

Supplemental Online Content

Quinn KL, Shurrab M, Gitau K, et al. Association of receipt of palliative care interventions with health care use, quality of life, and symptom burden among adults with chronic noncancer illness: a systematic review and meta-analysis. *JAMA*. Published October 13, 2020.
doi:10.1001/jama.2020.14205

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

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Supplementary Online Content

2 **Association of Receipt of Palliative Care Interventions with Healthcare Use, Quality of Life, and Symptom Burden 3 Among Adults with Chronic Noncancer Illness**

4 *A Systematic Review and Meta-analysis*

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39 **eText 1 - Methodological Details Regarding Search Strategy**

40 Medline Search Strategy

- 42 1. palliative care/ or terminal care/ or hospice care/
- 43 2. (palliative or hospice* or (terminal adj3 care)).ti,ab,kf.
- 44 3. "Hospice and Palliative Care Nursing"/
- 45 4. Hospices/
- 46 5. Palliative Medicine/
- 47 6. ((End of life or End-of-life) adj3 care).ti,ab,kf.
- 48 7. 1-6/OR
- 49 8. attitude to death/ or attitude to health/ or health services misuse/ or medical overuse/ or unnecessary procedures/ or "patient acceptance of health care"/
50 or patient compliance/ or patient dropouts/ or patient participation/ or patient satisfaction/ or patient preference/ or treatment refusal/
- 51 9. Health Services/ut [Utilization]
- 52 10. hospitalization/ or "length of stay"/ or patient admission/ or patient discharge/ or patient readmission/
- 53 11. Life Support Care/ut [Utilization]
- 54 12. Hospital Costs/
- 55 13. Diagnostic Tests, Routine/ut [Utilization]
- 56 14. "Diagnostic Techniques and Procedures"/ut [Utilization]
- 57 15. Quality Indicators, Health Care/
- 58 16. "Quality of Life"/
- 59 17. "costs and cost analysis"/ or health care costs/ or hospital costs/
- 60 18. sickness impact profile/
- 61 19. depression/ or stress, psychological/
- 62 20. Anxiety/
- 63 21. treatment outcome/
- 64 22. patient satisfaction/ or patient preference/
- 65 23. spirituality/
- 66 24. FACIT-Pal.ti,ab,kf.
- 67 25. functional assessment of chronic illness therapy palliative.ti,ab,kf.
- 68 26. (SF36 or SF-36 or short form 36).ti,ab,kf.
- 69 27. Kansas City Cardiomyopathy Questionnaire.ti,ab,kf.
- 70 28. KCCQ.ti,ab,kf.
- 71 29. Minnesota living with heart failure questionnaire.ti,ab,kf. Or MLHFQ.ti,ab,kf.
- 72 30. St Georges respiratory questionnaire.ti,ab,kf. Or SGRQ-C.ti,ab,kf.
- 73 31. COPD Assessment Test.ti,ab,kf.
- 74 32. quality of life in alzheimer's disease.ti,ab,kf.
- 75 33. QOL-AD.ti,ab,kf.

- 76 34. CHOICE health experience.ti,ab,kf.
77 35. Choices for healthy outcomes in caring.ti,ab,kf.
78 36. (Kidney disease quality of life* or KDQOL).ti,ab,kf.
79 37. parfrey test.ti,ab,kf.
80 38. (chronic liver disease questionnaire or CLDQ).ti,ab,kf.
81 39. (short form liver disease quality of life or SF-LDQOL).ti,ab,kf.
82 40. (Liver disease symptom index or LDSI).ti,ab,kf.
83 41. (Stroke specific quality of life scale or SSQoL).ti,ab,kf.
84 42. (stroke impact scale or SIS).ti,ab,kf.
85 43. (Stroke adapted sickness impact profile or SASIP).ti,ab,kf.
86 44. patient care planning/ or advance care planning/ or advance directives/ or living wills/
87 45. (goal* adj3 care).ti,ab,kf.
88 46. (care adj3 plan*).ti,ab,kf.
89 47. (advance* adj3 plan*).ti,ab,kf.
90 48. advance* directive*.ti,ab,kf.
91 49. power of attorney.ti,ab,kf.
92 50. (living will or living wills).ti,ab,kf.
93 51. place of death.ti,ab,kf.
94 52. home death.ti,ab,kf.
95 53. end of life care.ti,ab,kf.
96 54. resource allocation/ or health care rationing/
97 55. (resource* adj3 (allocat* or efficien*)).ti,ab,kf.
98 56. (healthcare adj3 ration*).ti,ab,kf. or (health care adj3 ration*).ti,ab,kf.
99 57. exp Death/
100 58. home death.ti,ab,kf.
101 59. non-hospital death.ti,ab,kf.
102 60. (location adj3 death).ti,ab,kf.
103 61. (attitude* adj3 (death* or health*)).ti,ab,kf.
104 62. (utiliz* adj3 (healthcare or health care or health service* or life support or test or tests or procedure*)).ti,ab,kf.
105 63. (Cost* adj3 (hospital or healthcare or health care or test or tests or procedure*)).ti,ab,kf.
106 64. (accept* adj3 death).ti,ab,kf.
107 65. ((treatment or patient*) adj3 (adherence or compliance or cooperation)).ti,ab,kf.
108 66. (length of stay or patient admission or patient readmission).ti,ab,kf.
109 67. quality of life.ti,ab,kf.
110 68. (depress* or stress*).ti,ab,kf.
111 69. anxiety.ti,ab,kf.
112 70. (treatment outcome* or patient satisfaction or patient preference*).ti,ab,kf.

- 113 71. (cost* adj3 (hospital or healthcare or health care or test or tests or procedure*)).ti,ab,kf.
114 72. 8-71/OR
115 73. heart failure/ or heart failure, diastolic/ or heart failure, systolic/ or pulmonary disease, chronic obstructive/ or bronchitis, chronic/ or pulmonary
116 emphysema/ or kidney failure, chronic/ or frasier syndrome/ or End Stage Liver Disease/
117 74. ((cardiac or heart or myocardial) adj3 (insufficiency or failure)).ti,ab,kf.
118 75. (liver failure* adj3 chronic).ti,ab,kf.
119 76. (liver disease* adj3 end).ti,ab,kf.
120 77. cirrhosis.ti,ab,kf.
121 78. exp Dementia/
122 79. stroke/ or brain infarction/ or brain stem infarctions/
123 80. ((non cancer* or non-cancer* or noncancer*) adj3 (disease* or diagnosis or patient*)).ti,ab,kf.
124 81. (dementia* or amentia* or alzheimer*).ti,ab,kf.
125 82. Tauopathies/
126 83. tauopath*.ti,ab,kf.
127 84. cerebrovascular accident.ti,ab,kf.
128 85. stroke*.ti,ab,kf.
129 86. ((brain or cerebellum) adj3 infarction*).ti,ab,kf.
130 87. ((end-stage or end stage) adj3 (kidney or renal)).ti,ab,kf.
131 88. (chronic adj3 (kidney or renal) adj3 failure).ti,ab,kf.
132 89. (chronic adj3 airflow obstruct*).ti,ab,kf.
133 90. copd.ti,ab,kf.
134 91. ((cardiac or heart or myocardial) adj3 (failure* or insufficiency)).ti,ab,kf.
135 92. (chronic obstruc*.adj3 disease).ti,ab,kf.
136 93. (heart edema or diastolic dysfunction or systolic dysfunction).ti,ab,kf.
137 94. ((Cardiac or heart) adj2 (edema or oedema)).ti,ab,kf.
138 95. Lewy body disease.ti,ab,kf.
139 96. Senility.ti,ab,kf.
140 97. Mental deteriorat*.ti,ab,kf.
141 98. Frasier syndrome.ti,ab,kf.
142 99. (Heart edema or Diastolic dysfunction or Systolic dysfunction).ti,ab,kf.
143 100. Dialysis/
144 101. Hemodialysis/
145 Renal Dialysis/ or Hemodiafiltration/ or Hemodialysis, Home/ or Peritoneal Dialysis/ or Peritoneal Dialysis, Continuous Ambulatory/
146 102. (Dialysis or hemodialysis or hemodiafiltration).ti,ab,kf.
147 103.73-103/OR
148 104.7 AND 72 AND 104
149

150 Limits
151 NOT (adolescent/ or child/ or child, preschool/ or infant/ or exp infant, newborn/) not exp Adult/
152 NOT exp animal/ not human/
153 English only
154 No books, book chapters or dissertations
155
156
157

158 **eText 2. Methodological Details Regarding Risk of Bias Assessment**

159 All studies were assessed for their risk of bias using the Cochrane Collaboration's Risk of Bias tool version 2. This tool contains five domains: risk
160 of bias arising from the randomization process; due to deviations from the intended interventions; due to missing outcome data; from
161 measurement of the outcome; or in selection of the reported result. Judgement about the overall risk of bias arising from the five domains was
162 made using the published algorithm based on answers to the signalling questions within the tool. Within each domain, the risk of bias was
163 assessed by two independent reviewers. Judgements could be 'Low', 'High' or 'Some Concerns' risk of bias.

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165 Because our study included both objective (e.g. hospitalizations, emergency department visits) and subjective (e.g. patient-reported quality of life
166 and symptom measures) outcomes, we assessed each separately with respect to their risk of bias. We reported two summary risks of bias for
167 each trial. When assessing the risk of bias for subjective outcomes, we made the following modifications based on recommendations from the
168 Cochrane Collaboration because it is impractical to blind study participants to a complex behavioral intervention such as palliative care:

- 169 1. For domain 1, allocation sequences were only considered concealed if a statement was explicitly made regarding concealment or if a
170 computer-generated sequence was used for randomization.
- 171 2. For domain 2, we omitted item 2.3 ("Were *important co-interventions balanced across intervention groups?*") from the final judgement
172 decisions because all studies were subject to the risk of unintended co-interventions regardless of whether they were reported or not.
- 173 3. For domain 4, items 4.3 ("Were *outcome assessors aware of the intervention received by study participants ?*"), 4.4 ("Could *assessment of the outcome have been influenced by knowledge of intervention received?*") and 4.5 ("Is it likely that *assessment of the outcome was influenced by knowledge of intervention received?*") were omitted from final risk of bias judgements for all subjective outcomes as all
174 studies were judged 'High' risk for this domain.

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180 **eText 3. Translation of Standardized Mean Differences to Clinical Values**

181 For measures of both general and disease-specific quality of life (QOL), we translated the standardized mean difference (SMD) to the Functional
182 Assessment of Chronic Illness Therapy – Palliative (FACIT-Pal) scale - a validated patient-reported measure of QOL in people with serious
183 illness.¹ We used the standard deviation (SD) from a randomized control trial of patients with advanced heart failure (n=150).² For measures of
184 symptom burden, we translated the SMD to the Edmonton Symptom Assessment Scale (ESAS) – a validated patient-reported measure that is
185 commonly used in palliative populations.³ We used the standard deviation (SD) from a multicenter randomized control trial of patients with
186 advanced heart failure (n=84).⁴ We intentionally used trials of patients with HF that measured the FACIT-Pal and ESAS because 40% of the trials
187 in this systematic review were in patients with HF.

