Palliative Care Interventions at High Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
								Questionnaire] Dyspnea, OR, 6.07 (95% Cl, 1.04 to 35.56) • [Brief Pain Inventory] Mean pain, F=1.03 (P=0.32) • [Medical Outcomes Study Survey] Sleep quality, F=0.14 (P=0.71) **Mood** • [POMS] Anxiety (F=4.09; P=0.05) • [CES-D] Depression (F=0.71; P=0.40) **Utilization** • Primary care visits, mean, 7.5 vs. 10.6 (P=0.03) • Urgent care visits, mean, 0.3 vs. 0.6 (P=0.04) • Specialty		

eTable 3. Trial Characteristics and Outcomes of 26 Palliative Care Interventions at High Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
								clinic visits, mean, 7.0 vs. 4.9 (P=0.25) • ED visits, mean, 1.7 vs. 1.6 (P=0.81) • Hospitalizations, mean, 0.8 vs. 1.2 (P=0.21) **Expenditures** • Total charges, mean [SD], $47,211USD [$73,009USD] vs. $43,338USD [$69,647USD] (P=0.80) **Advance care planning** • Completion of healthcare power of attorney, 55% vs. 28% (P=0.12) **Site of death** • Data not reported (P=0.40) **Satisfaction** • [Group Health Association		

eTable 3. Trial Characteristics and Outcomes of 26 Palliative Care Interventions at High Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
								of America Consumer Satisfaction Survey]: F=0.61 (P=0.44)		

Legend:
[a] Primary outcome measure; otherwise, not defined in article.
[b] Explicitly labeled as a pilot (or hypothesis generating, not hypothesis testing) study.
[c] Data analyzed and presented at dyad level
[d] Study closed early due to releasing of results of a different study.
[e] Assessed with an unvalidated instrument.
[f] Study does not provide number of patients in each experimental condition.

ES, effect size. NS, not significant. d, Hedges' d. g, Hedges' g. h, Hedges' h. OR, odds ratio. CI, confidence interval. HF, heart failure. COPD, chronic obstructive pulmonary disease. MSAS, Memorial Symptom Assessment Scale. CHF, congestive heart failure. ED, emergency department. GI, gastrointestinal. QOL, quality of life. FACIT-Pal, Functional Assessment of Chronic Illness Therapy – Palliative care. TOI, Trial Outcome Index. QUAL-E, Quality of Life at the End of Life. CESD, Center for Epidemiologic Studies Depression Scale. RR, risk ratio. CQOL-C, Caregiver Quality of Life Index – Cancer. MBCB, Montgomery Borgatta Caregiver Burden scale. PG13, Prolonged Grief – short form. NYHA, New York Heart Association. EQ-5D, EuroQOL Five Dimensions Scale. KCCQ, Kansas City Cardiomyopathy Questionnaire. SD, standard deviation. ICU, intensive care unit. EOL, end of life. IQR, interquartile range. LOS, length of stay. FACT-G, Functional Assessment of Cancer Therapy – General. POMS, Profile of Mood States. LASA, Linear Analog Scale Assessment. NRS, Numerical Rating Scale. HADS, Hospital Anxiety and Depression Scale. SF-36, 36-Item Short Form Survey. AIDS, Acquired immunodeficiency syndrome. GP, general practitioner. DNR, do not resuscitate. VA, Veterans Administration. FACT-B, Functional Assessment of Cancer Therapy-Breast. PC, palliative care. DM, diabetes mellitus. ESLD, End-stage liver disease. ALS, Amyotrophic lateral sclerosis. CMSAS, Condensed Memorial Symptom Assessment Scale. ACP, advance care planning. POS, Palliative Care Outcome Scale. ESAS, Edmonton Symptom Assessment Scale. HR, hazard ratio. PHQ-9, Patient Health Questionnaire 9. BPI, Brief Pain Inventory. FACT-L, Functional Assessment of Cancer Therapy-Lung. LCS, Lung Cancer Subscale.

Structure, Structure and processes of care. Psychological, Psychological and psychiatric aspects of care. Social, Social aspects of care. Cultural, Cultural aspects of care. Spiritual, Spiritual, religious, and existential aspects of care. EOL, Care of the imminently dying patient. Legal, Ethical and legal aspects of care.

Note: Primary outcome reported, regardless of whether it is one of our pre-specified outcomes of interest. If no primary outcome specified in paper, and the outcome is not one of our outcomes of interest, it is not reported here. All comparisons are intervention versus control, if not otherwise specified. Ambulatory interventions refer to those interventions where patients were required to travel to either an outpatient clinic or an intervention delivery site. Subjective outcomes include all patient-reported outcomes (e.g., QOL, symptoms, mood), whereas objective outcomes include those outcomes which are not subject to detection bias (e.g., survival, healthcare utilization and expenditures abstracted from clinical or administrative records).

eTable 4. Trial Characteristics and Outcomes of 11 Palliative Care Interventions at Unclear Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
Trials with patient-level randomization										
Ahronheim et al, 2000[42] (USA)	Parallel	Inpatients with advanced dementia; Mean age: 85	Structure, Physical, Legal	Daily PC consultations (from MD and RN) to provide recommendations to enhance patient comfort	48	Usual care	51	**Utilization** • LOS, 8.8 vs. 9.7 days (P=0.46) • Receipt of IV therapy during hospitalization, 66% vs. 81% (P=0.03) **ACP** • Discharged with a palliative care plan, 23% vs. 4% (P=0.008) **Survival** • In-hospital mortality, 12 vs. 12 (P=0.96)	Unclear	Unclear

eTable 4. Trial Characteristics and Outcomes of 11 Palliative Care Interventions at Unclear Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
Bekelman et al, 2015[43] (USA)	Parallel	CHF with poor QOL, limited functional status, and significant symptoms (KCCQ score <60); Mean age: 68	Structure, Physical, Psychological	Multidisciplinary collaborative CHF disease management, and tele-monitoring with patient self-care support	193	Usual care	199	**QOL** • [KCCQ][a] one year, overall KCCQ score, 54.2 (95% CI, 51.7 to 56.6) vs. 53.6 (95% CI, 51.1 to 56.0) **Survival** • One-year mortality (4.3% vs. 9.67%; P=0.04) **Mood** • [PHQ-9]: among patients with positive depression screen, 2.1 points lower (95% CI, 0.43 to 3.78); P=0.01 **Utilization** • One-year hospitalization 29.4% vs. 29.9%; P=0.87	Unclear	Unclear
Brumley et al, 2007[44] (USA)	Parallel	Cancer (type not specified) (47%), CHF (33%), or COPD (21%); Prognosis: ≤ 1 year; Mean age: 74	Structure, Physical, Psychological, Social, Spiritual, Legal	Multidisciplinary home-based palliative care	155	Usual care	155	**Utilization** • ED utilization, 20% vs. 33%; P=0.01 • Hospitalization, 36% vs. 59%; P<0.001 • Hospice enrollment, 25% vs. 36%; P=0.15	Unclear	Unclear

eTable 4. Trial Characteristics and Outcomes of 11 Palliative Care Interventions at Unclear Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
								Site of death • In-home death OR=2.20; 95% CI=1.3 to 3.7; P<0.001 **Satisfaction** • [Reid-Gundlach]: OR=3.37, 95% CI=0.65-4.96; P=0.03 **Expenditures** • Decreased healthcare costs, 33% reduction; 95% CI= -$12,411USD to -$780USD; P=0.03		
Edmonds et al, 2010[45-47] (UK)[b]	Waitlist, parallel	Multiple sclerosis with clinician-identified palliative needs; Mean age: 53	Structure, Physical, Psychological, Social, Legal	Assessment and follow-up from multidisciplinary palliative care consultative service, focusing on symptom management, psychological concerns, social issues, caregiver concerns, and advance care planning (n=26 patients, 26 caregivers)[c]; C: (n=26 patients, 24	26 patients, 21 care-givers	Delayed intervention (12 weeks)	26 patients, 22 caregivers	**Symptom burden** • [MS Palliative Outcome Scale-S5][a]: ES, -0.8 (P=0.035) **Expenditures** • Total costs, difference, -£1,789 (95% CI, -£5,224 to £1,902). **Other** • [Palliative Outcomes Scale][a] Palliative care needs subscale, ES, 0.2 (P=0.30) • [Modified Lawton	Unclear	Unclear

eTable 4. Trial Characteristics and Outcomes of 11 Palliative Care Interventions at Unclear Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
				caregivers)[d]				scale][a]: Caregiver positivity ES, -0.3 (P=0.75) **Caregiver burden** • [Zarit][a]: ES, -1.3 (P=0.013)		
Gade et al, 2008[48] (USA)	Parallel	Life limiting illness (31% cancer (type not specified), 7% CHF); Prognosis: < 1 year; Mean age:73	Structure, Physical, Psychological, Social, Spiritual, EOL	Inpatient consultative palliative care service	280	Usual care	237	**Symptom burden** • [Modified City of Hope Patient Questionnaire] [a] NS at hospital discharge (4.0 vs. 4.1l *P*=0.91) **Survival** • Median survival NS, 30 vs. 36 days; *P*=0.08 **Utilization** • Fewer ICU admissions (12 vs. 21; *P*=0.04) • Longer median hospice stays (24 vs. 12 days; *P*=0.04) • Admission to hospice NS (*P*=0.50) **ACP** • Increased proportion of patients with advance directives at discharge (91.1% vs. 77.8%;	Unclear	Unclear

eTable 4. Trial Characteristics and Outcomes of 11 Palliative Care Interventions at Unclear Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
								P<0.001) **Satisfaction** • [Modified City of Hope Patient Questionnaire] [a]: Improved satisfaction regarding place of care (6.8 vs. 6.4; *P*<0.001) and improved satisfaction with provider communication (8.3 vs. 7.2; *P*<0.001) **Expenditures** [a] • Decreased mean 6-month total costs per patient by $6,766 (*P*=0.001)		
Grudzen et al, 2016[49] (USA)	Parallel	Stage III-IV cancer (solid or hematological (breast, colorectal, lung, other)) presenting to quaternary emergency department; Mean age: 57	Structure, Physical, Psychological, Social, Spiritual, EOL, Legal	Comprehensive, multidisciplinary palliative care consultation initiated while in the emergency department. Consultation comprised: symptom assessment and treatment; goals of care and ACP; and, transition	69	Usual care	67	**QOL** • [FACT-G] [a]: NS at six weeks, increase from baseline 4.78 points vs. 1.52 points (P=0.05); Improved at 12 weeks greater in intervention vs. control (5.91 points vs. 1.08 points; P=0.03) **Survival** • 289 days (95%	Unclear	Unclear

eTable 4. Trial Characteristics and Outcomes of 11 Palliative Care Interventions at Unclear Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
				planning				CI, 128-453) vs 132 days (95% CI, 80-302); P=0.20 **Mood** • [PHQ-9]: NS at 6 weeks (P=0.97); NS at 12 weeks (P=0.46). **Utilization** • Hospice use, 28% vs. 25%; P=0.85 • Hospital days at 180 days post-enrollment, 17.45±20.18 vs. 10.93±9.33; P=0.14 • ICU admission at 180 days post-enrollment, 9% vs. 7%; P>0.99		
Hanks et al, 2002[50] (UK)	Parallel	Inpatients referred to PC service (93% cancer (type not specified)); Prognosis: > 24 hours; Mean age: 68	Structure, Physical, Psychological, Social, Spiritual	Multidisciplinary hospital-based specialist palliative care consultation	175 patients, 85 caregivers	Limited telephone-based palliative care consultation provided to referring clinician	86 patients, 42 caregivers	**QOL** • [EORTC QLQ-C30][a] Mean difference at 1 week, 2.35 (95% CI, -3.7, 8.4); *P*=0.45 **Symptom burden** • [VAS][a] Severity of most bothersome symptom, mean difference at 1 week, 2.94 (95%	Unclear	Unclear

