

**Appendix Table 1. PubMed Search Strategy**

<b>Set</b>	<b>Terms</b>	<b>Results</b>
#1	"Neoplasms"[Mesh] OR neoplasms[tiab] OR neoplasm[tiab] OR cancer[tiab] OR cancers[tiab] OR malignancy[tiab] OR malignant[tiab] OR carcinoma[tiab] OR carcinomas[tiab] OR blastoma[tiab]	<b>3312258</b>
#2	"Hospice and Palliative Care Nursing"[Mesh] OR "Palliative Medicine"[Mesh] OR "Palliative Care"[Mesh] OR "Terminal Care"[Mesh:NoExp] OR "Hospice Care"[Mesh] OR "Hospices"[Mesh] OR palliative[tiab] OR palliation[tiab] OR hospice[tiab] OR "end of life care"[tiab]	<b>100731</b>
#3	"Ambulatory Care"[Mesh] OR "Ambulatory Care Facilities"[Mesh] OR "Primary Health Care"[Mesh] OR "Home Care Services"[Mesh] OR "Residential Facilities"[Mesh] OR "Physicians, Primary Care"[Mesh] OR "Physicians, Family"[Mesh] OR "Outpatients"[Mesh] OR "Emergency Medical Services"[Mesh] OR ambulatory[tiab] OR primary care[tiab] OR outpatient[tiab] OR outpatients[tiab] OR clinic[tiab] OR clinics[tiab] OR home[tiab] OR community[tiab] OR "emergency department"[tiab] OR "out patient"[tiab] OR "out patients"[tiab]	<b>1200038</b>
#4	("early palliative care"[tiab] OR "early palliative intervention"[tiab])	<b>166</b>
#5	(#2 AND #3) OR #4	<b>16509</b>
#6	((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR randomised[tiab] OR randomization[tiab] OR randomisation[tiab] OR placebo[tiab] OR randomly[tiab] OR trial[tiab] OR groups[tiab] OR "Comparative Study"[Publication Type] OR "Controlled Clinical Trial"[Publication Type] OR Nonrandom[tiab] OR non-random[tiab] OR nonrandomized[tiab] OR non-randomized[tiab] OR nonrandomized[tiab] OR non-randomised[tiab] OR quasi-experiment*[tiab] OR quasiexperiment*[tiab] OR quasirandom*[tiab] OR quasi-random*[tiab] OR quasi-control*[tiab] OR quasicontrol*[tiab] OR (controlled[tiab] AND (trial[tiab] OR study[tiab]))) NOT (animals[mh] NOT humans[mh]) NOT (Editorial[ptyp] OR Letter[ptyp] OR Case Reports[ptyp] OR Comment[ptyp]))	<b>3043573</b>
#7	#1 AND #5 AND #6	<b>1364</b>