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193 **eTable 1 – Study Inclusion and Exclusion Criteria**

Inclusion Criteria	Exclusion Criteria
<ul style="list-style-type: none"> • Sample: <ul style="list-style-type: none"> ○ Adults \geq18 years ○ Main diagnosis of heart failure, chronic obstructive pulmonary disease, end-stage renal disease, cirrhosis, dementia or stroke • Intervention <ul style="list-style-type: none"> ○ Described as palliative care or contain \geq2 domains of palliative care as defined by the 2018 National Consensus Project on Clinical Practice Guidelines for Quality Palliative Care⁵ • Comparator: <ul style="list-style-type: none"> ○ Usual care, social calls, educational materials, ad hoc palliative care • Outcomes: <ul style="list-style-type: none"> ○ Healthcare use (hospitalizations and emergency department visits), general and disease-specific quality of life, symptom burden • Study Design: <ul style="list-style-type: none"> ○ Randomized clinical trials 	<ul style="list-style-type: none"> • Sample: <ul style="list-style-type: none"> ○ Individuals $<$18 years old ○ Co-morbid cancer in \geq50% of enrolled patients • Intervention: <ul style="list-style-type: none"> ○ Palliative care consultation for withdrawal of life-sustaining therapies in the ICU ○ Caregiver is the exclusive or primary target of intervention • Study Design: <ul style="list-style-type: none"> ○ Non-randomized studies

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196 **eTable 2. Trial Characteristics and Outcomes of 7 Palliative Care Interventions at Low Risk of Bias in Subjective
197 and Objective Outcomes.**

Study (Country)	Design	Patient Population	Died During Study (%)	Palliative Care Domains Addressed	Intervention			Control		Risk of Bias	
					Description	n	Presence of Palliative Care Physician	Description	n	Subjective Outcomes	Objective Outcomes
Janssens et al, 2019 (Switzerland) ⁶	Parallel	COPD, stage III or IV and/or treatment with either home oxygen or home mechanical ventilation and/or ≥ 1 hospital admissions in the previous year for an acute exacerbation	16.3	Structure and Process; Physical; Psychological; Social; Spiritual; Ethical and Legal	Home visits by nurses focused on coordination of care, symptoms, nutrition, social and spiritual needs, illness understanding and ACP, and caregiver support. All cases discussed with a palliative care physician.	26	Yes	Usual Care	23	Low	N/A
Possin et al, 2019 (USA) ⁷	Parallel	Dementia	12.2	Structure and Process; Physical; Psychological; Social; Ethical and Legal	The Care Ecosystem: telephone- and internet-based supportive care (education, symptoms, legal and financial, safety concerns) delivered by care team navigators and APN, SW, and pharmacist. Monthly telephone calls for 12 months.	512	No	Usual Care	268	Low	Low

Study (Country)	Design	Patient Population	Died During Study (%)	Palliative Care Domains Addressed	Intervention			Control		Risk of Bias	
					Description	n	Presence of Palliative Care Physician	Description	n	Subjective Outcomes	Objective Outcomes
Wong et al, 2016 (Hong Kong) ⁴	Parallel	HF with ≥2 of: NYHA class III or IV; ≤ 1-year estimated life expectancy, ≥3 HF-related hospitalizations within 1 year; physical or psychological symptoms despite optimal tolerated therapy	NR	Structure and Process; Physical; Psychological; Social; Spiritual; Care of the Imminently Dying; Ethical and Legal	Transitional care: RN-led case manager, volunteers conducted weekly visits and phone calls for 4 weeks then monthly for 12 weeks. Supported by palliative care MD.	43	Yes	Usual Care: Palliative care clinic consultation, discharge advice on symptom management and medication. Two social placebo calls; ad hoc home- visits.	41	Low	Low
Bekelman et al, 2015 (USA) ⁸	Parallel	HF with KCCQ<60	6.9	Structure and Process; Physical; Psychological; Social;	PCDM: RN, primary care MD, cardiologist, psychiatrist; collaborative care HF disease management, screening for and treatment of depression, and daily telemonitoring with patient self- care support.	187	No	Usual Care ± telemonitoring	197	Low	Low

					Intervention			Control		Risk of Bias	
Study (Country)	Design	Patient Population	Died During Study (%)	Palliative Care Domains Addressed	Description	n	Presence of Palliative Care Physician	Description	n	Subjective Outcomes	Objective Outcomes
Higginson et al, 2014 (UK) ⁹	Parallel	Mixed: cancer (20%), COPD (54%), HF (5%), interstitial lung disease (18%), and other (3%). and MRC dyspnea scale ≥2	3.8	Structure and Process; Physical; Psychological; Social; Spiritual	Breathlessness Support Service: interprofessional service, respiratory MD, palliative care MD, PT and OT. Two clinic visits and home assessment.	53	Yes	Usual Care	52	Low	Low
Au et al, 2012 (USA) ¹⁰	Cluster, Parallel	COPD: COPD as defined by the GOLD criteria and identify primary COPD MD	NR	Social, Ethical	One-page feedback form addressing goals of care, communication and dying preferences distributed to MDs to increase the self-efficacy of clinicians and patients for discussing end- of-life care.	194	No	Usual Care	182	Low	Low
					Intervention			Control		Risk of Bias	
Study	Design	Patient	Died During	Palliative Care	Description	n	Presence of	Description	n	Subjective	Objective

(Country)		Population	Study (%)	Domains Addressed			Palliative Care Physician			Outcomes	Outcomes
Gade et al, 2008 (Australia) ¹¹	Parallel	Mixed: hospitalized patients with a life limiting illness ≤ 1-year estimated life expectancy – HF (7.6%), COPD (12.9%), cancer (31.5%), dementia (4.2%), stroke (6.9%), CKD (3.7%)	59	Structure and Process; Physical; Psychological; Social; Spiritual; Ethical and Legal	IPCS: consultation with palliative care MD, RN, SW and chaplain who assessed and managed symptoms, psychosocial and spiritual support, end-of-life planning, and post-hospital care.	275	Yes	Usual Care	237	Low	Low

198 HF – Heart failure, COPD – Chronic obstructive pulmonary disease, CAD – coronary artery disease, ESRD – End-stage renal disease, AML – Amyotrophic lateral sclerosis, MD -
 199 Physician, RN – Registered nurse, NP – Nurse practitioner, SW – Social work, ACP – Advance care plan, GOLD - Global Initiative for Chronic Obstructive Lung Disease, NYHA – New
 200 York Heart Association, KCCQ – Kansas City cardiomyopathy questionnaire , EFFECT - Enhanced Feedback for Effective Cardiac Treatment, ESCAPE - Evaluation Study of
 201 Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness, CASA – Collaborative Care to Alleviate Symptoms and Adjust to Illness, PREFER - Palliative Advanced
 202 Home Care and Heart Failure Care, PCDM – Patient-Centred Disease Management, IPCS – interdisciplinary palliative care service, PPS - Palliative Performance scale, NR – Not
 203 reported

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207**eTable 3. Trial Characteristics and Outcomes of 18 Palliative Care Interventions at High Risk of Bias in Either Subjective or Objective Outcomes.**

Study (Country)	Design	Patient Population	Died During Study (%)	Palliative Care Domains Addressed	Intervention			Control		Risk of Bias	
					Description	n	Presence of Palliative Care Physician	Description	n	Subjective Outcomes	Objective Outcomes
Van den Block et al, 2019 (Belgium, England, Finland, Italy, the Netherlands, Poland, and Switzerland) ¹²	Cluster, Parallel	Mixed, nursing home (12% cancer)	100	Structure and Process; Physical; Psychological; Social; Spiritual; Care of the Imminently Dying; Ethical and Legal	6-step program implemented over a 12-month period: (1) ACP; (2) review of resident needs and problems; (3) coordination of care via monthly multidisciplinary meetings; (4) symptom management; (5) end-of-life care; and (6) care after death	830	No	Usual Care	704	High	High
Van Spall et al, 2019 (Canada) ¹³	Cluster, Parallel	HF, hospitalized with a most responsible diagnosis of HF	9.9	Structure and Process; Physical; Social	Nurse-led self-care education, structured hospital discharge summary, family physician follow-up appointment less than 1 week after discharge, and, for high-risk patients, structured nurse home visits and heart function clinic care	1104	No	Usual Care (transitional care occurred at the discretion of clinicians)	1390	High	Low

Study (Country)	Design	Patient Population	Died During Study (%)	Palliative Care Domains Addressed	Intervention			Control		Risk of Bias	
					Description	n	Presence of Palliative Care Physician	Description	n	Subjective Outcomes	Objective Outcomes
Bekelman et al, 2018 (USA) ¹⁴	Parallel	HF, KCCQ≤70 and 1 symptom (fatigue, shortness of breath, pain, and/or depression)	7.3	Structure and Process; Physical; Psychological; Social; Spiritual	CASA: clinical team (RN, SW, primary care MD, palliative care MD, and cardiologist) reviewed symptoms, psychosocial and provided orders for tests and medications. Twice monthly nurse-led phone calls for symptom assessment and up to 6 SW visits.	158	Yes	Usual Care: Primary care provider or NP provided unstructured symptom and psychosocial assessments; ad hoc visits (3-6 months); ad hoc social work, palliative care, and cardiologist involvement.	159	High	Low
O'Donnell et al, 2018 (USA) ¹⁵	Parallel	HF with NYHA II-IV; currently or recently hospitalized with at ≥1 poor prognostic indicator	38	Structure& and Process; Social; Ethical and Legal	SW-led structured goals of care discussion	26	No	Usual Care with educational materials on palliative care and ACP.	24	High	Low
Agar et al, 2017 (Australia) ¹⁶	Cluster, Parallel	Dementia (FAST ≥6a; Australia— modified Karnofsky Performance Status ≤50)	46	Structure and Process; Social; Ethical and Legal	Facilitated case conferencing: RN-led implementation of palliative care plans, training of RN and direct care staff in person-centred palliative care.	64	No	Usual Care	67	SC	High

Study (Country)	Design	Patient Population	Died During Study (%)	Palliative Care Domains Addressed	Intervention			Control		Risk of Bias	
					Description	n	Presence of Palliative Care Physician	Description	n	Subjective Outcomes	Objective Outcomes
Rogers et al, 2017 (USA) ²	Parallel	HF-related hospitalization with: acute HF; resting dyspnea plus ≥1 sign of volume overload; previous HF hospitalization within past year; ESCAPE risk score ≥4	28.7	Structure and Process; Physical; Psychological; Social; Spiritual; Care of the Imminently Dying; Ethical and Legal	PAL-HF: Palliative care NP and MD, cardiology team	75	Yes	Usual Care: cardiologist-directed team care with HF expertise, ad hoc palliative care referral.	75	High	Low
Steinhauser et al, 2017 (USA) ¹⁷	Parallel (3-arm)	Mixed: HF (NYHA III-IV), COPD (FEV1 ≤25% or O2-dependent), pulmonary fibrosis (TLC<50%), ESRD (on dialysis), cancer (stage IV solid tumors, stage IIIB NSCLC and pancreatic cancer, recurrent or refractory hematologic malignancy)	4.1	Spiritual, Psychological	SW-led in person interviews (x4) over 1 month focusing on life review, issues of forgiveness, regret, and things left unsaid or undone, and heritage and legacy.	75	No	Usual Care (attention control not included in this systematic review)	72	High	N/A

Study (Country)	Design	Patient Population	Died During Study (%)	Palliative Care Domains Addressed	Intervention			Control		Risk of Bias	
					Description	n	Presence of Palliative Care Physician	Description	n	Subjective Outcomes	Objective Outcomes
Sidebottom et al, 2015 (USA) ¹⁸	Parallel	HF with HF-related hospitalization	8.2	Structure and Process; Physical; Psychological; Social; Spiritual; Ethical and Legal	Consultation with palliative care MD, nurse specialist, SW, and chaplain; assessed symptoms; emotional, spiritual, and psychosocial; coordination of care; recommendations for future treatment; referrals;	116	Yes	Usual Care	116	High	High
Brännström et al, 2014 (Sweden) ¹⁹	Parallel	HF with NYHA class III–IV and ≥1 of the following: HF-related hospitalization in the preceding 6 months; the need for frequent or continual intravenous medication support; poor quality of life; cardiac cachexia within 6–12 months; estimated life expectancy < 1 year.	16.7	Structure and Process; Physical; Psychological; Social; Spiritual; Care of the Imminently Dying; Ethical and Legal	PREFER: specialized nurses, palliative care nurses, cardiologist, palliative care MD, physiotherapist, and occupational therapist; structured, twice monthly person-centred care meetings at home.	36	Yes	Usual Care: provided mainly by general practitioners or doctors and/or the nurse-led heart failure clinic at the Medicine-Geriatrics department.	36	High	SC

Study (Country)	Design	Patient Population	Died During Study (%)	Palliative Care Domains Addressed	Intervention			Control		Risk of Bias	
					Description	n	Presence of Palliative Care Physician	Description	n	Subjective Outcomes	Objective Outcomes
Radwany et al, 2014 (USA) ²⁰	Parallel	Mixed (% not reported): cancer, HF (stage C), COPD (on home O2), diabetes with complications, ESRD on dialysis, Cirrhosis, AML with aspiration, Parkinson's disease (stage 3 or 4), pulmonary hypertension	17.5	Structure and Process; Physical; Psychological; Social; Spiritual; Care of the Imminently Dying; Ethical and Legal	Palliative care MD, geriatrician, care manager, nurse specialist, SW, spiritual advisor and pharmacist. 2 home visits for biopsychosocial, spiritual and symptom needs, emergency response plan, education, and completing ACP and legal documents. 24-hour phone availability, monthly phone calls for 1 year.	40	Yes	Usual Care	40	High	SC
Sampson et al, 2011 (UK) ²¹	Parallel	Dementia (FAST ≥ 6 d) hospitalized with a treatable acute medical illness	9.1	Physical, Psychological, Social, Spiritual, Ethical and Legal	Nurse-led consultation with input from interprofessional team and up to 4 visits to address illness understanding, symptoms, spiritual, psychological and social supports and advance directives.	22	No	Usual Care	11	High	High