eTable 4. Trial Characteristics and Outcomes of 11 Palliative Care Interventions at Unclear Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
								CI, -5.3, 11.1); *P*=0.48 **Mood** • [Memorial Pain Assessment Card][a] Mean difference at 1 week, 3.97 (95% CI, -2.5, 10.4); *P*=0.23 Utilization • Hospital LOS[a] NS, 14.7 vs. 13.2 days; *P* not reported • Readmissions[a] NS, 0.18 vs. 0.18; *P* not reported **Satisfaction** • [MacAdam's Assessment of Suffering] NS, data not reported **Caregiver satisfaction** • [FAMCARE] NS, data not reported		
Kane et al, 1984[51,52] (USA)	Parallel	Terminal cancer (lung, prostate, ear, nose, throat, brain, other); Prognosis: 2 weeks - 6 months; Mean age: 64	Structure, Physical, Psychological, Social, Spiritual, EOL	Inpatient and/or home hospice services	137[c]	Usual care	110[c]	**Symptom burden** • [California Pain Assessment Profile]: Pain NS, data not reported **Mood** • [CES-D] Depression NS, data not reported	Unclear	Unclear

eTable 4. Trial Characteristics and Outcomes of 11 Palliative Care Interventions at Unclear Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
								• [General Wellbeing Measure] Anxiety NS, data not reported **Utilization** • Total inpatient days NS, 51 vs. 47.5; P not reported • Nursing home days, 1.0 vs. 11.4; P≤0.05 • Chemotherapy treatments, 1.3 vs. 0.49; P=0.03 • Major surgical procedures, 0.09 vs. 0.01; P≤0.05 **Satisfaction** • [Ware scale]: Patient satisfaction improved, data not reported; P<0.01 **Expenditures** • Total inpatient cost NS, mean, $11,618 vs. $11,614; P not reported **Caregiver mood** • [CES-D] Depression NS, data not reported • [General		

eTable 4. Trial Characteristics and Outcomes of 11 Palliative Care Interventions at Unclear Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
								Wellbeing Measure] Anxiety improved, data not reported; P≤0.05 **Caregiver satisfaction** • [Ware scale]: Caregiver satisfaction improved, data not reported; P≤0.05		
Northouse et al, 2013[53] (USA)	Parallel	Advanced cancer (breast, colorectal, lung, prostate); Prognosis: ≥ 6 months; Mean age: 61	Physical, Psychological, Social	Home-based, dyadic intervention (see Northouse et al, 2005) including home visits and phone sessions 1. Brief: Two 90-min home visits, and one 30-min home phone session 2. Extensive: Four 90-min home visits, and two 30-min phone sessions	Brief: 159 patients, 159 caregivers; Extensive: 162 patients, 162 caregivers	Usual care	163 patients, 163 caregivers	**Patient and caregiver QOL** • [FACT-G][d]: Social QOL improved (F=4.28; P=0.002) • [FACT-G][d]: Emotional QOL (F=0.8; P=0.52) • [FACT-G][d]: Functional QOL (F=0.35; P=0.84) • [FACT-G][d]: Physical QOL (F=1.16; P=0.33) **Caregiver burden** • [Appraisal of Caregiving Scale]: (F=0.99; P=0.46)	Unclear	N/A
Trials with cluster randomization										
Jordhoy et al, 2001[54,55]	Cluster, parallel	Incurable cancer(gastrointe	Structure, Physical,	Comprehensive palliative care	235	Usual care	199	**QOL** • [EORTC QLQ-	Unclear	Unclear

eTable 4. Trial Characteristics and Outcomes of 11 Palliative Care Interventions at Unclear Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
(Norway)		stinal, lung, breast and female genitals, prostate and male genitals, kidney or vesical or ureter, lymphomas, skin, other); Prognosis: 2-9 months; Median age:70	Psychological, EOL	coordinated by hospital-based palliative medicine unit, providing inpatient, outpatient, and home-based services, as well as palliative care education for non-specialists				C30 Global Health] [a]: NS standardized AUC (-1.1 vs 1.1; P = 0.48) **Symptom burden** • [EORTC QLQ-C30 fatigue] [a]: NS standardized AUC (4.6 vs 1.2; P = 0.23) • [EORTC QLQ-C30 nausea/vomiting] [a]: NS standardized AUC (-0.7 vs 2.1; P = 0.27) • [EORTC QLQ-C30 pain] [a]: NS standardized AUC (-3.9 vs -1.6; P = 0.35) • [EORTC QLQ-C30 dyspnea] [a]: NS standardized AUC (2.8 vs 1.9; P = 0.95) • [EORTC QLQ-C30 diarrhea] [a]: NS standardized AUC (-0.4 vs -2.0; P = 0.68) • [EORTC QLQ-C30 constipation] [a]: NS standardized		

eTable 4. Trial Characteristics and Outcomes of 11 Palliative Care Interventions at Unclear Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
								AUC (-6.7 vs -0.5; P = 0.12) **Survival** • Median, 99 days vs. 127 days; P=0.1 **Mood** • [Impact of Event Scale] [a]: Avoidance SAUC I -1.5 vs. C -2.0, P=0.88; Intrusion SAUC I -1.5 vs. C -2.6, P=0.29 **Utilization** • [Time spent at home in last month of life] [a]: NS (52% vs 59%, P=0.15) • [Time in nursing homes during trial] decreased (3.0% vs 7.4%; P<0.05) • [Time in nursing homes during the last month of life] decreased (mean days, 7.2% vs. 14.6%; P<0.05) • [Admission to nursing home during the last month of life] NS (13% vs 24%, p=0.08 in		

eTable 4. Trial Characteristics and Outcomes of 11 Palliative Care Interventions at Unclear Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
								adjusted model) • [Inpatient time during study] NS (5.0 vs 9.3, P not reported) • [Inpatient days during last month of life] NS (2.2 vs 4.3, P not reported) **Site of death**[a]: • Increased death at home (25% vs. 15%; P=0.02) • Decreased nursing home deaths (9% vs. 21%; P<0.01)		
The SUPPORT Investigators 1995[56] (USA)	Cluster, parallel	Adults hospitalized with ≥ one of nine life-threatening diagnoses: Acute organ system failure (50%), chronic disease (29%); Mean age: 65	Physical, Psychological, Social, Legal	Nurse-led, patient-tailored intervention to improve communication by providing timely and reliable prognostic information, by eliciting and documenting patient/family preferences and understanding of diagnosis, prognosis and treatment, and to facilitate	2652	Usual care	2152	**Symptom burden** • [Scale not reported]: Pain NS (adjusted ratio, 1.15 [95% CI, 1.00, 1.33]) **ACP** • Time until DNR order entered NS (adjusted ratio, 1.02 [95% CI, 0.90, 1.15]) • Physician-patient DNR agreement NS (adjusted ratio, 1.22 [95% CI, 0.99, 1.49]) **Expenditures** • Hospital	Unclear	Unclear

eTable 4. Trial Characteristics and Outcomes of 11 Palliative Care Interventions at Unclear Risk of Bias

Study (Country)	Design	Patient Population	Domains Addressed	Intervention		Control		Main Results	Risk of Bias	
				Description	n	Description	n		Subjective Outcomes	Objective Outcomes
				family meeting				expenditures NS, adjusted ratio, 1.05 [95% CI, 0.99, 1.12]) **Utilization** • Days in ICU, comatose, or receiving mechanical ventilation NS (adjusted ratio, 0.97 [95% CI, 0.87, 1.07]) **Survival** • Six-month mortality NS (adjusted relative hazard, 0.95 [95% CI, 0.87, 1.04])		

Legend:
[a] Primary outcome measure; otherwise, not defined in article.
[b] Explicitly labeled as a pilot (or hypothesis generating, not hypothesis testing) study.
[c] Study does not provide number of caregivers in each experimental condition.
[d] Data analyzed and presented at dyad level.

ES, effect size. NS, not significant. d, Hedges' d. g, Hedges' g. h, Hedges' h. OR, odds ratio. Cl, confidence interval. LOS, length of stay. MD, medical doctor. RN, registered nurse. PC, palliative care. IV, intravenous. ACP, advance care planning. CHF, congestive heart failure. QOL, quality of life. KCCQ, Kansas City Cardiomyopathy Questionnaire. PHQ-9, Patient Health Questionnaire 9. COPD, chronic obstructive pulmonary disease. ED, emergency department. MS, multiple sclerosis. EOL, end of life. ICU, intensive care unit. FACT-G, Functional Assessment of Cancer Therapy-General. EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire. VAS, visual analog scale. CESD, Center for Epidemiologic Studies Depression Scale. AUC, area under curve. SAUC, standardized area under curve. DNR, do not resuscitate.

Structure, Structure and processes of care. Psychological, Psychological and psychiatric aspects of care. Social, Social aspects of care. Cultural, Cultural aspects of care. Spiritual, Spiritual, religious, and existential aspects of care. EOL, Care of the imminently dying patient. Legal, Ethical and legal aspects of care.

Note: Primary outcome reported, regardless of whether it is one of our pre-specified outcomes of interest. If no primary outcome specified in paper, and the outcome is not one of our outcomes of interest, it is not reported here. All comparisons are intervention versus control, if not otherwise specified. Ambulatory interventions refer to those interventions where patients were required to travel to either an outpatient clinic or an intervention delivery site. Subjective outcomes include all patient-reported outcomes (e.g., QOL, symptoms, mood), whereas objective outcomes include those outcomes which are not subject to detection bias (e.g., survival, healthcare utilization and expenditures abstracted from clinical or administrative records).

eTable 5. Risk of Bias Assessments of 43 Randomized Clinical Trials of Palliative Care Interven-tions

Trials with patient-level randomization

First author, year	Sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of subjective outcomes	Blinding of objective outcomes	Incomplete outcome data	Selective outcome reporting	Other sources of bias	Summary of bias: subjective outcomes	Summary of bias: objective outcomes
Ahronheim JC et al., 2000[42]	Low	Unclear	High	N/A	Low	Low	Low	Low	Unclear	Unclear
Aiken LS et al., 2006[11]	Low	Low	High	High	Low	High	High	High	High	High
Bakitas M et al., 2009[4]	Low	Low	High	High	Low	Low	Low	Low	Low	Low
Bakitas MA, 2015[12]	Low	Low	High	High	Low	Low	Low	High	High	High
Bekelman DB et al., 2015[43]	Low	Low	High	High	Low	Low	Low	Unclear	Unclear	Unclear
Brannstrom M et al., 2014[14]	Unclear	Low	High	High	Low	High	High	High	High	High
Brumley R et al., 2007[44]	Low	Low	High	High	Low	Low	Unclear	Unclear	Unclear	Unclear
Chapman DG et al., 2007[16]	Low	Unclear	High	High	N/A	Unclear	Unclear	High	High	N/A
Cheung W et al., 2010[17]	Low	Low	High	High	Low	High	Low	High	High	High
Clark MM et al., 2013[18]	Low	Unclear	High	High	N/A	High	Low	Low	High	N/A
Dyar S et al., 2012[19]	Low	Unclear	High	High	N/A	High	High	High	High	N/A
Edmonds P et al., 2010[45]	Low	Low	High	High	Low	Unclear	Low	Unclear	Unclear	Unclear
Engelhardt JB et al., 2006[20]	Low	Low	High	High	Low	High	Unclear	High	High	High
Farquhar MC et al., 2014[21]	Low	Low	High	High	Low	High	Low	Low	High	High
Farquhar MC et al., 2016[22]	Low	Low	High	High	Low	High	Low	Low	High	High
Gade G et al., 2008[48]	Low	Unclear	High	High	Low	Low	Low	Unclear	Unclear	Unclear
Given B et al., 2002[57]	Unclear	Unclear	High	High	N/A	Unclear	High	Low	High	N/A
Grande GE et al., 1999[24]	Low	Low	High	High	Low	Unclear	Low	High	High	High
Grudzen C et al., et al 2016[49]	Low	Low	High	High	Low	Low	Low	Unclear	Unclear	Unclear
Hanks GW et al., 2002[50]	Low	Low	High	High	Low	Unclear	Unclear	Unclear	Unclear	Unclear
Higginson IJ et al., 2014[6]	Low	Low	High	High	Low	Low	Low	Low	Low	Low
Hopp et al., 2016[25]	Unclear	Unclear	High	N/A	Low	Low	Unclear	High	N/A	High
Hughes SL et al., 1992[26]	Low	Unclear	High	High	Low	High	Unclear	High	High	High
Kane RL et al., 1984[51]	Low	Unclear	High	High	Low	Unclear	Unclear	Low	Unclear	Unclear
Lowther K et al., 2015[7]	Low	Low	High	High	N/A	Low	Low	Low	Low	N/A
McCorkle R et al., 1989[27]	Low	Low	High	High	Low	High	Unclear	Low	High	High
Northouse LL et al., 2005[28]	Low	Low	High	High	N/A	Low	High	Low	High	N/A
Northouse LL et al., 2007[8]	Low	Low	High	High	N/A	Low	Low	Low	Low	N/A
Northouse LL et al., 2013[53]	Low	Low	High	High	N/A	Low	Unclear	Low	Unclear	N/A
Pantilat SZ et al., 2010[29]	Unclear	Unclear	High	High	N/A	Unclear	Unclear	High	High	N/A
Radwany SM et al., 2014[30]	Low	Low	High	High	Low	High	Unclear	Low	High	High
Rummans TA et al., 2006[10]	Low	Low	High	High	N/A	Low	Low	Low	Low	N/A
Sidebottom AC et al., 2015[31]	Unclear	Unclear	High	High	Low	Unclear	High	High	High	High
Steel JL et al., 2016[32]	Low	Low	High	High	Low	Low	High	High	High	High

eTable 5. Risk of Bias Assessments of 43 Randomized Clinical Trials of Palliative Care Interven-tions