**Appendix Table 2. Eligibility Criteria**

<b>PICOTS Study Element</b>	<b>Inclusion Criteria</b>	<b>Exclusion Criteria</b>
Population	<p>Adults <math>\geq 18</math> years of age with symptomatic or advanced malignancy defined as one of the following:</p> <ul style="list-style-type: none"> <li>• Malignancy causing symptoms such as fatigue, pain, or breathlessness, or unmet needs related to the malignancy</li> <li>• Malignancy without curative treatment options</li> <li>• Advanced stage (<i>eg</i>, stage III or IV malignancy), including statements of “late stage” or “advanced cancer”</li> </ul>	<ul style="list-style-type: none"> <li>• Patients with cancer not associated with systemic symptoms (<i>eg</i>, non-melanoma skin cancer)</li> <li>• Patients with non-cancer advanced illness</li> <li>• Studies enrolling mixed samples unless the majority are enrolled because of a symptomatic or advanced malignancy</li> </ul>
Intervention	<p>Integrated palliative care meeting the following definition:</p> <ul style="list-style-type: none"> <li>• An individual or multidisciplinary team of clinicians working together with a patient’s oncology physician(s) and having a focus on relief of symptoms and stress of serious illness. Goal is to improve quality of life for the patient and family.</li> <li>• One or more of the palliative care clinicians must have specialized training in palliative care, and the intervention must be multidimensional (<i>ie</i>, targeting at least the physical and psychosocial domains of quality of life).</li> </ul> <p>Integration may be broad, ranging from basic collaboration at a distance (<i>eg</i>, information exchanged to address specific patient treatment issues) to co-located care, to fully integrated care.</p> <p>Studies that evaluate barriers to implementing an integrated palliative care program in a research or clinical context are included</p>	<ul style="list-style-type: none"> <li>• Standalone palliative care interventions (<i>eg</i>, palliative chemotherapy, palliative radiotherapy)</li> <li>• Palliative care services delivered by clinicians without specialized training</li> <li>• Palliative care services (<i>ie</i>, hospice) delivered exclusively in the home (no outpatient clinic-based assessment) for the terminal stages of illness</li> <li>• Palliative care consultation without longitudinal services</li> <li>• Palliative care restricted to care for a single symptom (<i>eg</i>, opioids for dyspnea)</li> <li>• Palliative care intervention that targets only the caregiver</li> </ul>
Comparators	<p>KQ 1, KQ 2: Usual oncology care</p> <p>KQ 3: No comparator required for studies conducted in VA settings. For studies conducted outside of VA settings, the study must have an eligible comparator as specified for KQ 1 and KQ 2.</p>	No eligible comparator

PICOTS Study Element	Inclusion Criteria	Exclusion Criteria
Outcomes	<p>KQ 1, KQ 2:</p> <ul style="list-style-type: none"> <li>Care recipient primary outcomes: <ul style="list-style-type: none"> <li>Functional status or healthcare quality of life, defined as overall quality of life (<i>ie</i>, global quality of life) and then further defined as functional status, including physical functioning (<i>eg</i>, activities of daily living), general psychological functioning (<i>eg</i>, psychological well-being) and social functioning (<i>eg</i>, social well-being)</li> <li>Disease-related symptoms, overall symptom burden (if overall symptom burden was not reported, then include symptom assessment of fatigue, pain, or sleep)</li> <li>Care experience</li> </ul> </li> <li>Care recipient secondary outcomes: <ul style="list-style-type: none"> <li>Survival</li> <li>Site of death</li> <li>Healthcare utilization such as emergency department, inpatient, intensive care unit days, total costs</li> <li>Adverse effects</li> </ul> </li> <li>Caregiver outcomes: <ul style="list-style-type: none"> <li>Care experience</li> <li>Caregiver burden (<i>eg</i>, Caregiver Strain Index), depression (<i>eg</i>, PHQ-9)</li> </ul> </li> </ul> <p>The foregoing outcomes must be assessed using a standard instrument.</p> <p>KQ 3: Barriers to implementation, including workforce, stigma, financial, logistical (<i>eg</i>, space, communication and coordination between clinicians)</p>	Studies that do not plan to report any included outcomes; but studies that plan to report an included outcome but give only cursory results ( <i>eg</i> , p not significant) were included
Timing	<p>KQ 1, KQ 2: Studies reporting outcomes at <math>\geq 28</math> days (approximately 1 month) following initiation of integrated palliative care intervention</p> <p>KQ 3: No followup requirement; may be cross-sectional</p>	KQ 1, KQ 2: Studies reporting outcomes at $< 28$ days
Setting	<p>All KQs: Outpatient palliative care integrated with outpatient oncology services. Palliative care may be co-located or located in a separate outpatient setting. Services may be delivered in the emergency department, patient's home, by telephone, or by video.</p> <p>KQ 3: VA settings for any studies that address implementation barriers but were not eligible for KQ 1 or KQ 2</p>	Institutional settings ( <i>eg</i> , skilled nursing facility) or interventions delivered primarily to hospitalized patients