Study (Country)	Design	Patient Population	Died During Study (%)	Palliative Care Domains Addressed	Intervention			Control		Risk of Bias	
					Description	n	Presence of Palliative Care Physician	Description	n	Subjective Outcomes	Objective Outcomes
Pantilat et al, 2010 (USA) ²²	Parallel	Mixed: hospitalized patients with HF (51%), cancer (22%), COPD (20%), cirrhosis (6%)	NR	Structure and Process; Physical; Psychological; Social; Spiritual;	Consultation and daily inpatient visit from palliative care MD who assessed symptoms and psychosocial and spiritual needs and discussed treatment preferences.	54	Yes	Usual Care with education on diet and exercise	53	High	N/A
Farquhar et al, 2016 (UK) ²³	Parallel	Mixed: COPD (83% - 47% severe/very severe), other noncancer illness (17%)	2	Structure and Process; Physical; Psychological; Social;	BIS: PT-led and MD with home and telephone visits over 8 weeks addressed symptoms, psychological, ACP, education and self- management.	44	Yes	Usual Care	43	High	Low

Study (Country)	Design	Patient Population	Died During Study (%)	Palliative Care Domains Addressed	Intervention			Control		Risk of Bias	
					Description	n	Presence of Palliative Care Physician	Description	n	Subjective Outcomes	Objective Outcomes
Aiken et al, 2006 (USA) ²⁴	Parallel	Mixed: HF (NYAH III-IV – 67.8%) and COPD (O2-dependent – 32.2%) with ≤2 years estimated life expectancy and treatment in an emergency department, urgent care facility, or hospital within 3 months.	NR	Structure and Process; Physical, Social, Spiritual, Psychological, Ethical and Legal	PhoenixCare: RN-led home-based case management (medical director, SW, and pastoral counselor); facilitated care plan (symptoms, psychological, spiritual and financial needs, ACP, and provided educational) to primary care MD, patient/family, and community agencies.	100	No	Usual Care	90	High	High
Rabow et al, 2004 (USA) ²⁵	Parallel	Mixed: HF (34%), COPD (34%), cancer (35%) with a 1 to 5 year estimated life expectancy and who were not yet ready for hospice care.	NR	Structure and Process; Physical; Psychological; Social; Spiritual; Ethical and Legal	Comprehensive Care Team: consultation, follow-up and outpatient case management in (SW, MD, RN, chaplain, pharmacist, psychologist, art therapist, volunteer) to address physical, emotional, and spiritual needs.	50	Yes	Usual Care	40	High	High

Study (Country)	Design	Patient Population	Died During Study (%)	Palliative Care Domains Addressed	Intervention			Control		Risk of Bias	
					Description	n	Presence of Palliative Care Physician	Description	n	Subjective Outcomes	Objective Outcomes
Harrison et al, 2002 (Canada) ²⁶	Parallel	HF: hospitalized patients residing in the regional home care radius expected to be discharged with home nursing care.	10.4	Structure and Process; Social	RN-led support using structured, comprehensive, evidenced-based protocol for self- management and communications between inpatient and outpatient care teams and family to improve the transfer from hospital to home.	92	No	Usual Care	100	High	High
SUPPORT Investigators, 1995 (USA) ²⁷	Cluster, Parallel	Mixed: hospitalized patients with acute organ system failure (respiratory and multiple organ system failure ± sepsis, chronic disease [HF, COPD or cirrhosis] and cancer	45.6	Structure and Process; Social; Ethical and Legal	RN-led intervention to improve communication by addressing illness understanding about prognosis, addressing goals of care, and facilitating family meetings.	2652	No	Usual Care	2152	High	SC

Study (Country)	Design	Patient Population	Died During Study (%)	Palliative Care Domains Addressed	Intervention			Control		Risk of Bias	
					Description	n	Presence of Palliative Care Physician	Description	n	Subjective Outcomes	Objective Outcomes
Zimmer, et al, 1985 (USA) ²⁸	Parallel	Mixed: home-bound patients with cancer (19%), stroke (14.6%), rheumatoid arthritis (10.1%), or Other (dementia, CAD, chronic lung disease, multiple sclerosis – 56.4%; each condition less than 10%).	44	Structure and Process; Physical; Psychological; Social; Spiritual; Ethical and Legal	Home Healthcare Team: MD, NP and SW provided 24/7 telephone support as well as home visits and care during hospitalization. Addressed symptoms, emotional, social and financial needs.	82	Yes	Usual Care	76	High	High

208 HF – Heart failure, COPD – Chronic obstructive pulmonary disease, CAD – coronary artery disease, ESRD – End-stage renal disease, AML – Amyotrophic lateral sclerosis, MD -
 209 Physician, RN – Registered nurse, NP – Nurse practitioner, APN – Advanced practice nurse, SW – Social work, PT – Physiotherapy, OT – Occupational therapy, ACP – Advance care
 210 plan, GOLD - Global Initiative for Chronic Obstructive Lung Disease, NYHA – New York Heart Association, KCCQ – Kansas City cardiomyopathy questionnaire , EFFECT - Enhanced
 211 Feedback for Effective Cardiac Treatment, ESCAPE - Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness, CASA – Collaborative Care to
 212 Alleviate Symptoms and Adjust to Illness, PREFER - Palliative Advanced Home Care and Heart Failure Care, PCDM – Patient-Centred Disease Management, IPCS – interdisciplinary
 213 palliative care service, PPS - Palliative Performance scale, NR – Not reported

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215 **eTable 4. Trial Characteristics and Outcomes of 3 Palliative Care Interventions with Some Concerns Risk of Bias**
 216 **in Either Subjective or Objective Outcomes.**

Study (Country)	Design	Patient Population	Died During Study (%)	Palliative Care Domains Addressed	Intervention			Control		Risk of Bias	
					Description	n	Presence of Palliative Care Physician	Description	n	Subjective Outcomes	Objective Outcomes
Hopp et al, 2016 (USA) ²⁹	Parallel	Hospitalized patients with HF with ≥1 of: EFFECT score indicating ≥33% 1-year mortality risk; NYHA class III or IV.	23.8	Structure and Process; Physical; Social; Ethical and Legal	Clinical interviews with palliative care MD and RN for symptoms, goals of care, advance care planning, code status, and desired post-treatment residential setting. All had ≥1 palliative care consultation. Ad hoc chaplains and SW.	43	Yes	Usual Care	42	N/A	SC
Brumley et al, 2007 (USA) ³⁰	Parallel	Mixed: HF (33%), COPD (21%), cancer (47%) with ≤ 1-year estimated life expectancy, ≥1 ED visit or hospitalization within 1 year, and PPS score ≤ 70%.	75	Structure and Process; Physical; Psychological; Social; Spiritual; Ethical and Legal	Palliative care MD, RN and SW provided home-based care to assess and manage physical, medical, psychological, social, and spiritual needs with 24-hour call availability	152	Yes	Usual Care (Medicare guidelines for home healthcare criteria)	145	SC	SC

Study (Country)	Design	Patient Population	Died During Study (%)	Palliative Care Domains Addressed	Intervention			Control		Risk of Bias	
					Description	n	Presence of Palliative Care Physician	Description	n	Subjective Outcomes	Objective Outcomes
Ahronheim et al, 2000 (USA) ³¹	Parallel	Dementia: hospitalized patients with advanced dementia (FAST≥6d) with stable neurological deficits for ≥ 1 month	24	Structure and Process; Physical; Psychological; Social; Ethical and Legal	Consultation and daily visits by MD and RN to address symptoms, advance directives, goals of care, patient rights, emotional support, discussions surrounding place of death.	48	Yes	Usual Care	51	N/A	SC

217 HF – Heart failure, COPD – Chronic obstructive pulmonary disease, CAD – coronary artery disease, ESRD – End-stage renal disease, AML – Amyotrophic lateral sclerosis, MD -
 218 Physician, RN – Registered nurse, NP – Nurse practitioner, SW – Social work, ACP – Advance care plan, GOLD - Global Initiative for Chronic Obstructive Lung Disease, NYHA – New
 219 York Heart Association, KCCQ – Kansas City cardiomyopathy questionnaire , EFFECT - Enhanced Feedback for Effective Cardiac Treatment, ESCAPE - Evaluation Study of
 220 Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness, CASA – Collaborative Care to Alleviate Symptoms and Adjust to Illness, PREFER - Palliative Advanced
 221 Home Care and Heart Failure Care, PCDM – Patient-Centred Disease Management, IPCS – interdisciplinary palliative care service, PPS - Palliative Performance scale, NR – Not
 222 reported

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224 **eTable 5. Risk of Bias Assessments (Subjective Outcomes) of 26 Randomized Clinical Trials of Palliative Care
225 Interventions**

226 Trials with patient-level randomization

First author, year	Randomization	Deviation from Intended Interventions	Missing Outcome Data	Measurement of the Outcome	Selection of the Reported Result	Summary of Bias ^a
Aiken LS et al., 2006 ²⁴	Low	Low	High	High	SC	High
Bekelman DB et al., 2018 ¹⁴	Low	Low	High	High	Low	High
Bekelman DB et al., 2015 ⁸	Low	Low	Low	High	Low	Low
Brännström M et al., 2014 ¹⁹	SC	Low	Low	High	Low	High
Brumley R et al., 2007 ³⁰	Low	Low	SC	High	SC	SC
Farquhar MC et al., 2016 ²³	Low	Low	High	High	Low	High
Gade G et al., 2008 ¹¹	Low	Low	Low	High	Low	Low
Harrison MB et al., 2002 ²⁶	Low	Low	High	High	SC	High
Higginson IJ et al., 2014 ⁹	Low	Low	Low	High	Low	Low
Janssens JP et al., 2019 ⁶	Low	Low	Low	High	Low	Low
O'Donnell AE et al., 2018 ¹⁵	Low	Low	High	High	Low	High
Pantilat SZ et al., 2010 ²²	SC	High	High	High	SC	High
Possin KL et al, 2019 ⁷	Low	Low	Low	High	Low	Low
Rabow MW et al., 2004 ²⁵	High	High	Low	High	SC	High
Radwany SM et al., 2014 ²⁰	SC	Low	High	High	Low	High

Rogers JG et al., 2017 ²	Low	Low	High	High	Low	High
Sampson EL et al., 2011 ²¹	Low	High	High	High	SC	High
Sidebottom AC et al., 2015 ¹⁸	Low	High	High	High	Low	High
Steinhauser KE et al., 2017 ¹⁷	Low	Low	High	High	Low	High
Wong FKY et al., 2016 ⁴	Low	Low	Low	High	Low	Low
Zimmer JG et al., 1985 ²⁸	High	High	High	High	SC	High

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^aDomain #4 is omitted from summary judgements as all studies are high risk of bias.

RCTs without subjective outcome measures: Ahronheim JC et al., 2000³¹, Hopp FP et al., 2016²⁹

Trials with cluster-level randomization

First author, year	Randomization	Deviation from Intended Interventions	Missing Outcome Data	Measurement of the Outcome	Selection of the Reported Result	Summary of Bias ^a
Agar M et al., 2017 ¹⁶	Low	Low	SC	High	Low	SC
Au DH et al., 2012 ¹⁰	Low	Low	Low	High	Low	Low
SUPPORT Investigators, 1995 ²⁷	Low	Low	High	High	SC	High
Van den Block L et al., 2019 ¹²	Low	Low	High	High	Low	High
Van Spall HGC et al., 2019 ¹³	Low	Low	High	High	Low	High

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^aDomain #4 are omitted from summary judgements as all studies are high risk of bias.