Trials with patient-level randomization

First author, year	Sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of subjective outcomes	Blinding of objective outcomes	Incomplete outcome data	Selective outcome reporting	Other sources of bias	Summary of bias: subjective outcomes	Summary of bias: objective outcomes
Temel JS et al., 2010[33]	Low	Low	High	High	Low	Low	High	Low	Low	High/Low*
Wallen GR et al., 2012[36]	Low	Unclear	High	High	Low	High	Unclear	High	High	High
Wong FK et al., 2016[37]	Low	Low	Unclear	Low	Low	Low	High	Low	High	High
Zimmer JG et al., 1984[39]	Low	Unclear	High	High	Low	Unclear	High	Low	High	High

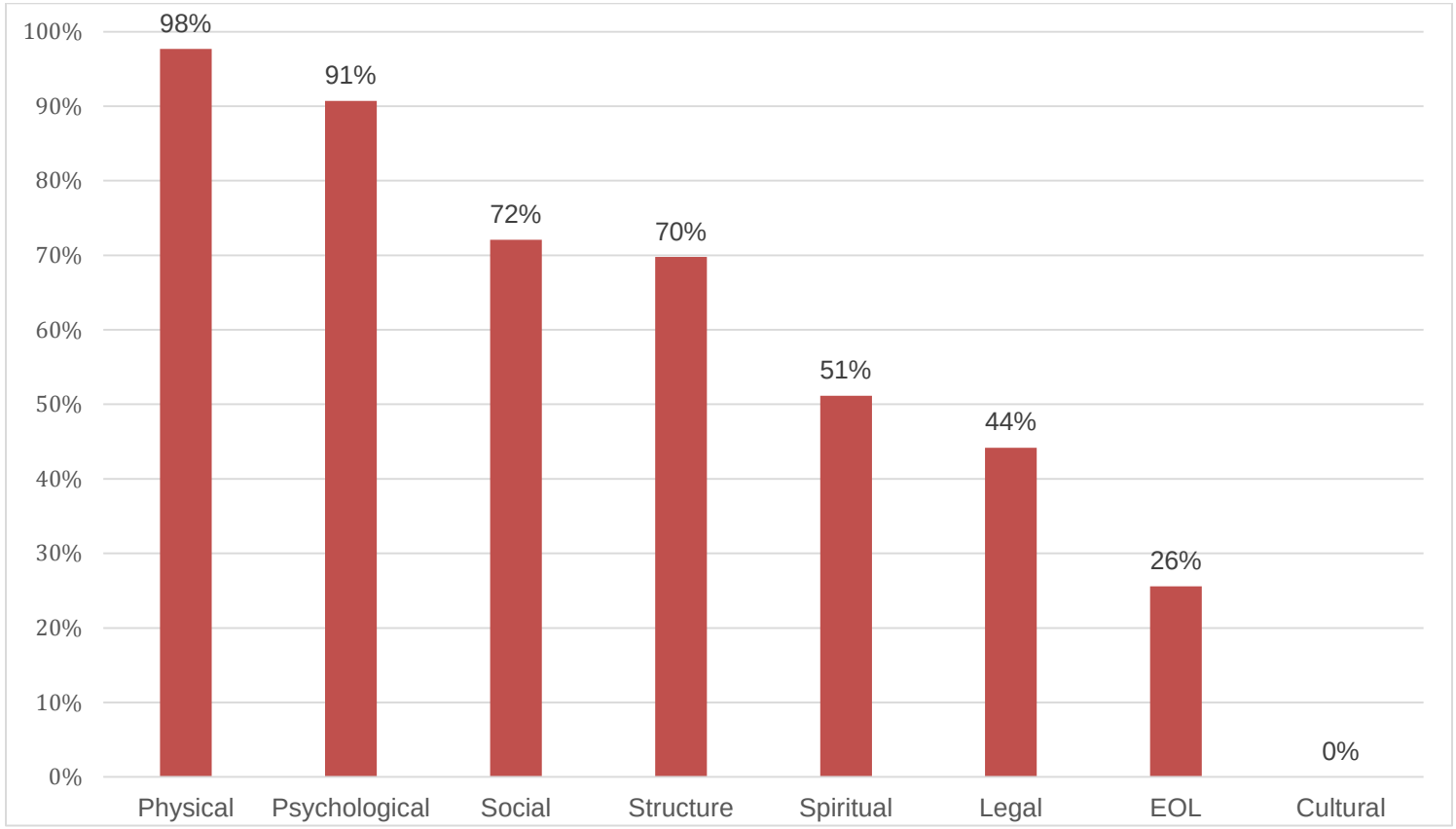
Trials with cluster-level randomization

First author, year	Sequence Generation	Recruitment Bias	Baseline Imbalance	Blinding of participants and	Blinding of subjective	Blinding of objective outcomes	Incomplete outcome data	Selective outcome reporting	Analysis accounted for clustering	Other sources of bias	Summary of bias: subjective outcomes	Summary of bias: objective outcomes
Jordhoy MS et al., 2001[54]	Unclear	Unclear	Low	High	High	Low	Low	Low	Low	Low	Unclear	Unclear
McCorkle R et al., 2015[40]	Low	High	High	High	High	N/A	Low	High	Low	Low	High	N/A
Rabow MW et al., 2004[41]	Low	High	Low	High	High	Low	Low	Low	High	Low	High	High
The SUPPORT Investigators, 1995[56]	Unclear	Unclear	Low	High	High	Low	Low	Low	Unclear	Low	Unclear	Unclear
Zimmermann C et al., 2014[3]	Low	High	Low	High	High	Low	Low	Low	Low	Low	Low	Low

eTable 6. Risk of Bias Judgments in 43 Randomized Clinical Trials of Palliative Care Interventions

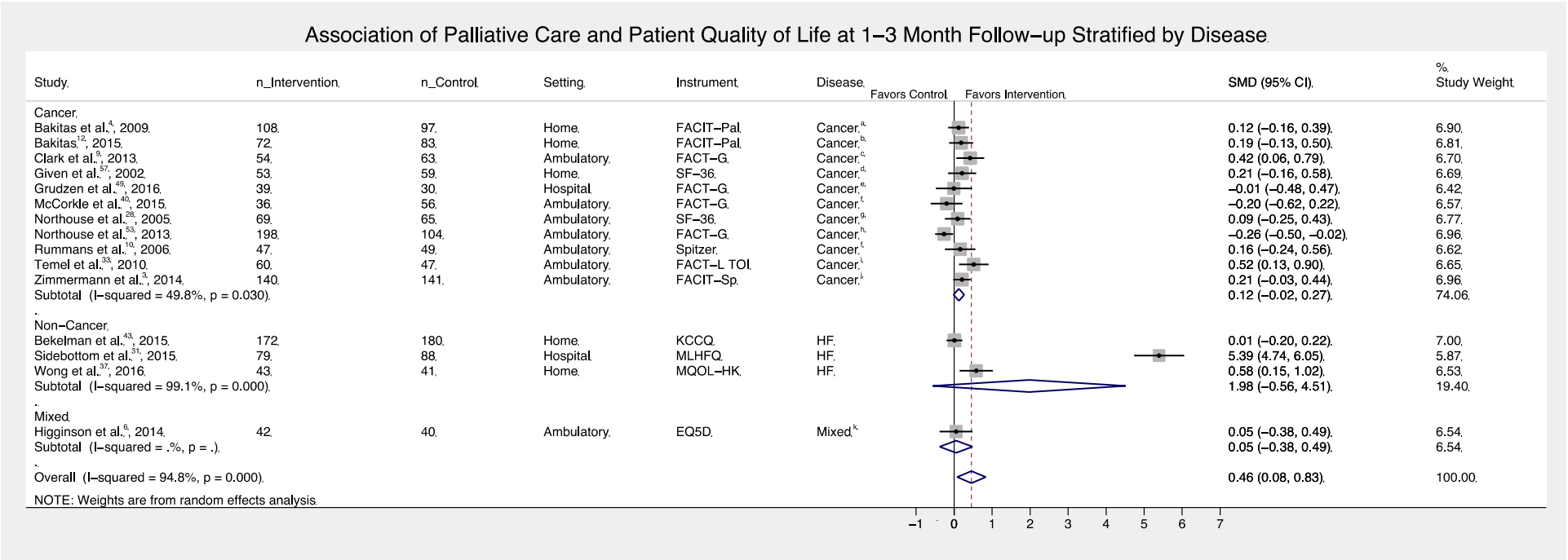
Risk Domain	Low risk of bias, No. of trials(%)	High risk of bias, No. of trials(%)	Unclear risk of bias, No. of trials(%)	Not applicable, No. of trials(%)
Trials with patient-level randomization (38 trials)				
Sequence generation (selection bias)	33 (87)	0 (0)	5 (13)	0 (0)
Allocation concealment (selection bias)	25 (66)	0 (0)	13 (34)	0 (0)
Blinding of participants and personnel (performance bias)	0 (0)	37 (97)	1 (3)	0 (0)
Blinding of subjective outcomes (detection bias)	1 (3)	35 (92)	0 (0)	2 (5)
Blinding of objective outcomes (detection bias)	28 (74)	0 (0)	0 (0)	10 (26)
Incomplete outcome data (attrition bias)	17 (45)	12 (32)	9 (24)	0 (0)
Selective outcome reporting (reporting bias)	16 (42)	10 (26)	12 (32)	0 (0)
Other sources of bias	18 (47)	14 (37)	6 (16)	0(0)
Trials with cluster-level randomization (5 trials)				
Sequence generation (selection bias)	3 (60)	0 (0)	2 (40)	0 (0)
Recruitment bias (selection bias)	0 (0)	3 (60)	2 (40)	0 (0)
Baseline imbalance (selection bias)	4 (80)	1 (20)	0 (0)	0 (0)
Blinding of participants and personnel (performance bias)	0 (0)	5 (100)	0 (0)	0 (0)
Blinding of subjective outcomes (detection bias)	0 (0)	5 (100)	0 (0)	0 (0)
Blinding of objective outcomes (detection bias)	4 (80)	0 (0)	0 (0)	1 (20)
Incomplete outcome data (attrition bias)	5 (100)	0 (0)	0 (0)	0 (0)
Selective outcome reporting (reporting bias)	4 (80)	1 (20)	0 (0)	0 (0)
Cluster-appropriate analysis	3 (60)	1 (20)	1 (20)	0 (0)
Other sources of bias	5 (100)	0 (0)	0 (0)	0 (0)

eFigure 1. Palliative Care Domains Addressed in 43 Randomized Clinical Trials of Palliative Care Interventions



Note: EOL, end of life.

eFigure 2. Association of Palliative Care and Patient Quality of Life at 1-3 Month Follow-up Stratified by Disease



Note: Cancer: P-value for pooled SMD=0.09, Tau^2=0.03, Q=19.93; Non-cancer: P-value for pooled SMD=0.13, Tau^2=4.96, Q=232.80; Mixed: P-value for pooled SMD=0.81, Tau^2<0.0001 Q<0.0001. Sample sizes in the figure are the number of patients analyzed corresponding to the studies at the specific time points.