<b>PICOTS Study Element</b>	<b>Inclusion Criteria</b>	<b>Exclusion Criteria</b>
Study design	<p>KQ 1, KQ 2:</p> <ul style="list-style-type: none"> <li>• Randomized controlled trials</li> <li>• Cluster-randomized trials</li> <li>• Nonrandomized cluster trials</li> <li>• Controlled before-and-after studies with at least 2 intervention sites and 2 control sites</li> </ul> <p>KQ 3: Quantitative studies (<i>eg</i>, surveys) and qualitative studies (<i>eg</i>, focus groups, key informant interviews, qualitative case studies) that address barriers to implementation related to studies eligible for KQ 1 or KQ 2 and studies addressing barriers in VA settings Study country limited to North America, Australia, New Zealand, and Western, Northern, and Southern Europe</p>	<ul style="list-style-type: none"> <li>• Case reports, case-series, cross-sectional studies, and all studies without a comparator</li> <li>• Sample size &lt;20 (<i>ie</i>, small pilot studies that are lower quality, prone to publication bias, and not powered to detect effects on clinically important outcomes)</li> </ul>
Publication type	<ul style="list-style-type: none"> <li>• English-language only</li> <li>• Peer-reviewed articles</li> <li>• Published from 1995 forward</li> </ul>	<ul style="list-style-type: none"> <li>• Non-English articles</li> <li>• Abstracts only</li> <li>• Letters to the editor</li> <li>• Editorials</li> <li>• Dissertations</li> </ul>

### Appendix Table 3. Author Survey to Determine Integration Elements

**Please provide your name. For each question, please answer to describe the intervention arm in the cited study.**

Q1. Are palliative care provider(s) and oncology provider(s) physically or virtually located in the same space?

Yes, co-located in the same clinical space

Yes, virtually co-located by video link or similar

No

Unsure

Q2. Is written or electronic information exchanged routinely between palliative and oncology clinicians? (*eg*, alert in medical record, faxed documents)

Yes

No

Unsure

Q3. Is communication between oncology and palliative care interactive? (*ie*, “two way”)

Yes

No, exchange of information is without interactive communication

Unsure

Q4. Do providers from palliative care and oncology communicate on a “standard and routine practice” basis to address specific patient treatment issues? Communication may be in person, by email exchange, team meeting, or phone call conversation.

Yes

No

Unsure

Q5. Do the palliative care and oncology care health providers have equal roles in decision making? Are they both involved in the approach to individual patient care?

Yes

No

Unsure

Q6. Were providers involved in care in a standard way across ALL patients? (eg, do all staff use the same tools and resources, and then ensure that all patients with the same score or outcome receives the same options for treatment?)

Yes

No

Unsure

Q7. Is there one joint treatment plan for cancer patients that is shared by palliative care and oncology care providers?

Yes

No

Unsure

#### Appendix Table 4. Excluded Studies

All studies listed below were reviewed in their full-text version and excluded for the reasons cited. Reasons for exclusion signify only the usefulness of the articles for this study and are not intended as criticisms of the articles. The reference list for these excluded studies follows the table.