232 **eTable 6. Risk of Bias Assessments (Objective Outcomes) of 26 Randomized Clinical Trials of Palliative Care
233 Interventions**

234 Trials with patient-level randomization

First author, year	Randomization	Deviation from Intended Interventions	Missing Outcome Data	Measurement of the Outcome	Selection of the Reported Result	Summary of Bias
Ahronheim JC et al., 2000 ³¹	SC	Low	Low	Low	SC	SC
Aiken LS et al., 2006 ²⁴	Low	Low	SC	Low	SC	High
Bekelman DB et al., 2018 ¹⁴	Low	Low	Low	Low	Low	Low
Bekelman DB et al., 2015 ⁸	Low	Low	Low	Low	Low	Low
Brännström M et al., 2014 ¹⁹	SC	Low	Low	Low	Low	SC
Brumley R et al., 2007 ³⁰	Low	Low	Low	Low	SC	SC
Farquhar MC et al., 2016 ²³	Low	Low	Low	Low	Low	Low
Gade G et al., 2008 ¹¹	Low	Low	Low	Low	Low	Low
Harrison MB et al., 2002 ²⁶	Low	Low	SC	Low	SC	High

Higginson IJ et al., 2014 ⁹	Low	Low	Low	Low	Low	Low
Hopp FP et al., 2016 ²⁹	SC	Low	Low	Low	SC	SC
Janssens JP et al., 2019 ⁶	Low	Low	Low	Low	Low	Low
O'Donnell AE et al., 2018 ¹⁵	Low	Low	Low	Low	Low	Low
Possin KL et al., 2019 ⁷	Low	Low	Low	Low	Low	Low
Rabow MW et al., 2004 ²⁵	High	High	Low	Low	SC	High
Radwany SM et al., 2014 ²⁰	SC	Low	Low	Low	Low	SC
Rogers JG et al., 2017 ²	Low	Low	Low	Low	Low	Low
Sampson EL et al., 2011 ²¹	Low	High	High	Low	SC	High
Sidebottom AC et al., 2015 ¹⁸	Low	High	SC	Low	Low	High
Wong FKY et al., 2016 ⁴	Low	Low	Low	Low	Low	Low
Zimmer JG et al., 1985 ²⁸	High	High	Low	Low	SC	High

235 RCTs without objective outcome measures: Janssens JP et al., 2019⁶, Pantilat SZ et al., 2010²², Steinhauser KE et al., 2017¹⁷
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Trials with cluster-level randomization

First author, year	Randomization	Deviation from Intended Interventions	Missing Outcome Data	Measurement of the Outcome	Selection of the Reported Result	Summary of Bias
Agar M et al., 2017 ¹⁶	Low	Low	High	Low	Low	High
Au DH et al., 2012 ¹⁰	Low	Low	Low	Low	Low	Low
SUPPORT Investigators, 1995 ²⁷	Low	Low	High	Low	SC	SC
Van den Block L et al., 2019 ¹²	Low	Low	High	Low	Low	High
Van Spall HGC et al, 2019 ¹³	Low	Low	Low	Low	Low	Low

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eTable 7. Results of Secondary Analyses of Palliative Care Interventions

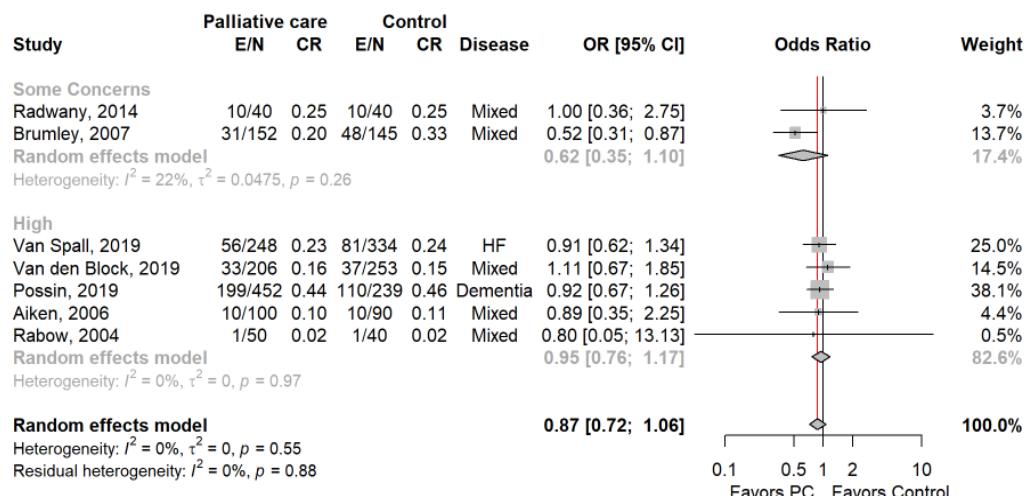
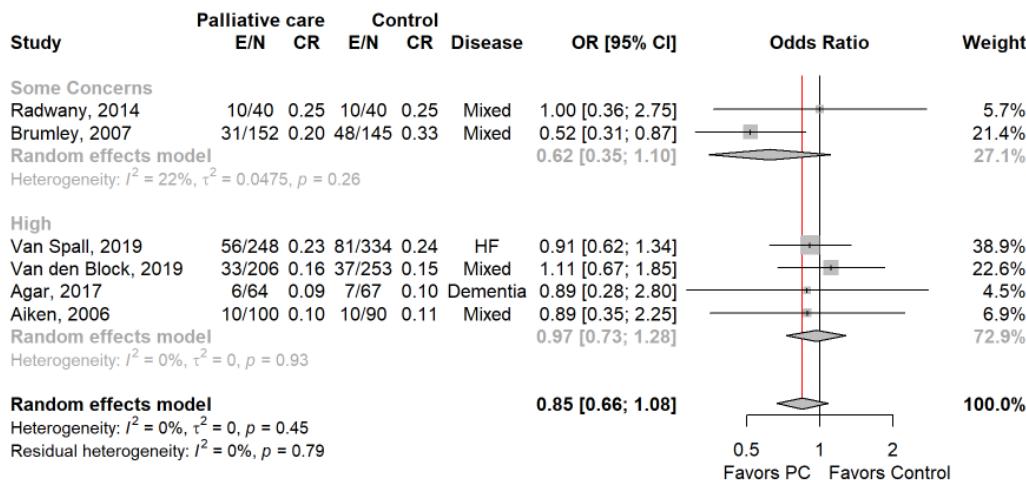
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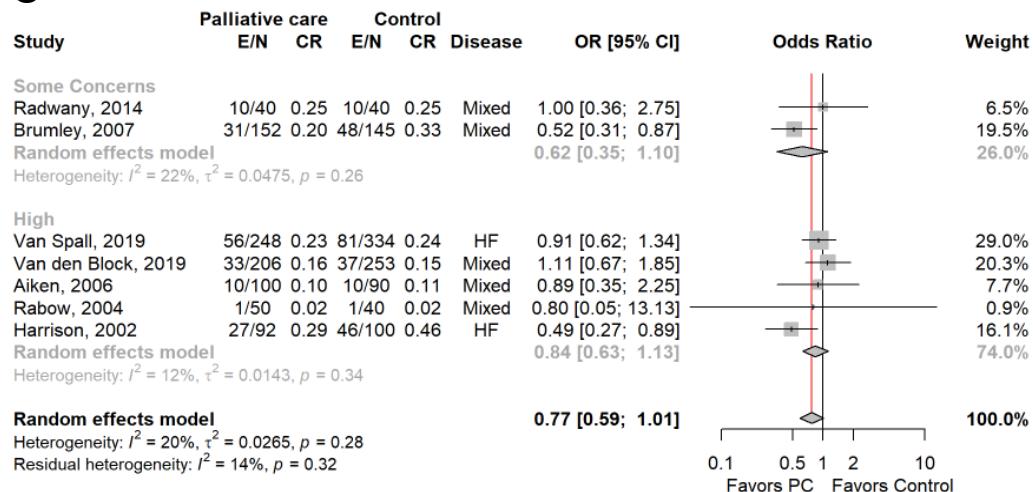
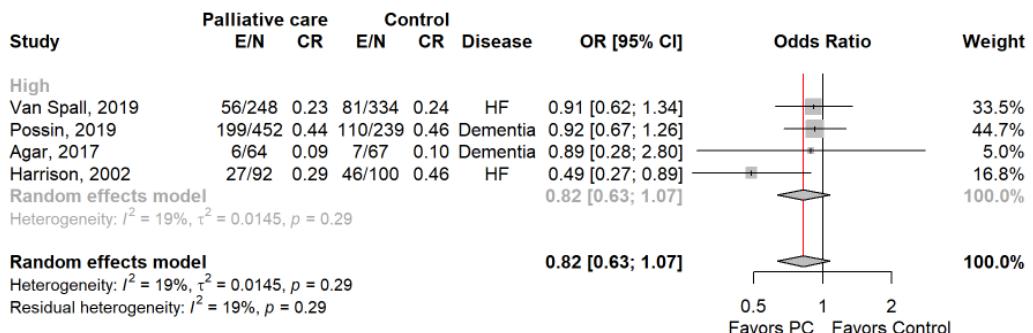
Outcome Measure	Summary Estimate (95% CI)*	p-value
Emergency Department Use		
<i>Meta-Regression Analyses</i>		
Presence of Palliative Care MD	0.60 (0.38-0.95)	0.03
Heart Failure	0.71(0.43-1.17)	0.18
Mixed Conditions	0.81 (0.53-1.24)	0.34
Dementia	0.92 (0.53-1.58)	0.75
Follow-up Time	1.03 (0.98-1.08)	0.27
<i>Other Secondary Analyses</i>		
Interdisciplinary Care Team	0.87 (0.72-1.06)	--
Home Visits	0.85 (0.66-1.08)	--
Dementia Excluded	0.77 (0.59-1.01)	--
Mixed (Cancer) Excluded	0.82 (0.63-1.07)	--
Hospitalization		
<i>Meta-Regression Analyses</i>		
Presence of Palliative Care MD	0.74 (0.55-1.00)	0.05
Heart Failure	0.83 (0.67-1.03)	0.09
Mixed Conditions	1.02 (0.64-1.63)	0.94
Dementia	1.04 (0.72-1.50)	0.85
Follow-up Time	1.00 (0.96-1.03)	0.77
<i>Other Secondary Analyses</i>		
Interdisciplinary Care Team	0.93 (0.78-1.11)	--
Home Visits	0.77 (0.53-1.12)	--
Dementia Excluded	0.88 (0.74-1.05)	--
Mixed (Cancer) Excluded	0.90 (0.76-1.06)	--
Disease-Generic QOL		
<i>Meta-Regression Analyses</i>		
Presence of Palliative Care MD	0.35 (0.13-0.57)	<0.001
Heart Failure	0.17 (-0.23-0.56)	0.40
Mixed Conditions	0.19 (-0.69-1.06)	0.67
Dementia	--	--
Follow-up Time	-0.07 (-0.21-0.08)	0.38
<i>Other Secondary Analyses</i>		
Interdisciplinary Care Team	0.18 (-0.29-0.64)	--
Home Visits	0.15 (-0.40-0.70)	--
Dementia Excluded	0.18 (-0.24-0.61)	--
Mixed (Cancer) Excluded	0.19 (-0.31-0.69)	--

Outcome Measure	Summary Estimate (95% CI)*	p-value
Disease-Specific QOL		
<i>Meta-Regression Analyses</i>		
Presence of Palliative Care MD	0.18 (-0.01-0.37)	0.06
Heart Failure	0.05 (-0.21-0.30)	0.73
Mixed Conditions	0.18 (-0.31-0.67)	0.47
Dementia	0.07 (-0.56-0.70)	0.83
Follow-up Time	-0.01 (-0.07-0.05)	0.75
<i>Other Secondary Analyses</i>		
Interdisciplinary Care Team	0.15 (0.02-0.29)	--
Home Visits	0.37 (0.05-0.69)	--
Dementia Excluded	0.13 (0.01-0.25)	--
Mixed (Cancer) Excluded	0.12 (0.00-0.23)	--
Symptoms		
<i>Meta-Regression Analyses</i>		
Presence of Palliative Care MD	-0.16 (-0.27--0.06)	0.002
Heart Failure	-0.16 (-0.32--0.01)	0.04
Mixed Conditions	-0.10 (-0.21-0.00)	0.05
Dementia	-0.20 (-1.43-1.03)	0.75
Follow-up Time	0.01 (0.00-0.02)	0.09
<i>Other Secondary Analyses</i>		
Interdisciplinary Care Team	-0.11 (-0.19--0.02)	--
Home Visits	-0.15 (-0.34-0.03)	--
Dementia Excluded	-0.12 (-0.20--0.03)	--
Mixed (Cancer) Excluded	-0.16 (-0.31--0.01)	--
Advance Care Planning		
<i>Meta-Regression Analyses</i>		
Presence of Palliative Care MD	3.98 (1.73-9.17)	0.001
Heart Failure	4.53 (1.16-17.71)	0.03
Mixed Conditions	1.72 (0.83-3.57)	0.20
Dementia	7.28 (1.16-45.81)	0.03
COPD	3.40 (1.33-8.68)	0.01
Follow-up Time	--	--
<i>Other Secondary Analyses</i>		
Interdisciplinary Care Team	3.34 (2.10-5.29)	--
Home Visits	--	--
Dementia Excluded	2.65 (1.35-5.21)	--
Mixed (Cancer) Excluded	3.74 (2.39-5.83)	--