Disease status: a: gastrointestinal, lung, genitourinary, and breast cancers. b: solid or hematological cancer. c: brain, gastrointestinal, head/neck, lung, and other cancers. d: breast, colon, lung, gynecological cancers, and lymphoma. e: breast, colon, lung, and other cancers. f: not further specified. g: breast cancer. h: breast, colon, lung, and prostate cancers. i: non-small cell lung cancer. j: lung, gastrointestinal, genitourinary, breast, and gynecological cancer. k: cancer, COPD, HF, ILD, ALS.

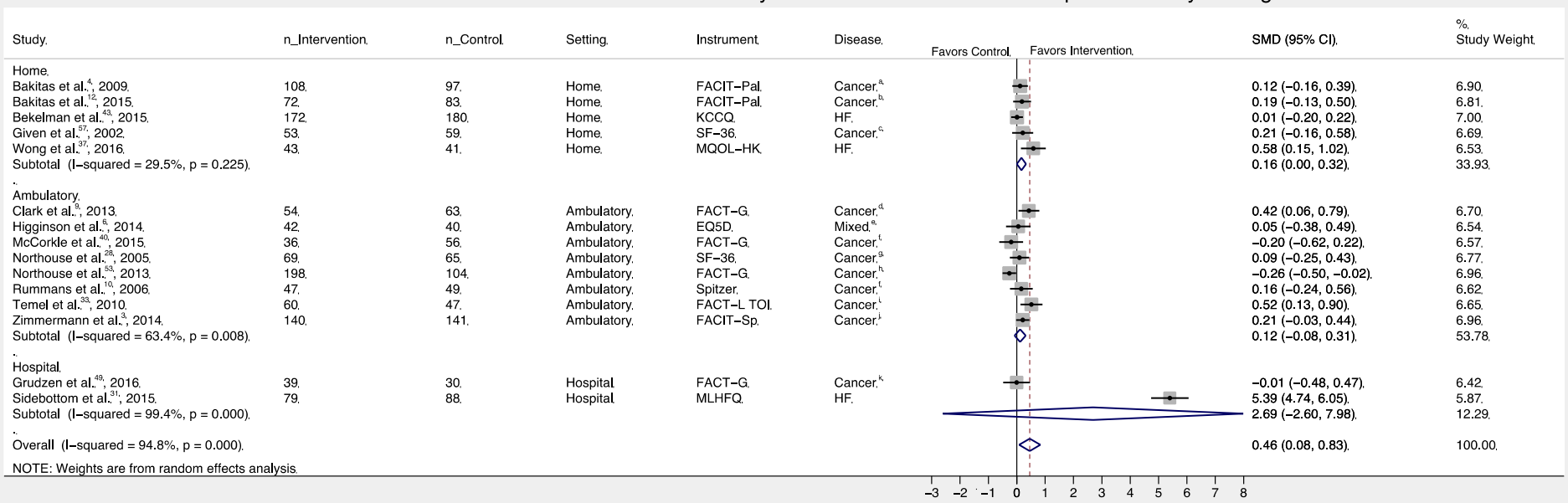
Legend: Data dots within shaded squares indicate SMDs from trials, with horizontal lines indicating 95% CI (confidence interval). The size of the shaded squares indicates study weight. Diamonds represent pooled SMDs and 95% CIs. The vertical dashed line indicates the pooled effect estimate, and the solid vertical line depicts a null effect (i.e., SMD = 0).

Abbreviations: SMD, standardized mean difference. SF-36, Short Form-36. EQ5D, EuroQol 5 Dimensions Questionnaire. FACIT-Pal, Functional Assessment of Chronic Illness Therapy-Palliative. FACT-L TOI, Functional Assessment of Cancer Therapy-Lung Treatment Outcome Index. FACT-G, Functional Assessment of Cancer Therapy- General. FACIT-Sp, Functional Assessment of Chronic Illness Therapy-Spirituality. KCCQ, Kansas City Cardiomyopathy Questionnaire. MLHFQ, Minnesota Living with Heart Failure Questionnaire. MQOL-HK, McGill Quality of Life Questionnaire – Hong Kong adaptation. HF, heart failure . COPD, chronic obstructive pulmonary disease. ILD, interstitial lung disease. ALS, amyotrophic lateral sclerosis.

Note: Ambulatory: P-value for pooled SMD=0.25, Tau^2= 0.05, Q=19.14; Hospital: P-value for pooled SMD=0.32, Tau^2=14.49, Q=169.31; Home: P-value for pooled SMD=0.05, Tau^2=0.01, Q=5.67. Sample sizes in the figure are the number of patients analyzed corresponding to the studies at the specific time points.

Disease status: a: gastrointestinal, lung, genitourinary, and breast cancers. b: solid or hematological cancer. c: breast, colon, lung, gynecological cancers, and lymphoma. d: brain, GI, head/neck, lung, and other cancers. e: cancer, COPD, HF, ILD, ALS. f: not further specified. g: breast cancer. h: breast, colon, lung, and prostate cancers. i: non-small cell lung cancer. j: lung, gastrointestinal, genitourinary, breast, and gynecological cancers. k: breast, colon, lung, and other cancers.

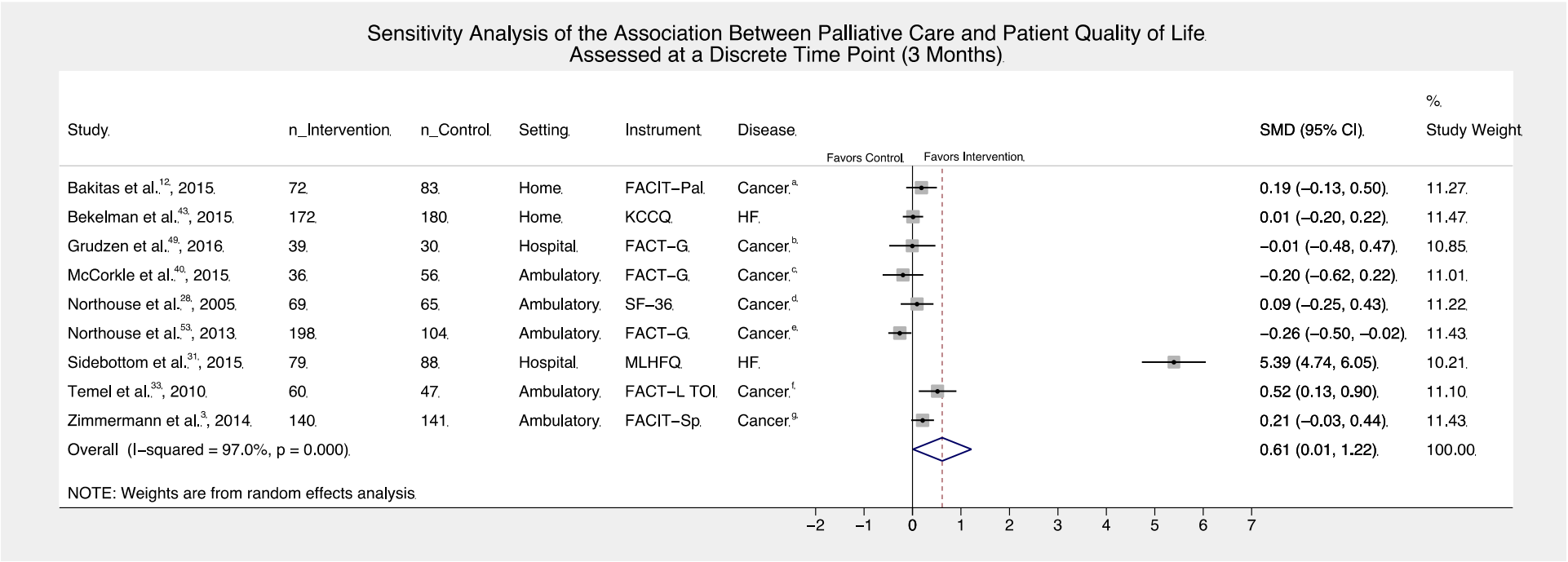
eFigure 3. Association of Palliative Care and Patient Quality of Life at 1-3 Month Follow-up Stratified by Setting



Legend: Data dots within shaded squares indicate SMDs from trials, with horizontal lines indicating 95% CI (confidence interval). The size of the shaded squares indicates study weight. Diamonds represent pooled SMDs and 95% CIs. The vertical dashed line indicates the pooled effect estimate, and the solid vertical line depicts a null effect (i.e., SMD = 0).

Abbreviations: SMD, standardized mean difference. SF-36, Short Form-36. EQ5D, EuroQol 5 Dimensions Questionnaire. FACIT-Pal, Functional Assessment of Chronic Illness Therapy-Palliative. FACT-L TOI, Functional Assessment of Cancer Therapy-Lung Treatment Outcome Index. FACT-G, Functional Assessment of Cancer Therapy- General. FACIT-Sp, Functional Assessment of Chronic Illness Therapy-Spirituality. KCCQ, Kansas City Cardiomyopathy Questionnaire. MLHFQ, Minnesota Living with Heart Failure Questionnaire. MQOL-HK, McGill Quality of Life Questionnaire – Hong Kong adaptation. HF, heart failure . COPD, chronic obstructive pulmonary disease. ILD, interstitial lung disease. ALS, amyotrophic lateral sclerosis.

eFigure 4. Sensitivity Analysis of the Association Between Palliative Care and Patient Quality of Life Assessed at a Discrete Time Point (3 Months)



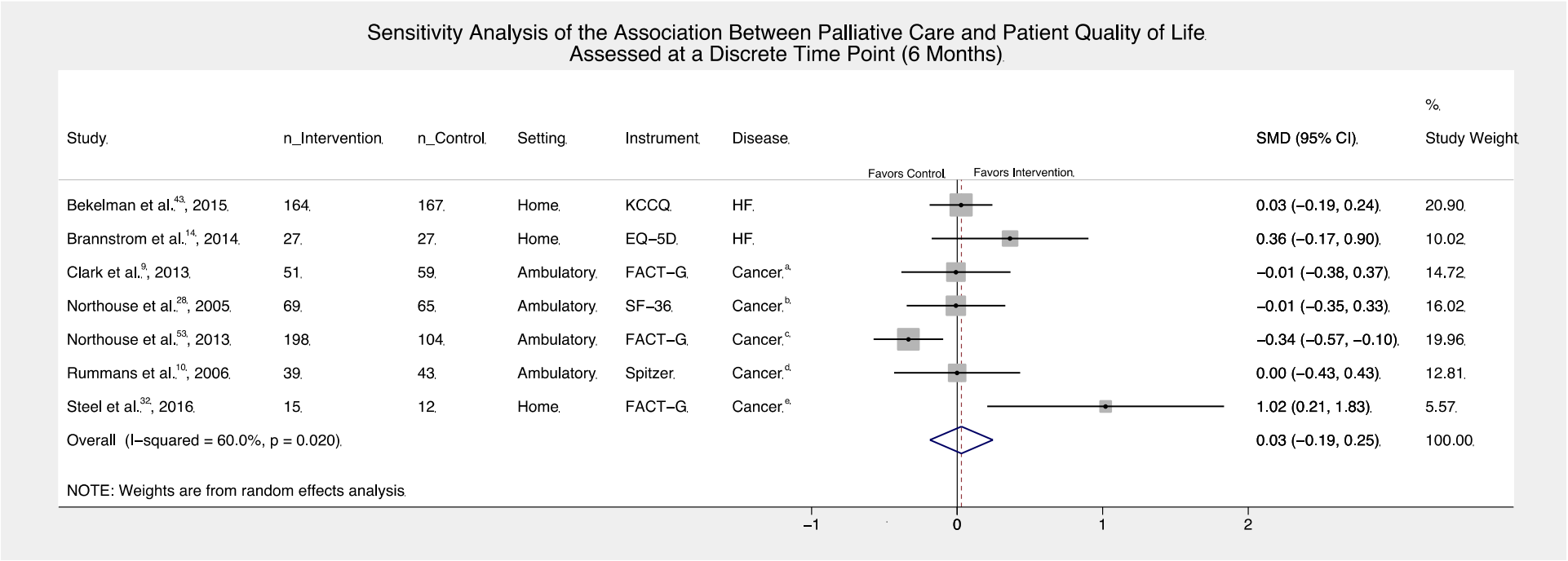
Note: P-value for pooled SMD=0.05, Tau^2=0.81 Q=262.75. Sample sizes in the figure are the number of patients analyzed corresponding to the studies at the specific time points.