Exclusion reason	Not English or primary study or Protocol	Not population of interest	Not eligible study design	Not eligible setting	Not eligible intervention	Not eligible outcomes	Not OECD country	N<20
<b>Study</b>								
Abernethy, 2013 <sup>1</sup>					X			
Acorn, 2008 <sup>2</sup>					X			
Addington-Hall, 1992 <sup>3</sup>	X							
Arnold, 2010 <sup>4</sup>	X							
Bagcivan, 2018 <sup>5</sup>				X				
Bakitas, 2009 <sup>6</sup>	X							
Barrett, 2009 <sup>7</sup>			X					
Barth, 2013 <sup>8</sup>			X					
Becker, 2017 <sup>9</sup>					X			
Beernaert, 2014 <sup>10</sup>				X				
Begue, 2012 <sup>11</sup>			X					
Blackhall, 2016 <sup>12</sup>			X					
Booth, 2010 <sup>13</sup>	X							
Borneman, 2008 <sup>14</sup>			X					
Breitbart, 2012 <sup>15</sup>					X			
Brumley, 2003 <sup>16</sup>		X						
Brumley, 2007 <sup>17</sup>		X						
Bucher, 2001 <sup>18</sup>			X					
Cameron, 2004 <sup>19</sup>			X					
Chambers, 2008 <sup>20</sup>	X							
Chochinov, 2011 <sup>21</sup>			X					
Critchley, 1999 <sup>22</sup>			X					
Daly, 2013 <sup>23</sup>			X					
Davis, 2012 <sup>24</sup>	X							
DeSanto-Madeya, 2009 <sup>25</sup>				X				
Dionne-Odom, 2016 <sup>26</sup>		X						
Dionne-Odom, 2016 <sup>27</sup>					X			
Dionne-Odom, 2016 <sup>28</sup>			X					
Dionne-Odom, 2018 <sup>29</sup>	X							
do Carmo, 2015 <sup>30</sup>					X			
do Carmo, 2017 <sup>31</sup>					X			

Exclusion reason	Not English or primary study or Protocol	Not population of interest	Not eligible study design	Not eligible setting	Not eligible intervention	Not eligible outcomes	Not OECD country	N<20
<b>Study</b>								
Douglas, 2014 <sup>32</sup>					X			
Duursma, 2011 <sup>33</sup>	X							
Dyar, 2012 <sup>34</sup>								X
Edwards, 2014 <sup>35</sup>					X			
El-Jawahri, 2010 <sup>36</sup>					X			
El-Jawahri, 2016 <sup>37</sup>		X						
Engelhardt, 2006 <sup>38</sup>		X						
Eschbach, 2014 <sup>39</sup>	X							
Farquhar, 2014 <sup>40</sup>					X			
Ferrell, 2015 <sup>41</sup>			X					
Fischer, 2015 <sup>42</sup>		X						
Follwell, 2009 <sup>43</sup>			X					
Fontani, 2011 <sup>44</sup>		X						
Geiger, 2011 <sup>45</sup>			X					
Given, 2002 <sup>46</sup>					X			
Gomes, 2013 <sup>47</sup>			X					
Gomez-Batiste, 2010 <sup>48</sup>					X			
Goodwin, 2003 <sup>49</sup>					X			
Gray, 1987 <sup>50</sup>	X							
Greer, 1986 <sup>51</sup>	X							
Greer, 2012 <sup>52</sup>	X							
Grudzen, 2014 <sup>53</sup>				X				
Grudzen, 2016 <sup>54</sup>				X				
Hainsworth, 2002 <sup>55</sup>			X					
Hanks, 2002 <sup>56</sup>				X				
Hannon, 2013 <sup>57</sup>	X							
Hannon, 2014 <sup>58</sup>	X							
Hannon, 2015 <sup>59</sup>	X							
Hannon, 2016 <sup>60</sup>						X		
Hannon, 2017 <sup>61</sup>					X			
Hermann, 2012 <sup>62</sup>					X			
Higginson, 2010 <sup>63</sup>			X					
Higginson, 2010 <sup>64</sup>		X						
Higginson, 2014 <sup>65</sup>					X			
Hinton, 1998 <sup>66</sup>			X					
Hoek 2017 <sup>67</sup>					X			