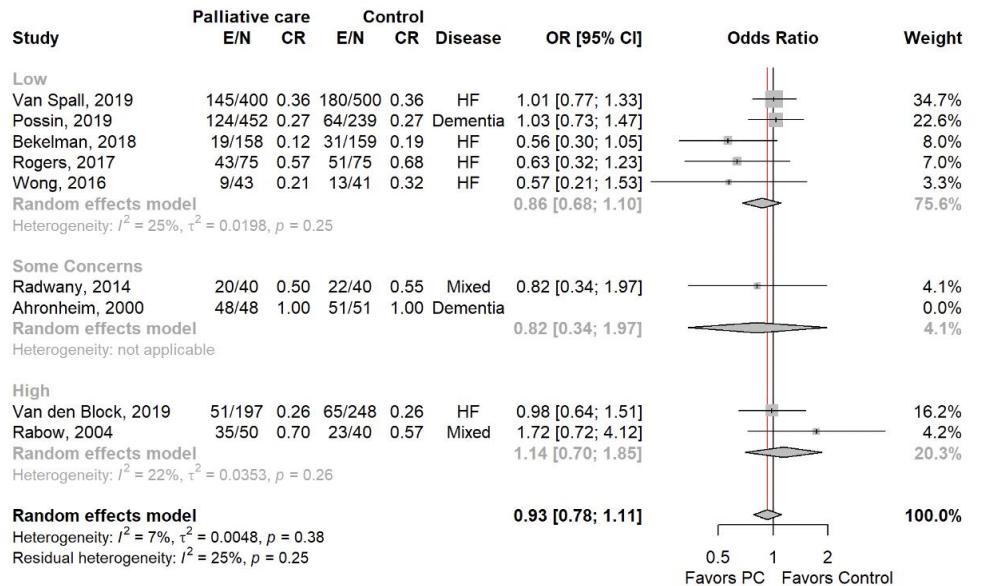
*All summary estimates are presented as OR (95% CIs) except for meta-regression analyses of measures of Quality of Life and Symptoms, which are presented as beta-estimates.
COPD – Chronic Obstructive Pulmonary Disease

250 **eFigure 1. Secondary Analysis of the Association Between Palliative Care and Healthcare Use for (A) Emergency**
251 **department use with interdisciplinary teams involving a physician, (B) Emergency department use with home**
252 **visits, (C) Emergency department use with trials of dementia excluded, (D) Emergency department use with trials**
253 **of mixed disease excluded, (E) Hospitalization with interdisciplinary teams involving a physician, (F)**
254 **Hospitalization with home visits, (G) Hospitalization with trials of dementia excluded, (H) Hospitalization with**
255 **trials of mixed disease excluded . Data are presented as the odds and 95% CIs (error bars) of at least one ED visit or**
256 **hospitalization during study follow-up. The shaded squares are proportionally sized to reflect study weight and the shaded**
257 **diamonds represent pooled odds and 95% CIs. The vertical red line indicates the pooled effect estimate, and the black**
258 **vertical line depicts a null effect. Studies are grouped according to their summary risk of bias (Low, High, Some Concerns)**
259 **HF – heart failure.**

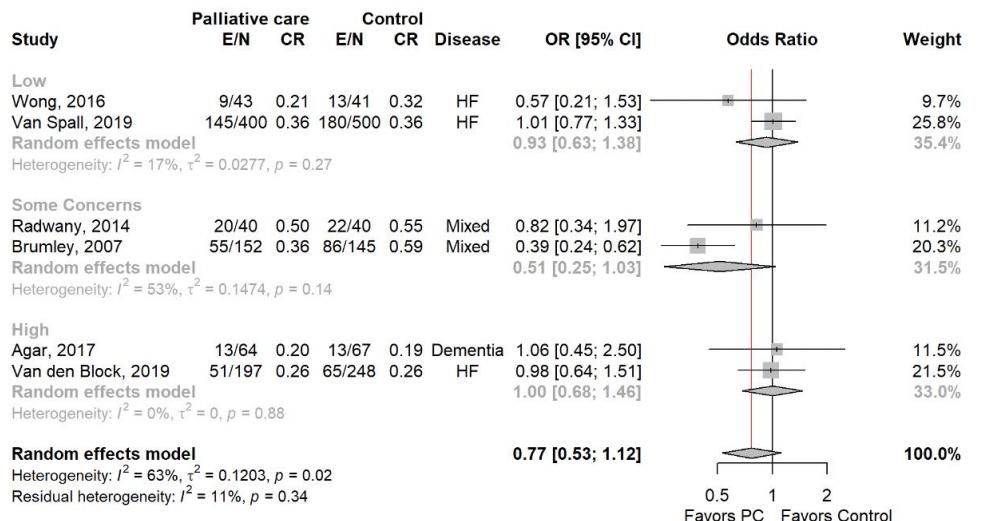
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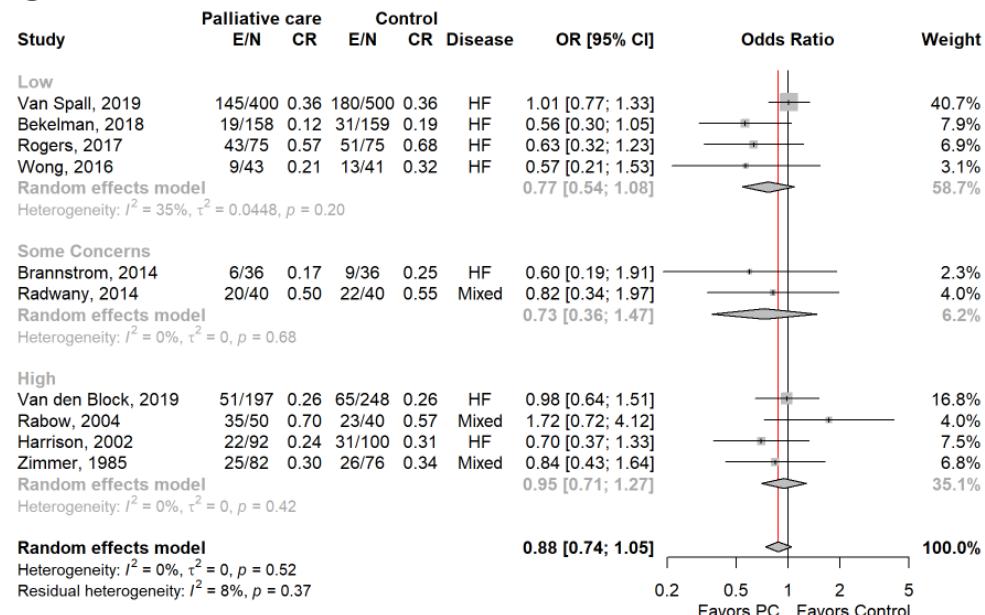
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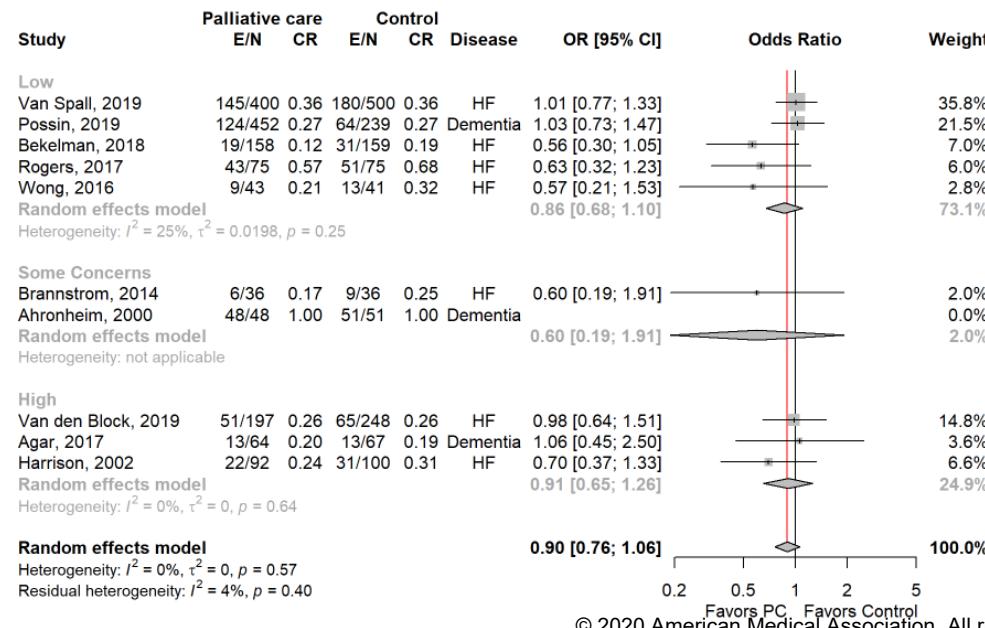
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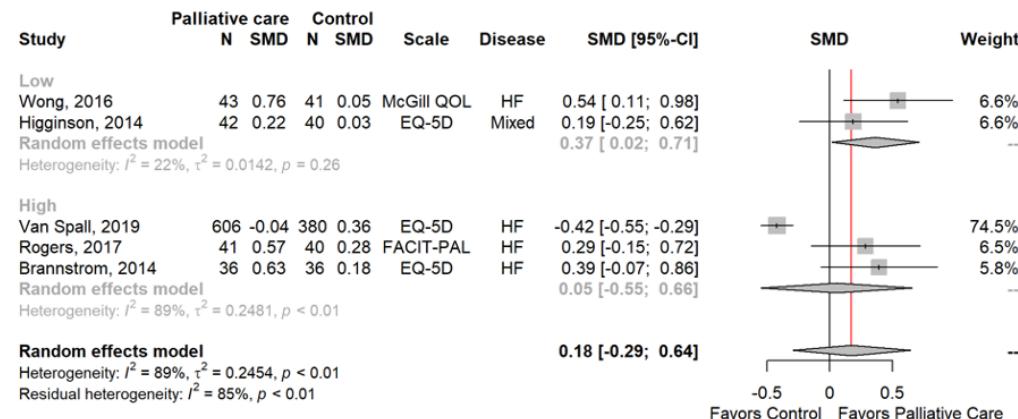
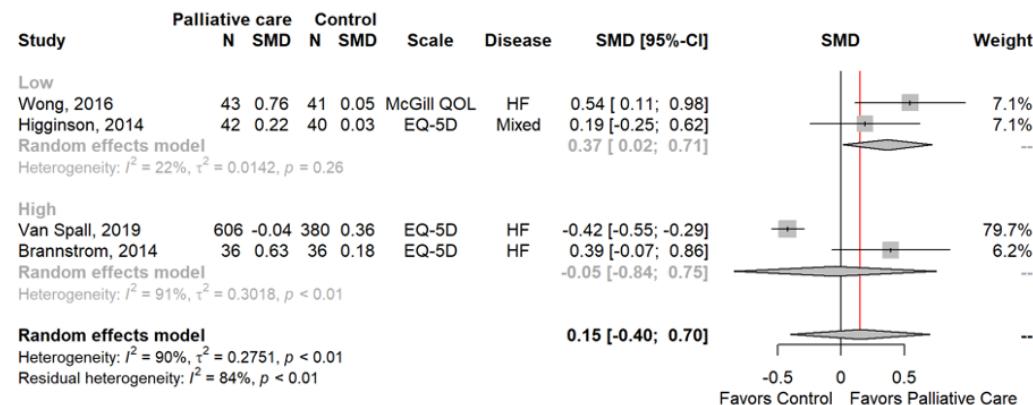