Disease status: a: solid or hematological cancer. b: breast, colon, lung, and other cancers. c: not further specified. d: breast cancer. e: breast, colon, lung, and prostate cancers. f: non-small cell lung cancer. g: lung, gastrointestinal, genitourinary, breast, and gynecological cancers.

Legend: Data dots within shaded squares indicate SMDs from trials, with horizontal lines indicating 95% CI (confidence interval). The size of the shaded squares indicates study weight. Diamonds represent pooled SMDs and 95% CIs. The vertical dashed line indicates the pooled effect estimate, and the solid vertical line depicts a null effect (i.e., SMD = 0).

Abbreviations: SMD, standardized mean difference. SF-36, Short Form-36. FACIT-Pal, Functional Assessment of Chronic Illness Therapy-Palliative. FACT-L TOI, Functional Assessment of Cancer Therapy-Lung Treatment Outcome Index. FACT-G, Functional Assessment of Cancer Therapy- General. FACIT-Sp, Functional Assessment of Chronic Illness Therapy-Spirituality. KCCQ, Kansas City Cardiomyopathy Questionnaire. MLHFQ, Minnesota Living with Heart Failure Questionnaire. HF, heart failure.

eFigure 5. Sensitivity Analysis of the Association Between Palliative Care and Patient Quality of Life Assessed at a Discrete Time Point (6 Months)



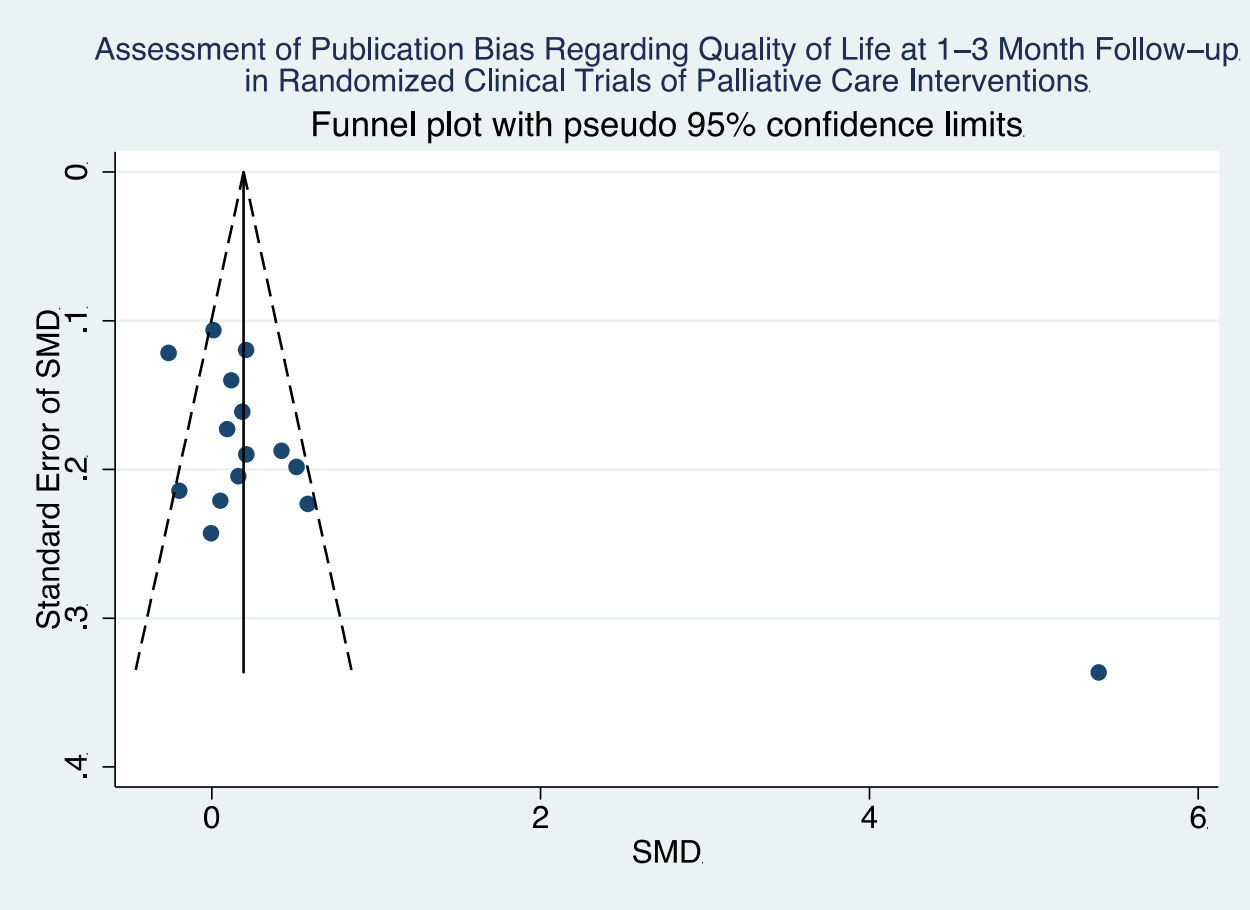
Note: P-value for pooled SMD=0.79, Tau^2=0.05 Q=15.01. Sample sizes in the figure are the number of patients analyzed corresponding to the studies at the specific time points.

Disease status: a: brain, gastrointestinal, head/neck, lung, and other cancers. b: breast cancer. c: breast, colon, lung, and prostate cancers. d: not further specified. e: upper gastrointestinal cancer.

Legend: Data dots within shaded squares indicate SMDs from trials, with horizontal lines indicating 95% CI (confidence interval). The size of the shaded squares indicates study weight. Diamonds represent pooled SMDs and 95% CIs. The vertical dashed line indicates the pooled effect estimate, and the solid vertical line depicts a null effect (i.e., SMD = 0).

Abbreviations: SMD, standardized mean difference. SF-36, Short Form-36. EQ-5D, EuroQol 5 Dimensions Questionnaire. FACT-G, Functional Assessment of Cancer Therapy- General. KCCQ, Kansas City Cardiomyopathy Questionnaire. HF, heart failure .

eFigure 6. Assessment of Publication Bias Regarding Quality of Life at 1-3 Month Follow-up in Randomized Clinical Trials of Palliative Care Interventions



Note: Egger's test bias estimate (SE): 8.25 (3.39), P=0.03.
Legend: Dotted lines indicate pseudo 95% confidence intervals around the overall summary estimate.
Abbreviation: SMD, standardized mean difference.

eTable 7. Meta-Regression Analysis to Explore Sources of Heterogeneity Among Randomized Clinical Trials of Palliative Care

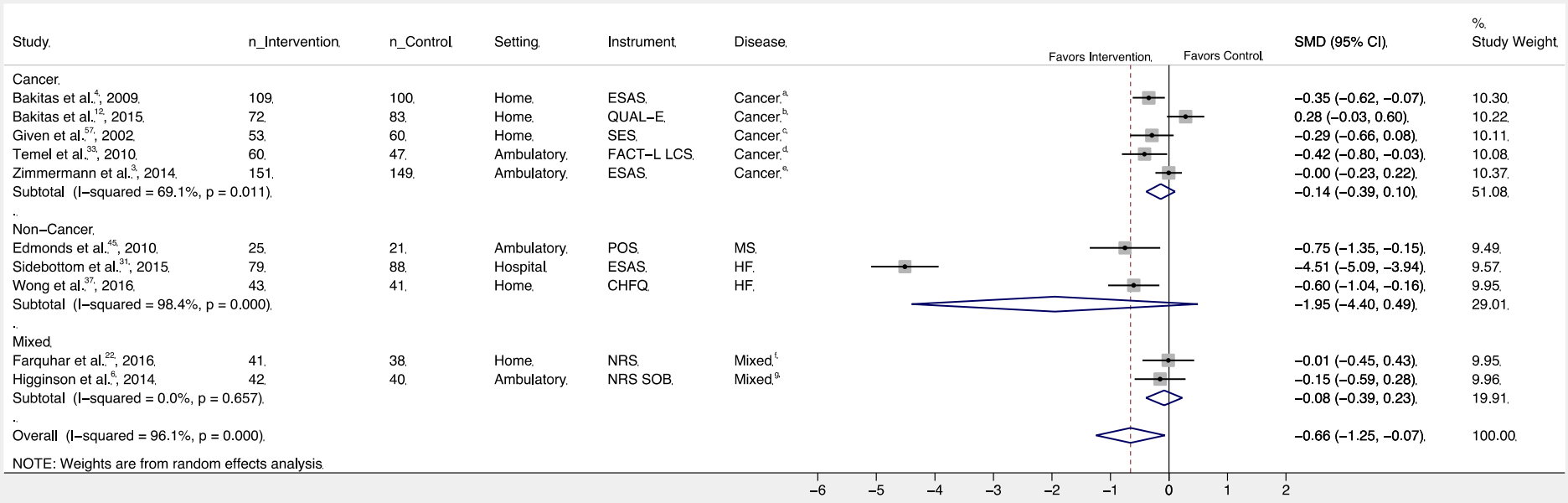
Subgroups by Trial Characteristics	No.			SMD or HR[a] (95% CI)	P Value for Heterogeneity
	Studies	Intervention	Control		
Association Between Palliative Care and Patient Quality of Life at 1-3 Months					
Risk of bias					
Low	5	397	374	0.20 (0.06, 0.34)	
High	7	406	455	0.93 (0.00, 1.85)	0.50
Unclear	3	409	314	-0.10 (-0.30, 0.09)	
Risk of bias					
Low & Unclear	8	806	688	0.08 (-0.08, 0.24)	0.25
High	7	406	455	0.93 (0.00, 1.85)	
Setting					
Ambulatory	8	646	565	0.12 (-0.08, 0.31)	
Hospital	2	118	118	2.69 (-2.60, 7.98)	0.04
Home	5	448	460	0.16 (0.00, 0.32)	
Disease					
Cancer	11	876	794	0.12 (-0.02, 0.27)	
Non-Cancer	3	294	309	1.98 (-0.56, 4.51)	0.11
Mixed	1	42	40	0.05 (-0.38, 0.49)	
No. of participants					
≥100	10	1005	927	0.63 (0.08, 0.83)	0.48
<100	5	207	216	0.12 (-0.13, 0.37)	
Intervention intensity					
High	9	642	639	0.80 (0.16, 1.45)	0.25
Low	6	570	504	-0.04 (-0.18, 0.11)	
Association Between Palliative Care and Symptom Burden at 1-3 Months					
Risk of bias					
Low	4	362	336	-0.21 (-0.42, 0.00)	
High	5	288	310	-1.01 (-2.37, 0.34)	0.74
Unclear	1	25	21	-0.75 (-1.35, -0.15)	
Risk of bias					
Low & Unclear	5	387	357	-0.27 (-0.50, -0.04)	0.47
High	5	288	310	-1.01 (-2.37, 0.34)	
Setting					
Ambulatory	4	278	257	-0.26 (-0.56, 0.04)	
Hospital	1	79	88	-4.51 (-5.09, -3.94)	<0.001
Home	5	318	322	-0.19 (-0.49, 0.12)	
Disease					
Cancer	5	445	439	-0.14 (-0.39, 0.10)	
Non-Cancer	3	147	150	-1.95 (-4.40, 0.49)	0.12
Mixed	2	83	78	-0.08 (-0.39, 0.23)	
No. of participants					
≥100	6	524	527	-0.85 (-1.75, 0.04)	0.61
<100	4	151	140	-0.35 (-0.68, -0.02)	
Intervention intensity					
High	7	539	529	-0.88 (-1.71, -0.06)	0.47
Low	3	136	138	-0.17 (-0.41, 0.07)	
Association Between Palliative Care and Survival					
Risk of bias					
Low	1	161	161	0.82 (0.64, 1.07)	
High	2	193	190	1.01 (0.32, 3.17)	0.97
Unclear	4	766	700	0.95 (0.70, 1.29)	
Risk of bias					
Low & Unclear	5	927	861	0.92 (0.71, 1.20)	0.92
High	2	193	190	1.01 (0.32, 3.17)	

eTable 7. Meta-Regression Analysis to Explore Sources of Heterogeneity Among Randomized Clinical Trials of Palliative Care

Subgroups by Trial Characteristics	No.			SMD or HR[a] (95% CI)	P Value for Heterogeneity
	Studies	Intervention	Control		
Setting					
Ambulatory	1	77	74	0.59 (0.39, 0.88)	
Hospital	3	460	420	1.11 (0.69, 1.77)	0.51
Home	3	583	557	0.87 (0.58, 1.29)	
Disease					
Cancer	4	542	501	0.82 (0.60, 1.13)	
Non-Cancer	2	303	313	0.93 (0.23, 3.77)	0.74
Mixed	1	275	237	1.22 (0.98, 1.53)	
No. of participants					
≥300	4	858	794	0.98 (0.75, 1.29)	0.73
<300	3	262	257	0.84 (0.48, 1.45)	
Intervention intensity					
High	5	698	655	0.90 (0.65, 1.25)	0.85
Low	2	422	396	0.79 (0.31, 1.99)	

Note: SMD, standardized mean difference. HR, hazard ratio. CI, confidence interval. [a]= SMDs provided for meta-regressions of quality of life and symptom burden, whereas HRs provided for meta-regressions of survival.

eFigure 7. Association of Palliative Care and Patient Symptom Burden at 1-3 Month Follow-up Stratified by Disease



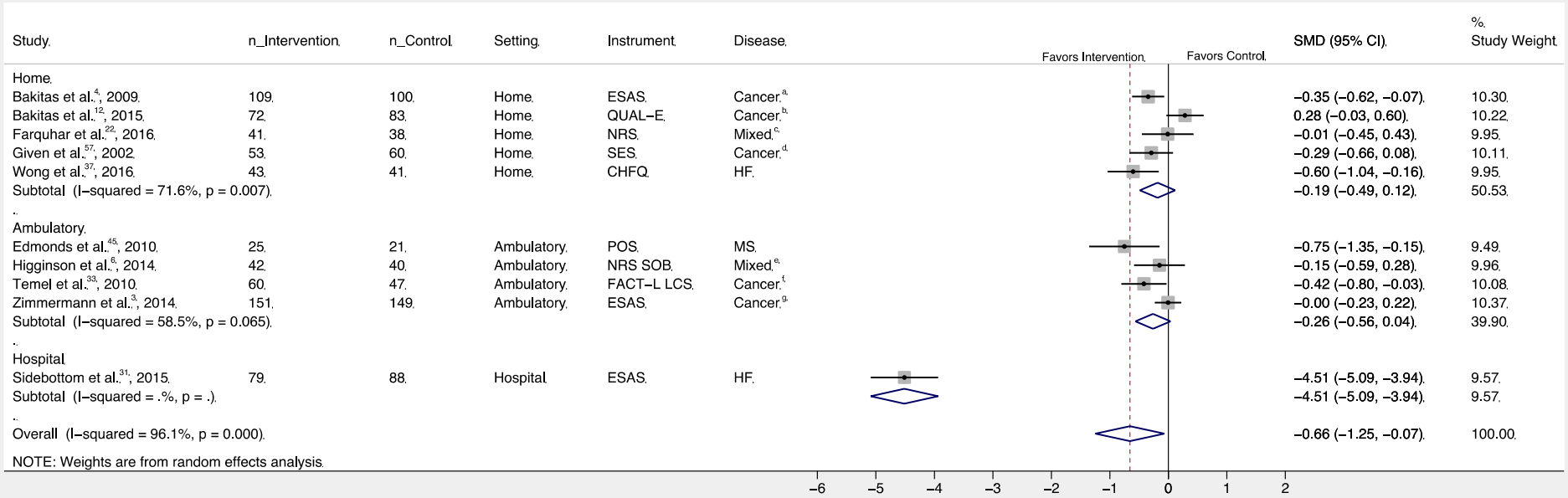
Note: Cancer: P-value for pooled SMD=0.26, Tau^2=0.05, Q=12.96; Non-cancer: P-value for pooled SMD=0.12, Tau^2=4.59, Q=125.21; Mixed: P-value for pooled SMD=0.60, Tau^2<0.0001, Q=0.20. Sample sizes in the figure are the number of patients analyzed corresponding to the studies at the specific time points.

Disease status: a: gastrointestinal, lung, genitourinary, and breast cancers. b: solid or hematological cancer. c: breast, colon, lung, and gynecological cancers, and lymphoma. d: non-small cell lung cancer. e: lung, gastrointestinal, genitourinary, breast, and gynecological cancers. f: COPD or other source of dyspnea. g: cancer, COPD, HF, ILD, ALS.

Legend: Dots within shaded squares indicate SMDs from trials, with horizontal lines indicating 95% CI (confidence interval). The size of the shaded squares indicates the study weight. Diamonds represent pooled SMDs and 95% CIs. The vertical dashed line indicates the pooled effect estimate, and the solid vertical line depicts a null effect (i.e., SMD=0).

Abbreviations: SMD, standardized mean difference. SES, Symptom Experience Scale. POS, Palliative Outcomes Scale. FACT-L LCS, Functional Assessment of Cancer Therapy-Lung Lung Cancer Scale. NRS SOB, Numerical Rating Scale Shortness of Breath. ESAS, Edmonton Symptom Assessment Scale. QUAL-E, Quality of Life at the End of Life. CHFQ, Chronic Heart Failure Questionnaire. MS, multiple sclerosis. HF, heart failure . COPD, chronic obstructive pulmonary disease. ILD, interstitial lung disease. ALS, amyotrophic lateral sclerosis.

eFigure 8. Association of Palliative Care and Patient Symptom Burden at 1-3 Month Follow-up Stratified by Setting



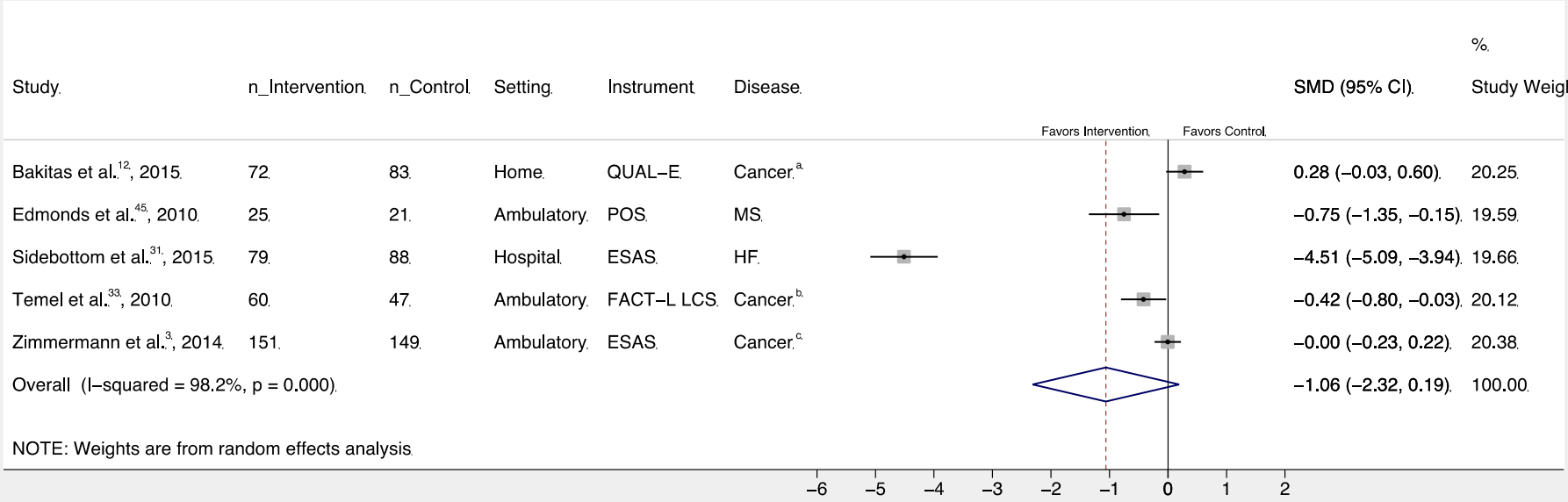
Note: Ambulatory: P-value for pooled SMD=0.09, Tau^2=0.05, Q=7.23; Hospital: P-value for pooled SMD<0.0001, Tau^2<0.0001, Q<0.0001; Home: P-value for pooled SMD=0.23, Tau^2=0.08, Q=14.09. Sample sizes in the figure are the number of patients analyzed corresponding to the studies at the specific time points.

Disease status: a: gastrointestinal, lung, genitourinary, and breast cancers. b: solid or hematological cancer. c: COPD or other source of dyspnea. d: breast, colon, lung, and gynecological cancers, and lymphoma. e: cancer, COPD, HF, ILD, ALS. f: non-small cell lung cancer. g: lung, gastrointestinal, genitourinary, breast, and gynecological cancers.

Legend: Dots within shaded squares indicate SMDs from trials, with horizontal lines indicating 95% CI (confidence interval). The size of the shaded squares indicates the study weight. Diamonds represent pooled SMDs and 95% CIs. The vertical dashed line indicates the pooled effect estimate, and the solid vertical line depicts a null effect (i.e., SMD=0).

Abbreviations: SMD, standardized mean difference. SES, Symptom Experience Scale. POS, Palliative Outcomes Scale. FACT-L LCS, Functional Assessment of Cancer Therapy-Lung Lung Cancer Scale. NRS SOB, Numerical Rating Scale Shortness of Breath. ESAS, Edmonton Symptom Assessment Scale. QUAL-E, Quality of Life at the End of Life. CHFQ, Chronic Heart Failure Questionnaire. MS, multiple sclerosis. HF, heart failure . COPD, chronic obstructive pulmonary disease. ILD, interstitial lung disease. ALS, amyotrophic lateral sclerosis.

eFigure 9. Sensitivity Analysis of the Association between Palliative Care and Patient Symptom Burden at a Discrete Timepoint (3 months)



Note: P-value for pooled SMD=0.10, Tau^2=2.00, Q=226.41. Sample sizes in the figure are the number of patients analyzed corresponding to the studies at the specific time points.

Disease status: a: solid or hematological cancer. b: non-small cell lung cancer. c: lung, gastrointestinal, genitourinary, breast, and gynecological cancer.

Legend: Dots within shaded squares indicate SMDs from trials, with horizontal lines indicating 95% CI (confidence interval). The size of the shaded squares indicates the study weight. Diamonds represent pooled SMDs and 95% CIs. The vertical dashed line indicates the pooled effect estimate, and the solid vertical line depicts a null effect (i.e., SMD=0).

Abbreviations: SMD, standardized mean difference. POS, Palliative Outcomes Scale. FACT-L LCS, Functional Assessment of Cancer Therapy-Lung Lung Cancer Scale. ESAS, Edmonton Symptom Assessment Scale. QUAL-E, Quality of Life at the End of Life. MS, multiple sclerosis. HF, heart failure