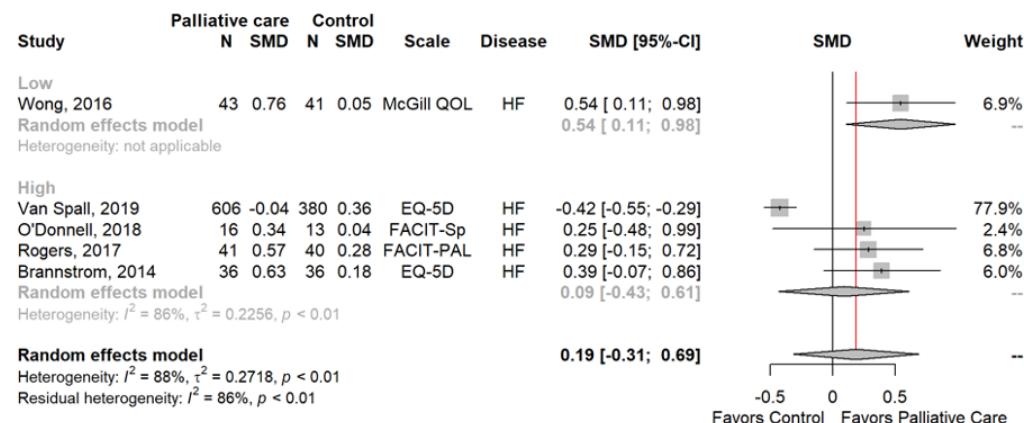
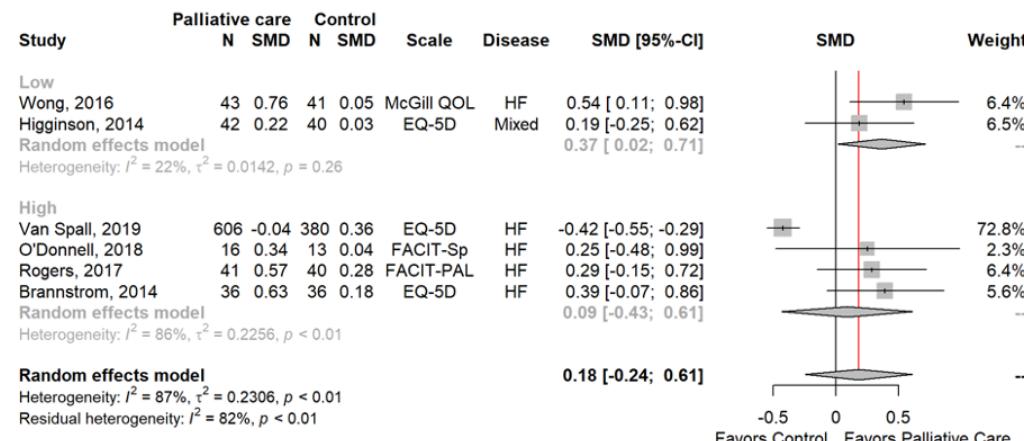
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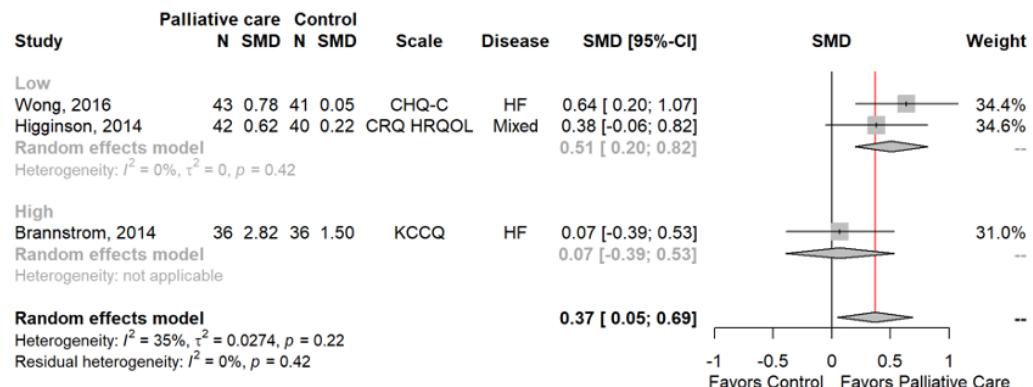
264 **eFigure 2. Secondary Analysis of the Association Between Palliative Care and Quality of Life for (A) Disease-**
265 **generic QOL with interdisciplinary teams involving a physician, (B) Disease-generic QOL with home visits, (C)**
266 **Disease-generic QOL with trials of dementia excluded, (D) Disease-generic QOL with trials of mixed disease**
267 **excluded, (E) Disease-specific QOL with interdisciplinary teams involving a physician, (F) Disease-specific QOL**
268 **with home visits, (G) Disease-specific QOL with trials of dementia excluded, (H) Disease-specific QOL with trials**
269 **of mixed disease excluded.** Data are presented as the means and 95% CIs (error bars) of the change in quality of life
270 measures from baseline to the end of study follow-up. The shaded squares are proportionally sized to reflect study weight
271 and the shaded diamonds represent pooled standardized mean difference and 95% CIs. The vertical red line indicates the
272 pooled effect estimate, and the black vertical line depicts a null effect. Studies are grouped according to their summary
273 risk of bias (Low, High, Some Concerns). HF – heart failure; EQ-5D – EuroQol-5D; FACIT - Functional Assessment of
274 Chronic Illness Therapy scale.

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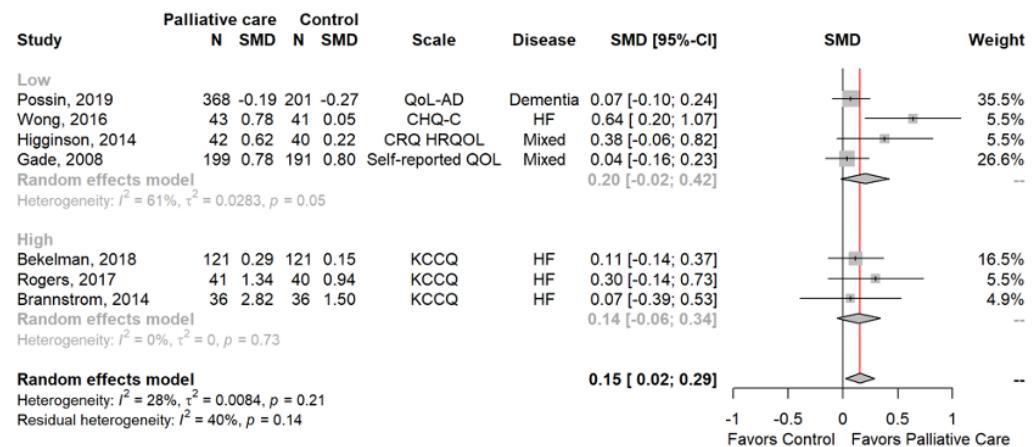
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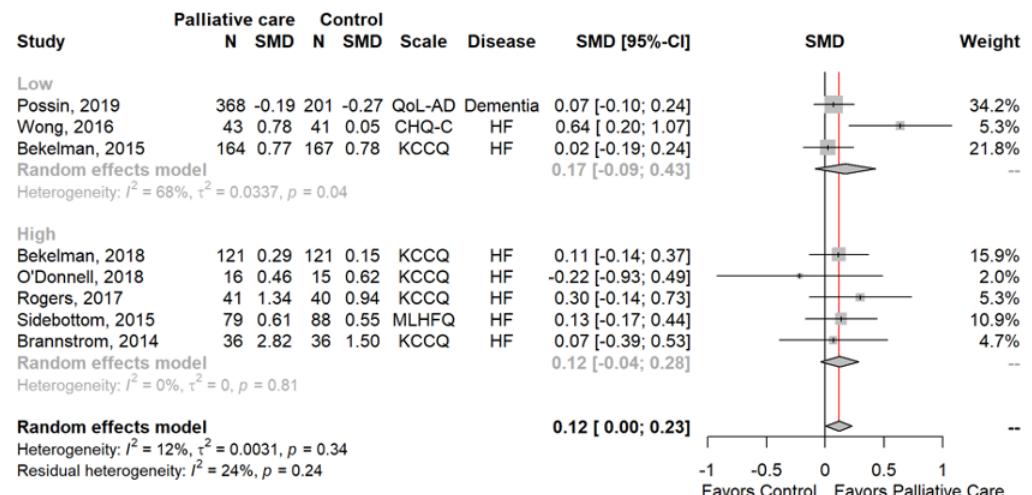
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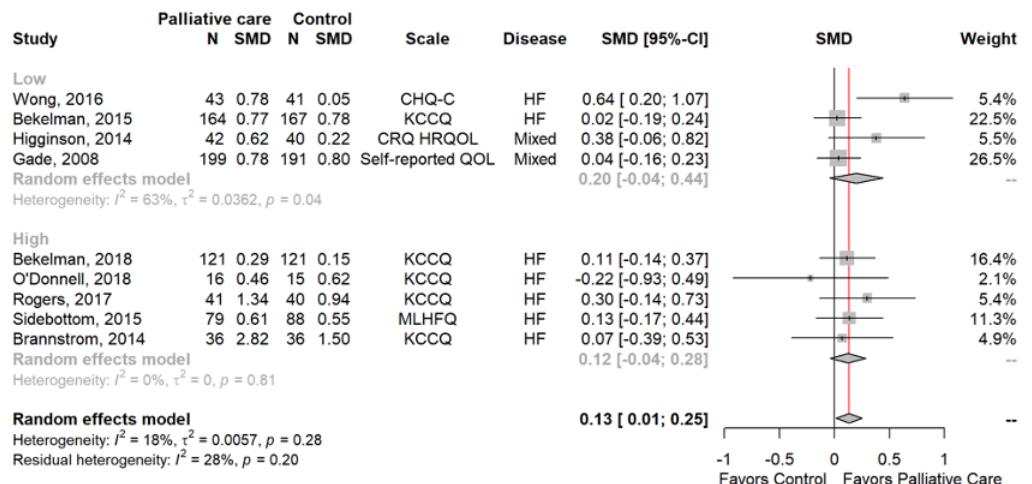
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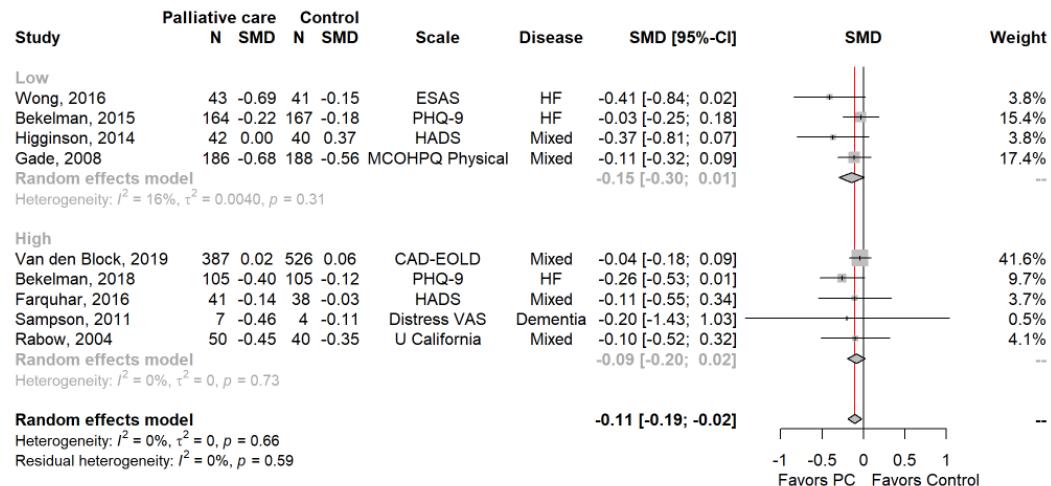


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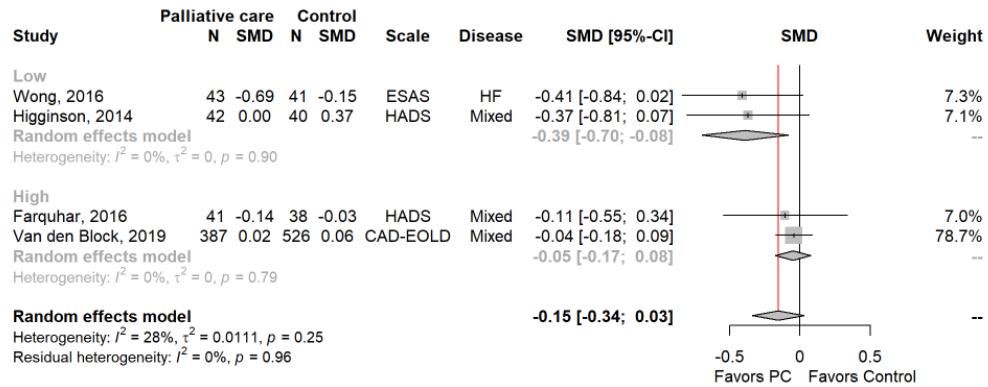


280 **eFigure 3. Subgroup Analysis of the Association Between Palliative Care and Symptoms for (A) Interdisciplinary**
281 **teams involving a physician, (B) Home visits, (C) Trials of dementia excluded, (D) Trials of mixed disease**
282 **excluded.** Data are presented as the means and 95% CIs (error bars) of the change in symptom measures from baseline
283 to the end of study follow-up. The shaded squares are proportionally sized to reflect study weight and the shaded
284 diamonds represent pooled standardized mean difference and 95% CIs. The vertical red line indicates the pooled effect
285 estimate, and the black vertical line depicts a null effect. Studies are grouped according to their summary risk of bias
286 (Low, High, Some Concerns). HF – heart failure; PHQ – Patient Health Questionnaire; HADS - Hospital Anxiety and
287 Depression Scale; VAS – Visual Analogue Scale; ESAS – Edmonton Symptom Assessment Scale; MCOHPQ - Modified
288 City of Hope Patient Questionnaire.