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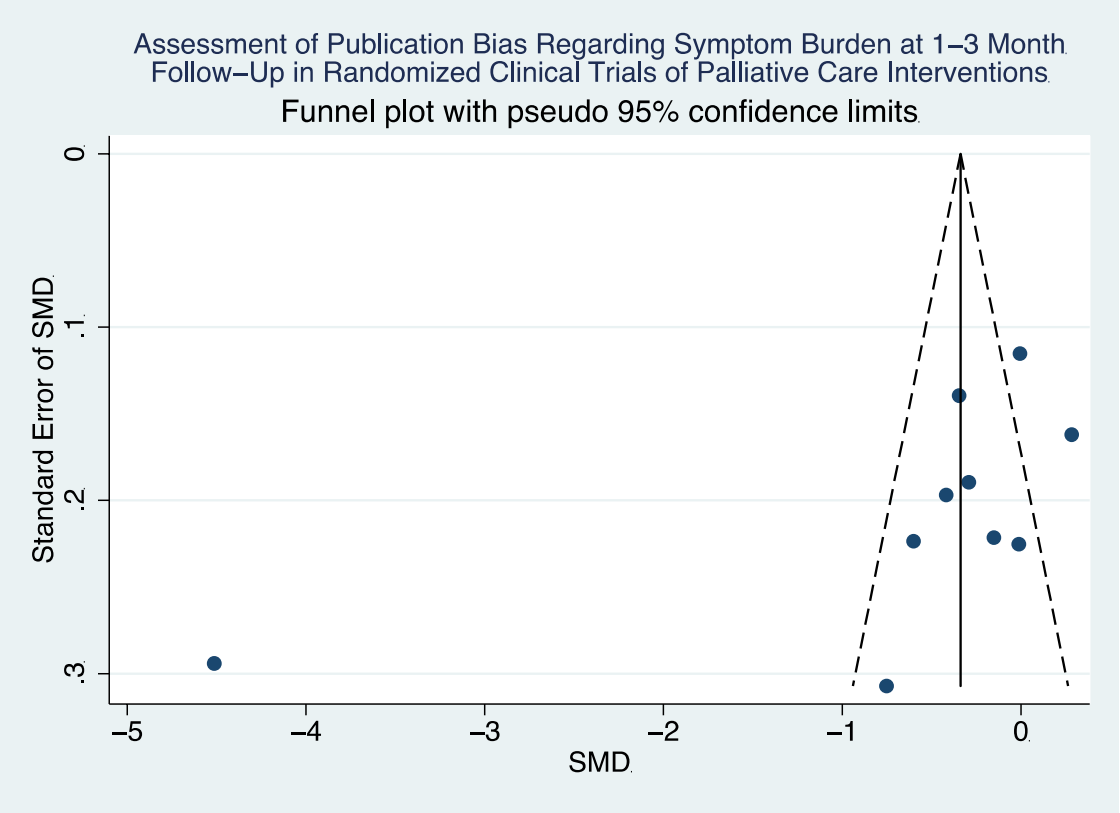
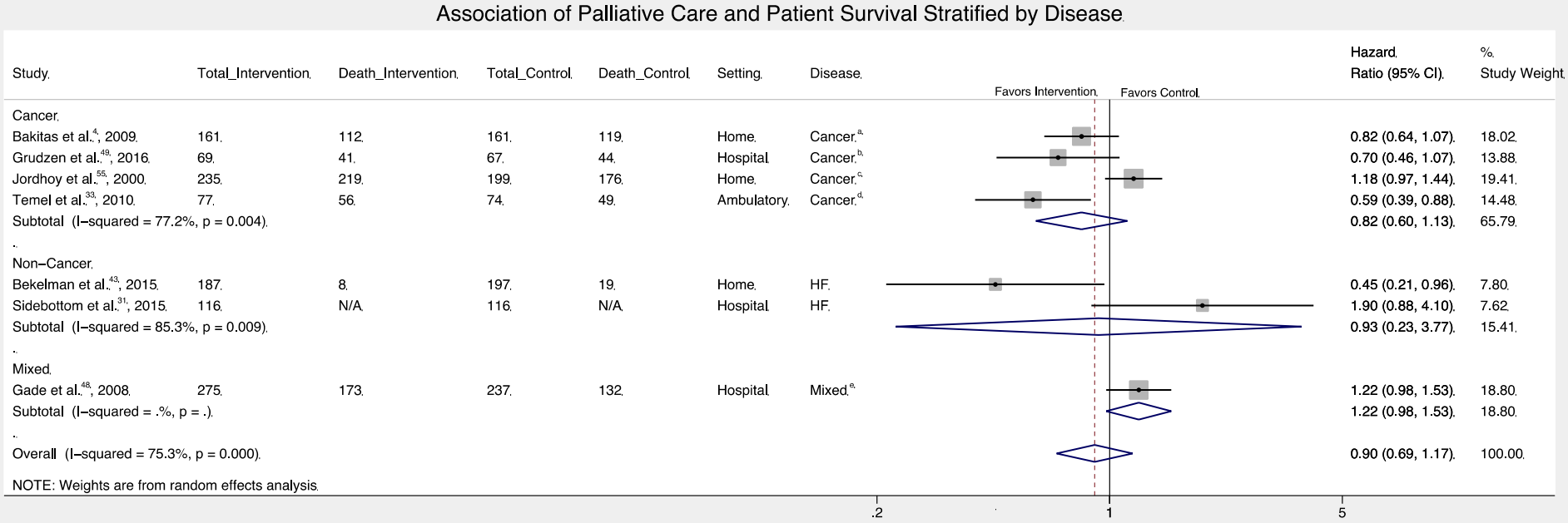
eFigure 10. Assessment of Publication Bias Regarding Symptom Burden at 1-3 Month Follow-Up in Randomized Clinical Trials of Palliative Care Interventions



Note: Egger's test bias estimate (SE): -9.33 (4.81), P=0.09.
Legend: Dotted lines indicate pseudo 95% confidence intervals around the overall summary estimate.
Abbreviation: SMD, standardized mean difference.

eFigure 11. Association of Palliative Care and Patient Survival Stratified by Disease



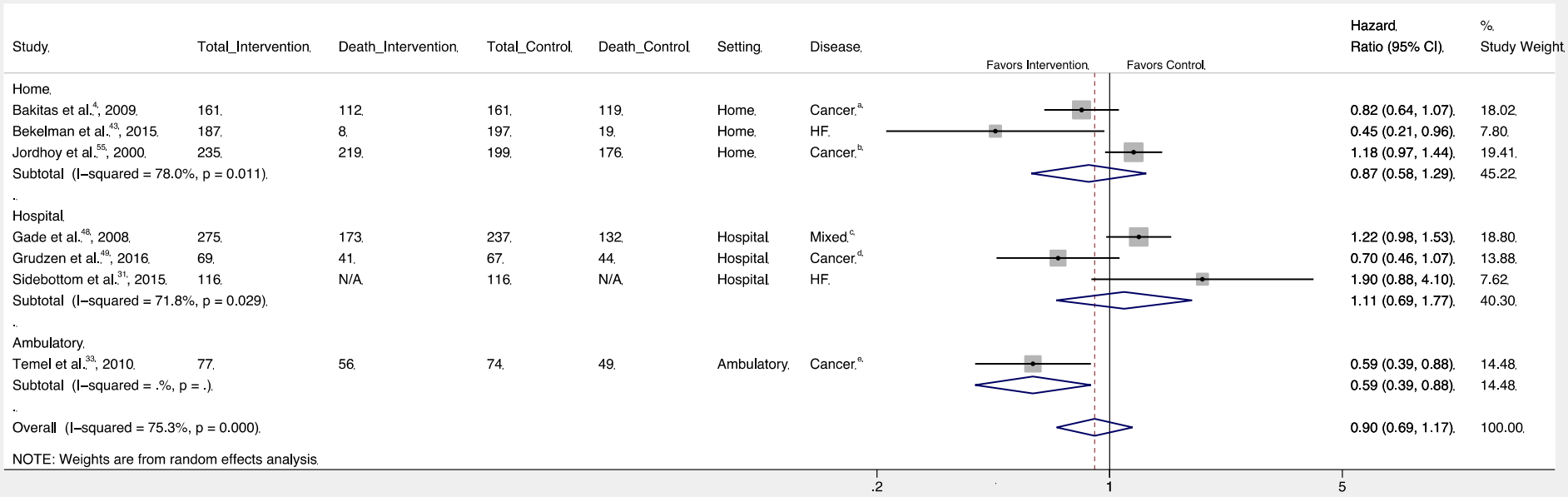
Note: Cancer: P-value for pooled HR=0.23, Tau^2=0.08, Q=13.18; Non-cancer: P-value for pooled HR=0.92, Tau^2=0.88, Q=6.80; Mixed: P-value for pooled HR=0.08, Tau^2=<0.0001, Q<0.0001.

Disease status: a: gastrointestinal, lung, genitourinary, and breast cancers. b: breast, colon, lung, and other cancers. c: GI, lung, breast, gynecological., genitourinary, kidney, lymph., skin, and other cancers. d: non-small cell lung cancers. e: cancer, HF, COPD, ESRD, stroke, dementia.

Legend: Data dots within shaded squares indicate HRs from trials, with horizontal lines indicating 95% CI (confidence interval). The size of the shaded squares indicates the study weight. Diamonds represent pooled HRs and 95% CIs. The vertical dashed line indicates the pooled effect estimate, and the solid vertical line depicts a null effect (i.e., HR=1).

Abbreviations: HF, heart failure. N/A, not applicable. COPD, chronic obstructive pulmonary disease. ESRD, end stage renal disease.

eFigure 12. Association of Palliative Care and Patient Survival Stratified by Setting



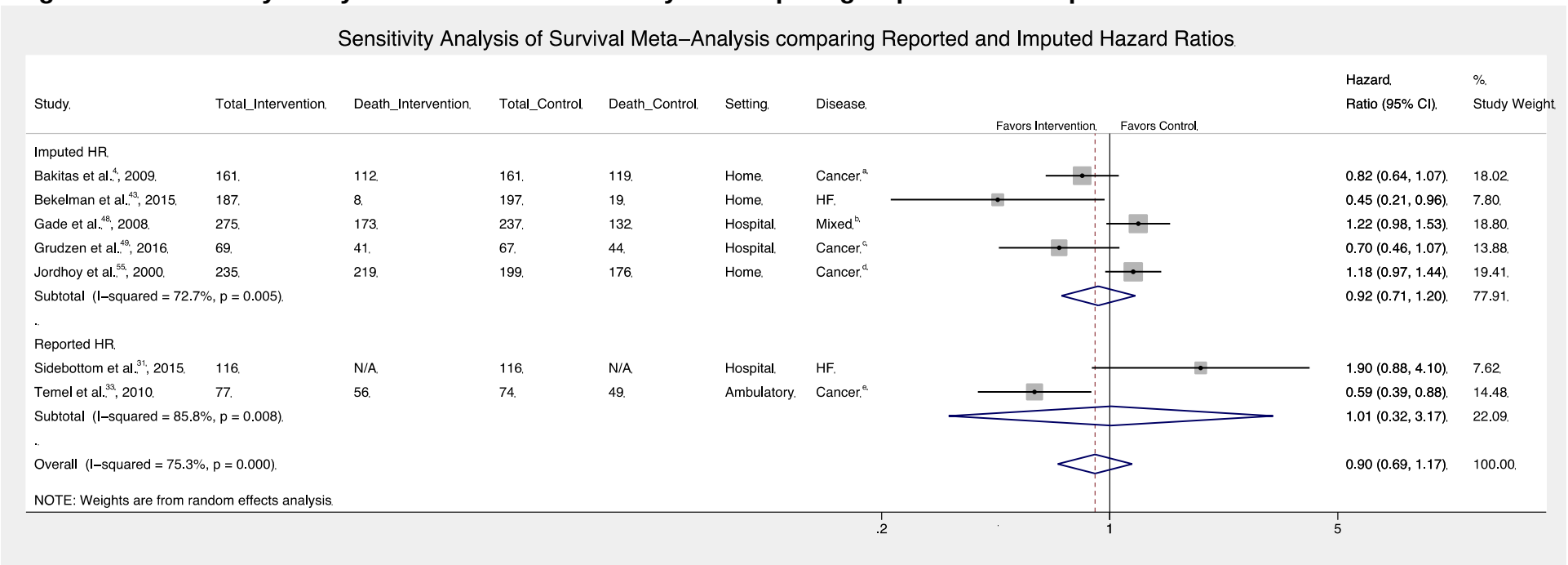
Note: Ambulatory: P-value for pooled HR=0.01, Tau^2<0.0001, Q<0.0001; Hospital: P-value for pooled HR=0.68, Tau^2=0.12, Q=7.10; Home: P-value for pooled HR=0.48, Tau^2=0.09, Q=9.10.

Disease status: a: gastrointestinal, lung, genitourinary, and breast cancers. b: gastrointestinal, lung, breast, gynecological, genitourinary, kidney, lymph., skin, and other cancers. c: cancer, HF, COPD, ESRD, stroke, dementia. d: breast, colon, lung, and other cancers. e: non-small cell lung cancer.

Legend: Data dots within shaded squares indicate HRs from trials, with horizontal lines indicating 95% CI (confidence interval). The size of the shaded squares indicates the study weight. Diamonds represent pooled HRs and 95% CIs. The vertical dashed line indicates the pooled effect estimate, and the solid vertical line depicts a null effect (i.e., HR=1).

Abbreviations: HF, heart failure. N/A, not applicable. COPD, chronic obstructive pulmonary disease. ESRD, end stage renal disease..

eFigure 13. Sensitivity Analysis of Survival Meta-Analysis comparing Reported and Imputed Hazard Ratios



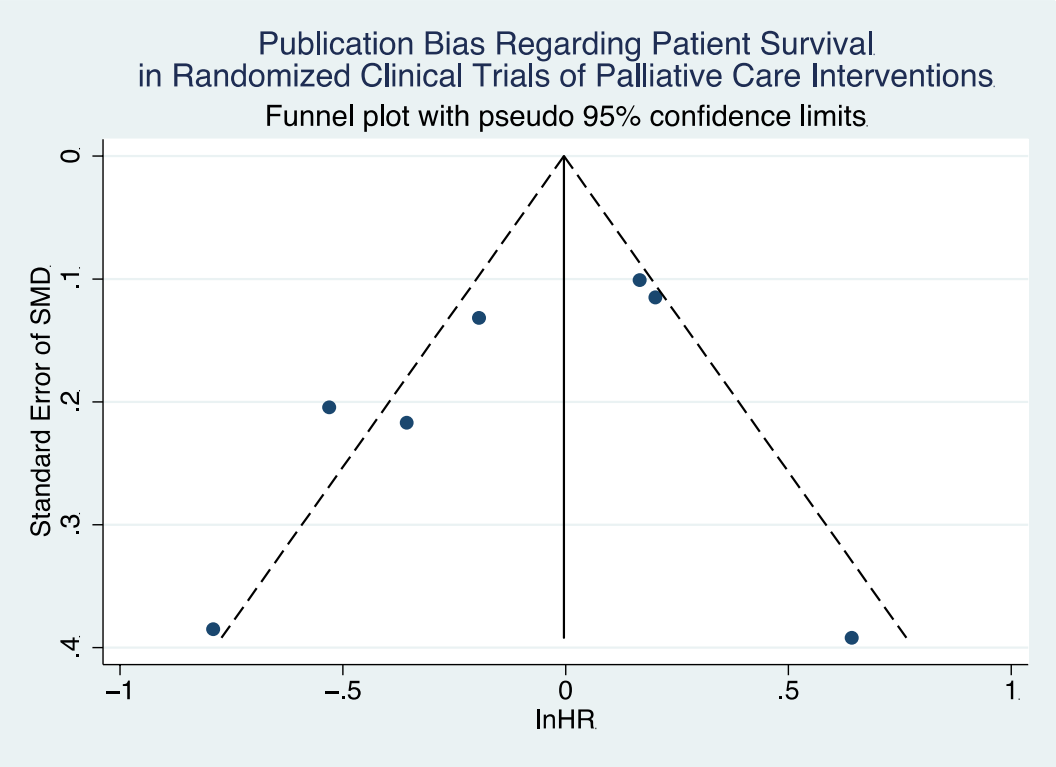
Note: Imputed HR: P-value for pooled HR=0.55, Tau^2=0.06, Q=14.66; Reported HR: P-value for pooled HR=0.99, Tau^2=0.59, Q=7.03.

Disease status: a: gastrointestinal, lung, genitourinary, and breast cancers. b: cancer, HF, COPD, ESRD, stroke, dementia. c: breast, colon, lung, and other cancers. d: gastrointestinal, lung, breast, gynecological, genitourinary, kidney, lymph., skin, and other cancers. e: non-small cell lung cancer.

Legend: Data dots within shaded squares indicate HRs from trials, with horizontal lines indicating 95% CI (confidence interval). The size of the shaded squares indicates the study weight. Diamonds represent pooled HRs and 95% CIs. The vertical dashed line indicates the pooled effect estimate, and the solid vertical line depicts a null effect (i.e., HR=1).

Abbreviation: HF, heart failure. N/A, not applicable. COPD, chronic obstructive pulmonary disease. ESRD, end stage renal disease.

eFigure 14. Publication Bias Regarding Patient Survival in Randomized Clinical Trials of Palliative Care Interventions



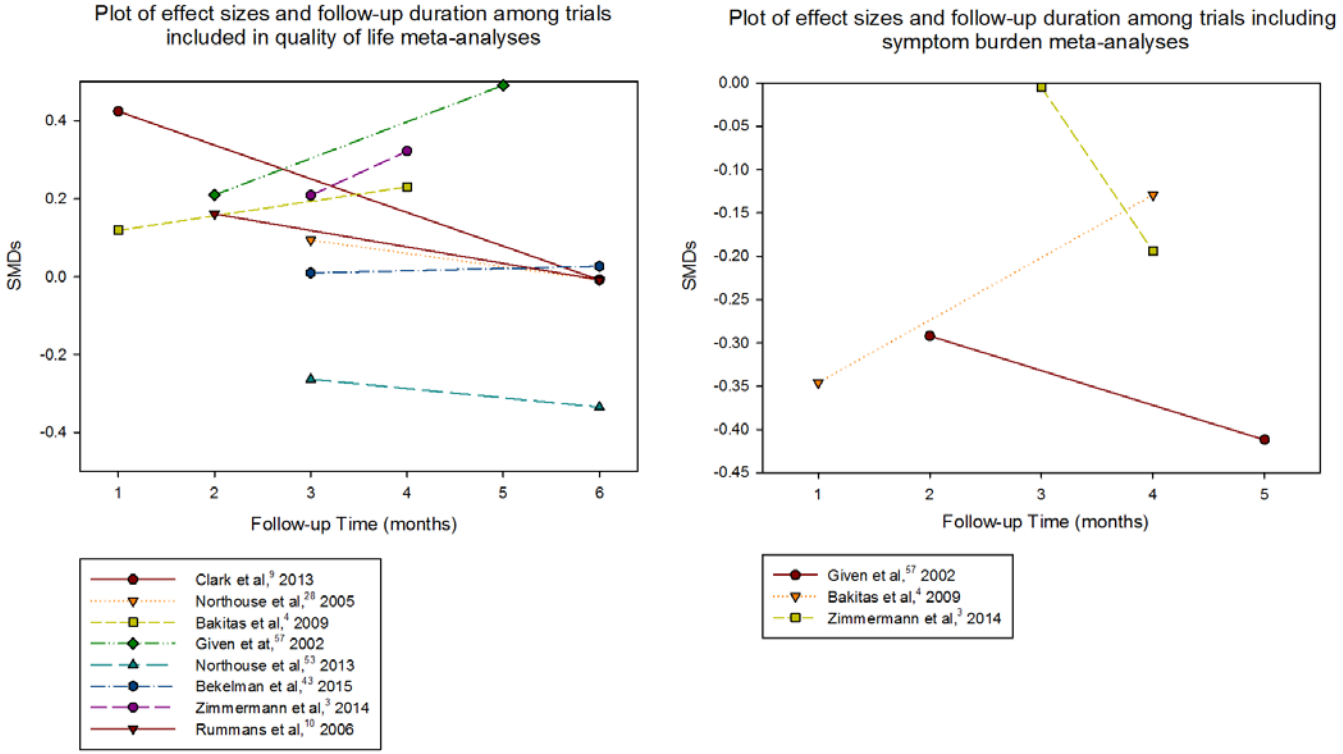
Note: Egger's test bias estimate (SE), -2.07 (1.75), P=0.29.
Legend: Dotted lines indicate pseudo 95% confidence intervals around the overall summary estimate.
Abbreviation: lnHR, natural log of hazard ratio.

eTable 8. Results of Univariable Meta-Regression Analysis to Identify Associations between Effect Size and Year of Publication and Intervention Intensity

	Coefficient	95% CI	P-value
Quality of life at 1-3 month follow-up			
Year of publication	0.053	(-0.127, 0.232)	0.538
Intervention intensity (reference: high)	-0.837	(-2.347, 0.674)	0.253
Symptom burden at 1-3 month follow-up			
Year of publication	-0.047	(-0.297, 0.203)	0.676
Intervention intensity (reference: high)	0.740	(-1.490, 2.969)	0.466
Survival			
Year of publication	-0.029	(-0.105, 0.048)	0.385
Intervention intensity (reference: high)	-0.079	(-1.121, 0.964)	0.854

Note: Coefficients for the meta-regressions related to year of publication indicate the difference in the standardized mean difference with every additional year. Coefficients for the meta-regressions related to intervention intensity indicate the difference in the standardized mean difference that studies with low intensity have relative to studies with high intervention intensity. Intervention intensity was dichotomized as “high” if an intervention comprised 6 or more domains of palliative care, whereas interventions comprising 5 or fewer domains were classified as “low” intensity. None of the tests presented are statistically significant (P>0.05); therefore, there is no evidence of association between year of publication and effect size, or between intervention intensity and effect size. CI, confidence interval.

eFigure 15. Plots of Effect Sizes and Follow-up Duration among Trials included in Quality of Life and Symptom Burden Meta-Analyses



Abbreviations: SMD, standardized mean difference. QoL, quality of life. Legend: Curves were calculated by plotting a line between the standardized mean differences of each trial at each of the two timepoints included. A SMD in the QoL meta-analyses >0 indicates better QoL associated with palliative care as compared to usual care, whereas a SMD<0 in the symptom burden meta-analyses indicates reduced symptom burden associated with palliative care as opposed to usual care.

Study	Timepoint (months), SMD	Timepoint (months), SMD
Quality of Life		
Bakitas et al, 2009[4]	1, 0.119	4, 0.231
Bekelman et al, 2015[43]	3, 0.01	6, 0.027
Clark et al, 2013[18]	1, 0.424	6, -0.008
Given et al, 2002[57]	2, 0.21	5, 0.094
Northouse et al, 2005[28]	3, 0.094	6, -0.008
Northouse et al, 2013[53]	3, -0.263	6, -0.335
Rummans et al, 2006[10]	2, 0.161	6, 0
Zimmermann et al, 2014[3]	3, 0.209	4, 0.322
Symptom Burden		
Bakitas et al, 2009[4]	1, -0.346	4, -0.129
Given et al, 2002[57]	2, -0.292	5, -0.412
Zimmermann et al, 2014[3]	3, -0.005	4, -0.194

eTable 9. Reasons for Trial Exclusion from Meta-Analysis

Trial	Reason for exclusion
Quality of Life	
Aiken et al, 2006[11]	Study reported linear trajectory analysis. Unable to extract standard deviations from data provided.
Dyar et al, 2012[19]	Follow-up time point not specified.
Farquhar et al, 2014[21]	Control group is a delayed intervention (by two weeks), and is therefore not comparable to the other included trials.
Jordhoy et al, 2001[54]	Standard deviations not reported.
Rabow et al, 2004[41]	Standard deviations not reported.
Radwany et al, 2014[30]	It is unclear how the mean difference (Table 3) is calculated.
Symptom Burden	
Aiken et al, 2006[11]	Study reported linear trajectory analysis. Unable to extract standard deviations from data provided.
Brannstrom et al, 2014[14]	Specific estimates not reported in paper.
Jordhoy et al, 2001[54]	Standard deviations not reported.
Kane et al, 1984[51]	Trial reports results as either statistically significant or not. No specific measurements included.
Gade et al, 2008[48]	Endpoint of symptom burden measure is at time of hospital discharge which varies by patient.
Rabow et al, 2004[41]	Unable to reverse-calculate standard deviation, as ANCOVA model also included other covariates.
Radwany et al, 2014[30]	It is unclear how the mean difference (Table 3) is calculated.
Rummans et al, 2006[10]	It is unclear how mean differences were calculated.
Wallen et al, 2012[36]	Unable to reverse-calculate standard deviation.
SUPPORT, 1995[56]	Timespan for outcome measure encompasses a two-year period; time point not comparable with other trials in this review.
Survival	
Ahronheim et al, 2000[42]	Reported deaths during hospitalizations and P-value using chi-square test. Chi-square test is only testing for difference in proportion of mortality and it's not the same as testing overall survival difference using log-rank or cox regression model.
Brannstrom et al, 2014[14]	Only reported a p-value regarding differences in survival. Did not specify the type of statistical test used.
Engelhardt et al, 2006[20]	Only survival rates at 18-month time point were reported. The log-rank test for time to completion was reported. This is not the same as overall survival.
Higginson et al, 2014[6]	Reports generalized Wilcoxon test, which is not comparable with other trials included in meta-analysis (which used log-rank tests).
Hughes et al, 1992[26]	Does mention survival days in each group, but unclear whether these estimates are mean or median. Paper doesn't mention the type of statistical method used to obtain these estimates.
SUPPORT, 1995[56]	Survival was included as a safety endpoint, not as an outcome of interest.
Wallen et al, 2012[36]	Hazard ratio reported is not for overall survival.
Zimmer et al, 1984[39]	Unable to convert results of log-likelihood ratio test to hazard ratios.

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