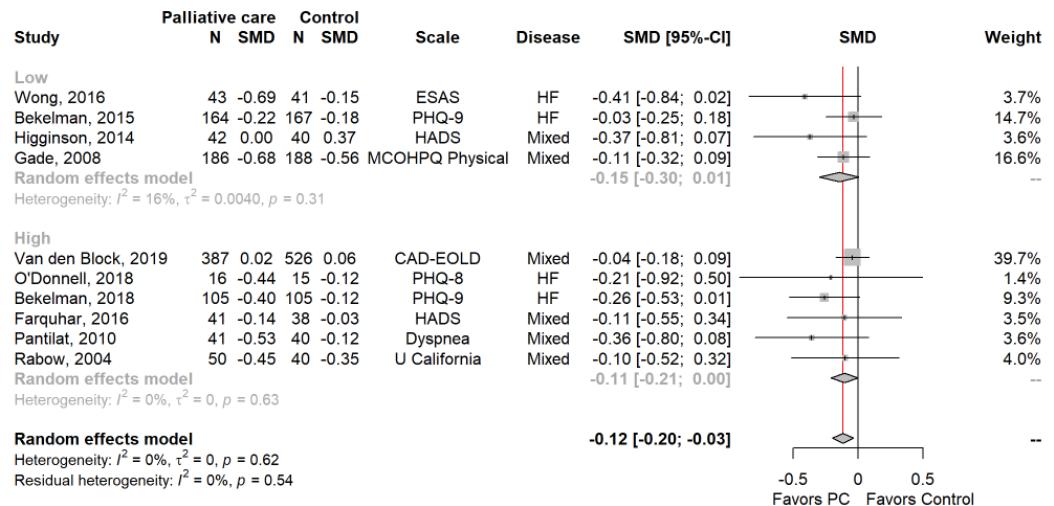
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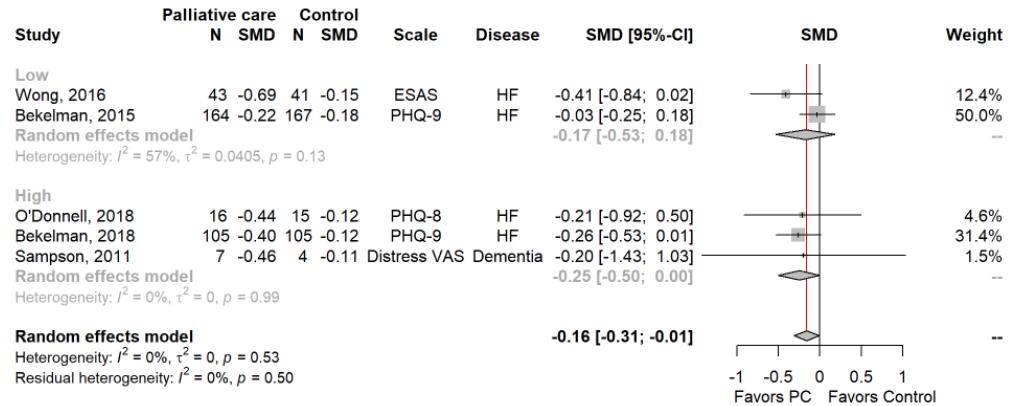
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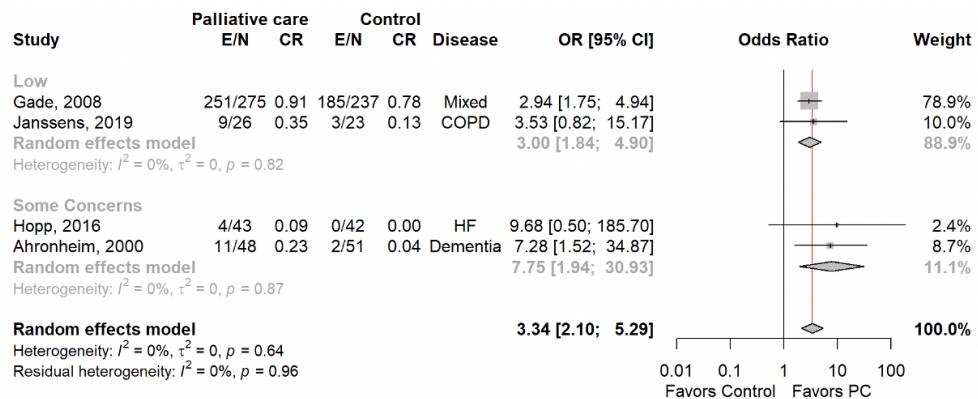
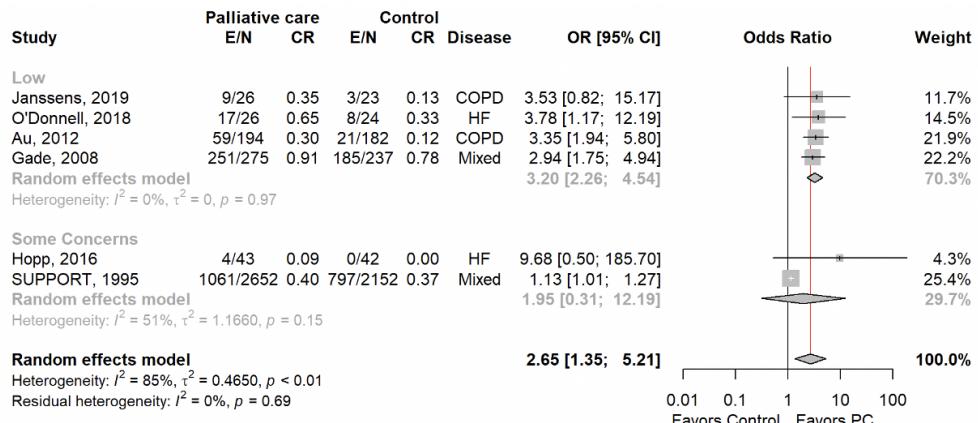
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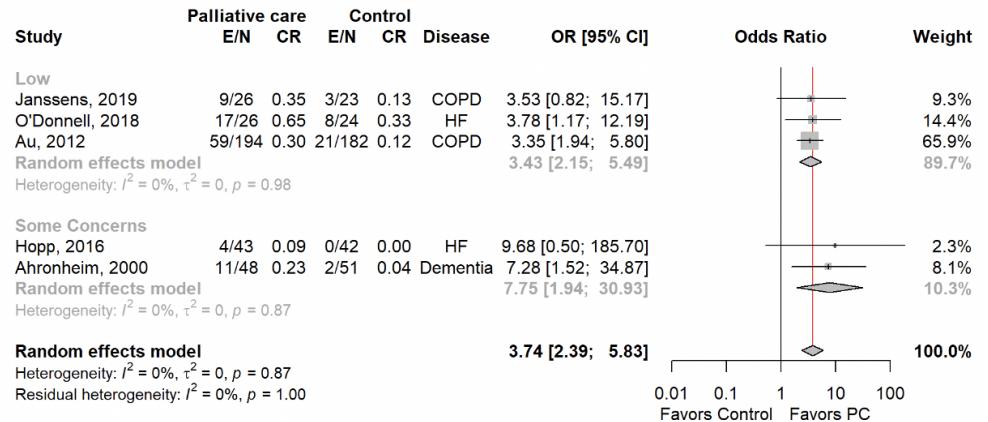
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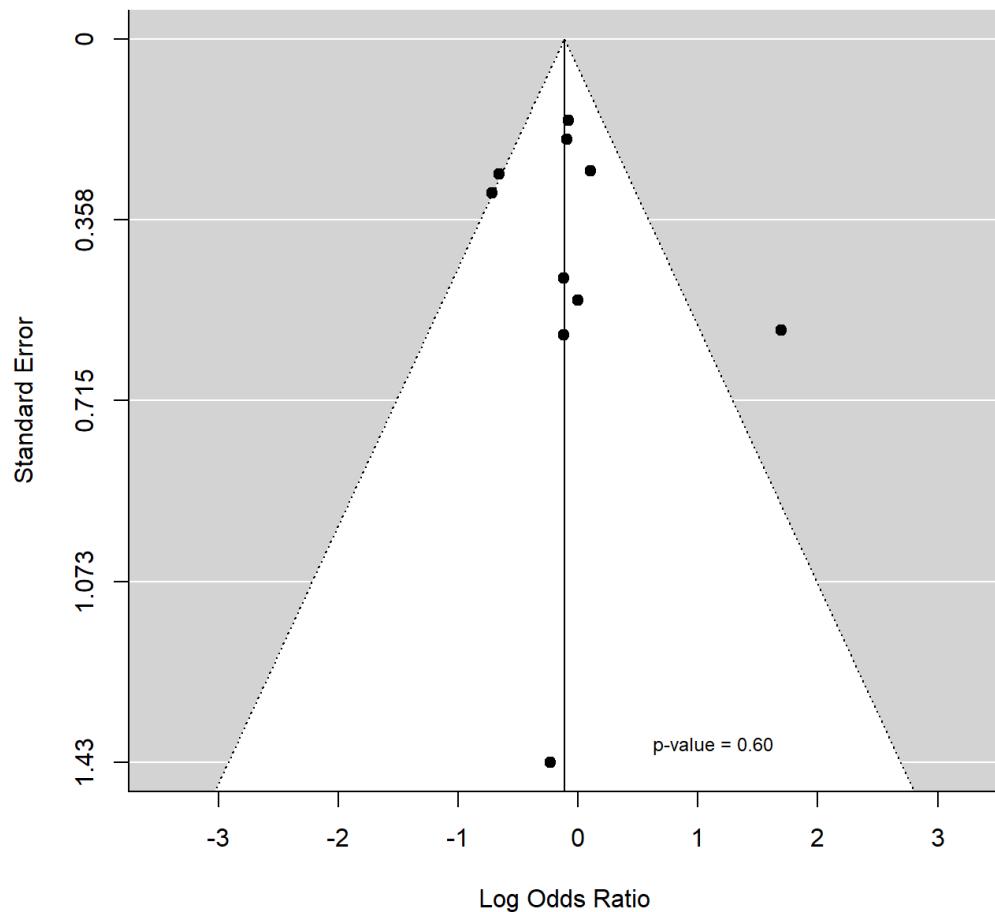
292 **eFigure 4. Subgroup Analysis of the Association Between Palliative Care and Advance Care Planning. (A)**
293 **Interdisciplinary teams involving a physician, (B) Trials of dementia excluded, (C) Trials of mixed disease**
294 **excluded.** Data are presented as the odds and 95% CIs (error bars) of a newly documented advanced care plan during
295 study follow-up. The shaded squares are proportionally sized to reflect study weight and the shaded diamonds represent
296 pooled odds and 95% CIs. The vertical red line indicates the pooled effect estimate, and the black vertical line depicts a
297 null effect. Studies are grouped according to their summary risk of bias (Low, High, Some Concerns). HF – heart failure

A**B**

C



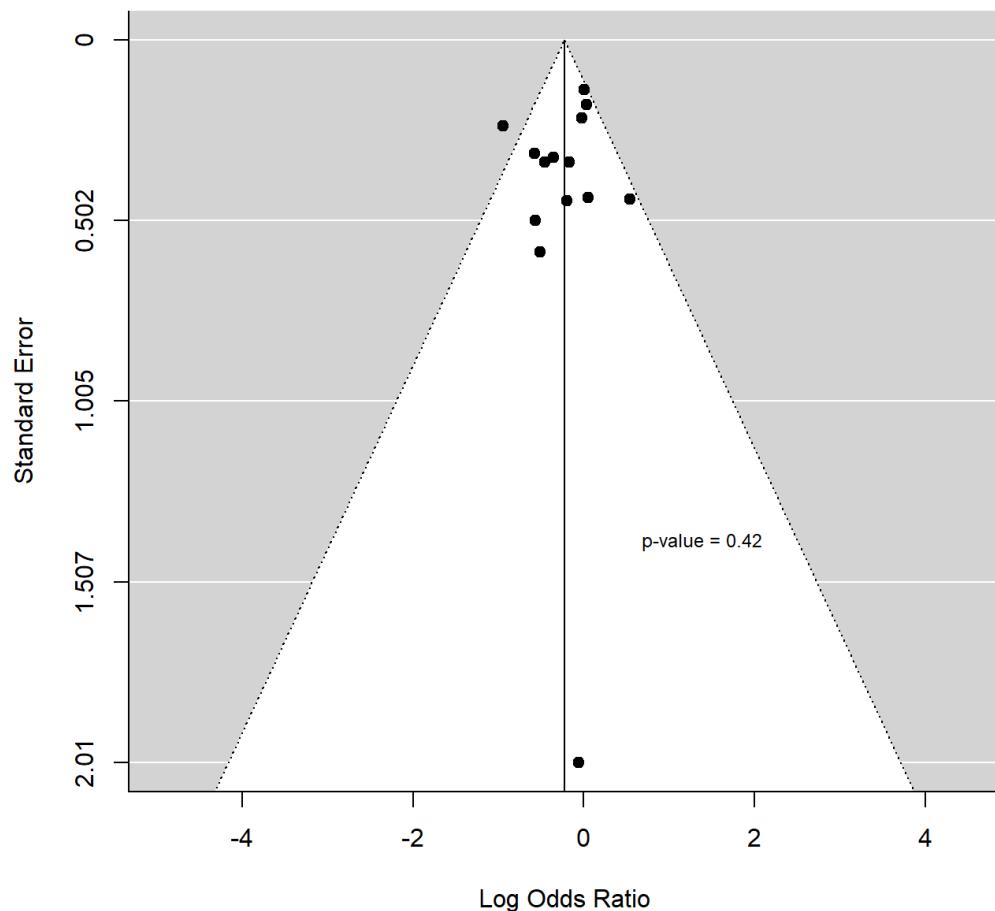
300 **eFigure 5. Funnel Plot and Egger Test to Assess the Presence of Publication Bias Among Randomized Clinical**
301 **Trials Included in the Review.** Individual studies are represented by black dots. The solid line represents the pooled
302 estimate of the effect on the outcome. The dashed lines represent the 95% confidence interval of the effect estimate.
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304 **Emergency Department Visits**



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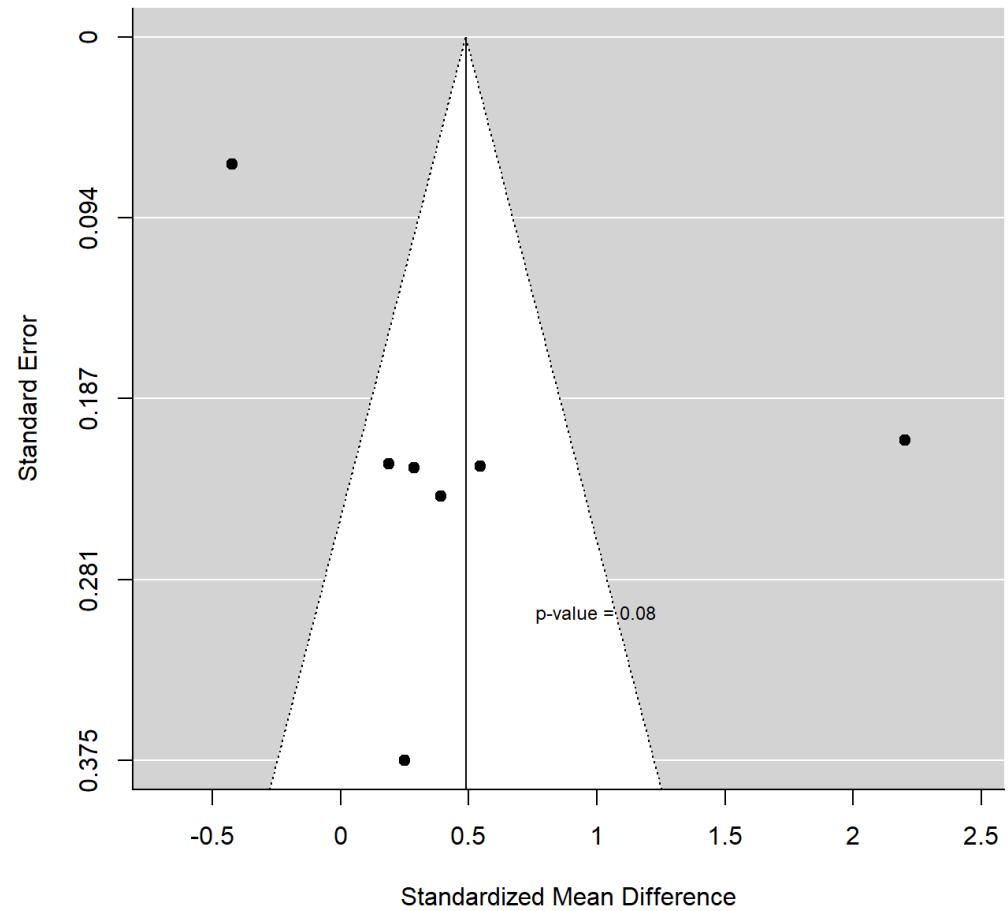
307 Hospitalization



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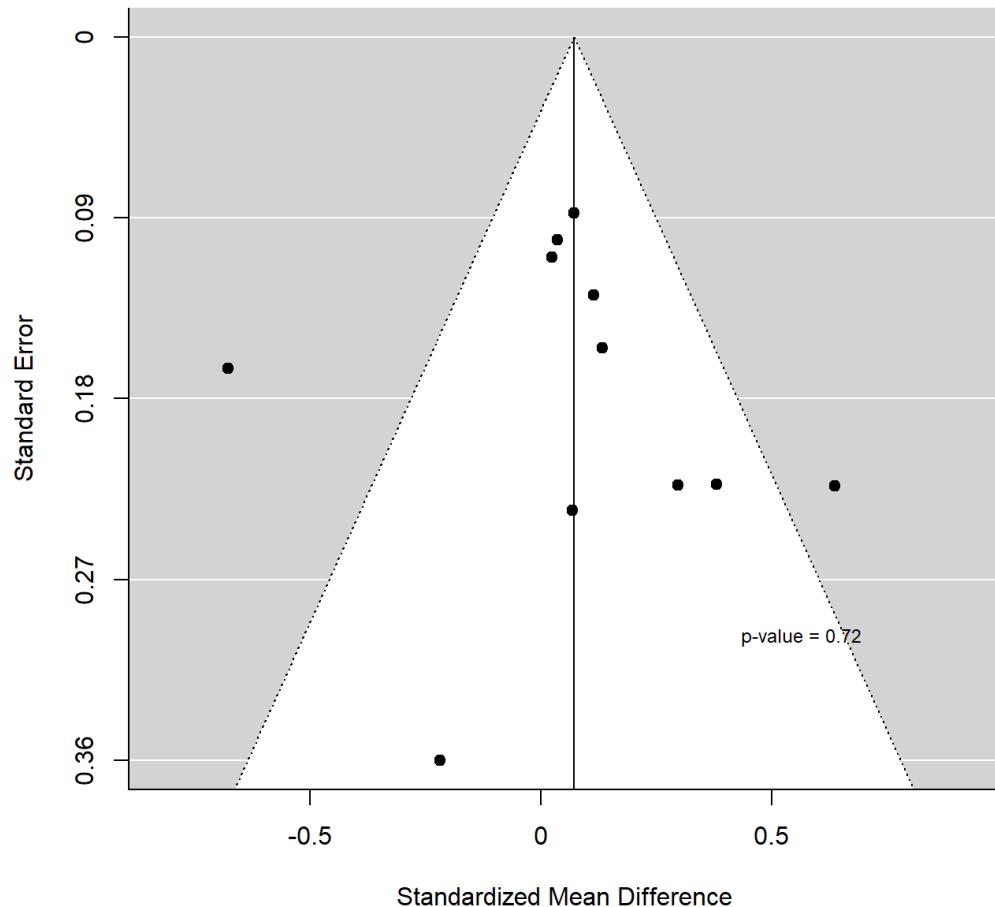
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310 Disease-Generic Quality of Life



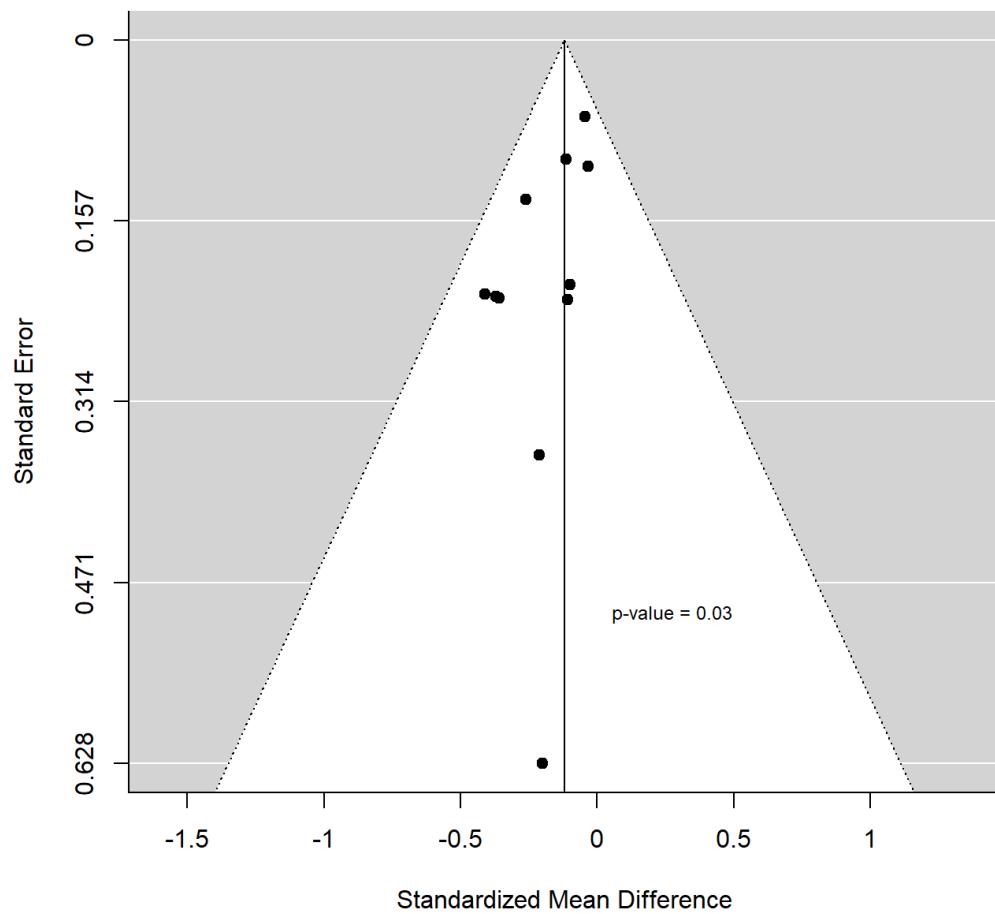
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313 Disease-Specific Quality of Life

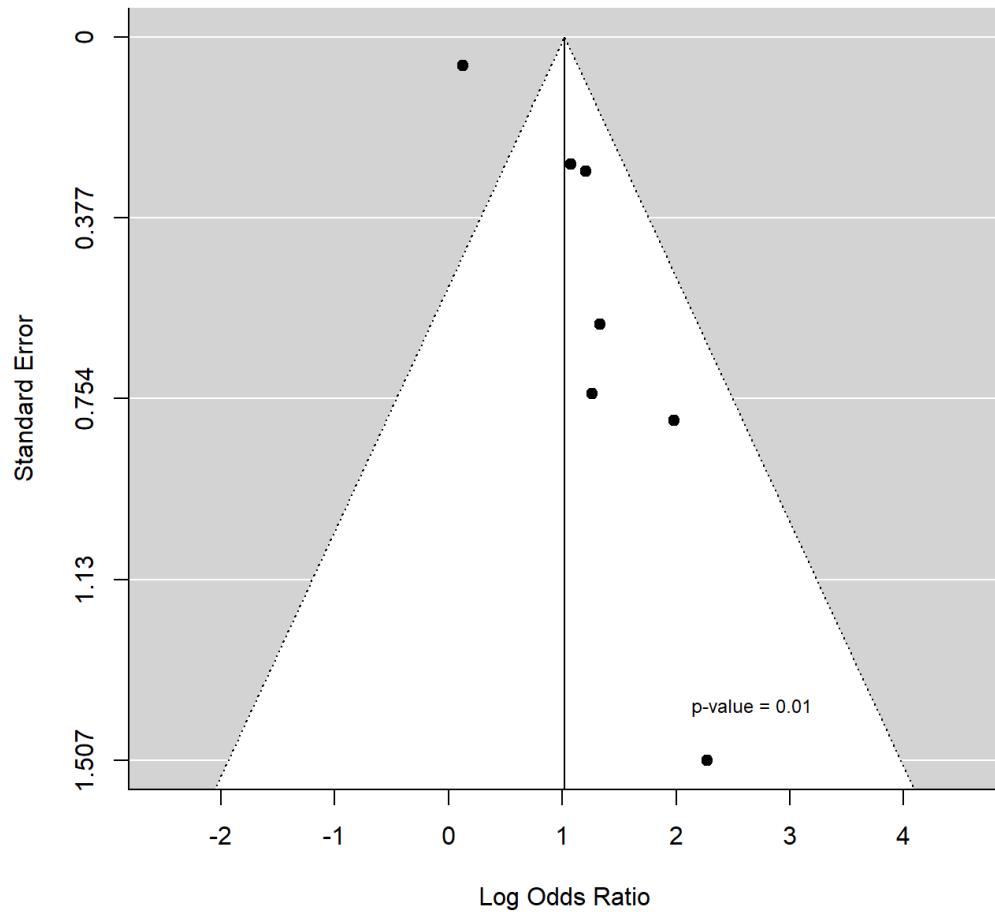


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316 **Symptoms**



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