Exclusion reason	Not English or primary study or Protocol	Not population of interest	Not eligible study design	Not eligible setting	Not eligible intervention	Not eligible outcomes	Not OECD country	N<20
<b>Study</b>								
Hollen, 2000 <sup>68</sup>		X						
Holm, 2016 <sup>69</sup>		X						
Holm, 2016 <sup>70</sup>					X			
Hughes, 1992 <sup>71</sup>	X							
Jack, 2003 <sup>72</sup>				X				
Jelinek, 2014 <sup>73</sup>				X				
Johnsen, 2014 <sup>74</sup>						X		
Johnson, 2011 <sup>75</sup>			X					
Jones, 2013 <sup>76</sup>				X				
Jordhøy, 2000 <sup>77</sup>					X			
Jordhoy, 2001 <sup>78</sup>					X			
Jung, 2013 <sup>79</sup>			X					
Kandarian, 2014 <sup>80</sup>						X		
Kane, 1984 <sup>81</sup>	X							
Keating, 2010 <sup>82</sup>			X					
Kissane, 2016 <sup>83</sup>					X			
Kotzsch, 2015 <sup>84</sup>			X					
Lau, 2012 <sup>85</sup>	X							
Lazenby, 2010 <sup>86</sup>	X							
Lidstone, 2003 <sup>87</sup>			X					
Lowe, 2009 <sup>88</sup>			X					
Lowery, 2013 <sup>89</sup>			X					
Lukas, 2013 <sup>90</sup>		X						
Maeda, 2016 <sup>91</sup>			X					
McCorkle, 1998 <sup>92</sup>					X			
McDonald, 2015 <sup>93</sup>	X							
McDonald, 2015 <sup>94</sup>	X							
McDonald, 2016 <sup>95</sup>						X		
McDonald, 2017 <sup>96</sup>		X						
McLoughlin, 2015 <sup>97</sup>	X							
McMillan, 2002 <sup>98</sup>			X					
McMillan, 2011 <sup>99</sup>		X						
Mills, 2009 <sup>100</sup>					X			
Moore, 2002 <sup>101</sup>					X			
Morita, 2009 <sup>102</sup>		X						
Nabal, 2013 <sup>103</sup>			X					

Exclusion reason	Not English or primary study or Protocol	Not population of interest	Not eligible study design	Not eligible setting	Not eligible intervention	Not eligible outcomes	Not OECD country	N<20
<b>Study</b>								
Nakajima, 2016 <sup>104</sup>			X					
Nipp, 2016 <sup>105</sup>			X					
Nipp, 2018 <sup>106</sup>	X							
Nordly, 2014 <sup>107</sup>						X		
Northouse, 2005 <sup>108</sup>					X			
Northouse, 2007 <sup>109</sup>					X			
Northouse, 2013 <sup>110</sup>					X			
Nottelmann, 2017 <sup>111</sup>	X							
Obel, 2014 <sup>112</sup>			X					
Obermeyer, 2016 <sup>113</sup>			X					
Odejide, 2014 <sup>114</sup>				X				
Oliver, 2012 <sup>115</sup>	X							
Ornstein, 2017 <sup>116</sup>					X			
Otsuka, 2013 <sup>117</sup>			X					
Ozcelik, 2014 <sup>118</sup>				X				
Pachman, 2011 <sup>119</sup>			X					
Parikh, 2013 <sup>120</sup>	X							
Phillips, 2008 <sup>121</sup>		X						
Rabow, 2003 <sup>122</sup>			X					
Rabow, 2003 <sup>123</sup>		X						
Rabow, 2004 <sup>124</sup>		X						
Raftery, 1996 <sup>125</sup>					X			
Ragnarson-Tennvall, 1999 <sup>126</sup>			X					
Raphaël, 2005 <sup>127</sup>			X					
Reville, 2009 <sup>128</sup>	X							
Schenker, 2015 <sup>129</sup>			X					
Schenker, 2018 <sup>130</sup>					X			
Sekelja, 2010 <sup>131</sup>		X						
Seow, 2014 <sup>132</sup>			X					
Silveira, 2011 <sup>133</sup>	X							
Skov Benthien, 2018 <sup>134</sup>						X		
Smeenk, 1998 <sup>135</sup>					X			
Smeenk, 1998 <sup>136</sup>				X				
Sochor, 2014 <sup>137</sup>	X							
Steel, 2016 <sup>138</sup>					X			
Steinhauser, 2008 <sup>139</sup>			X					

Exclusion reason	Not English or primary study or Protocol	Not population of interest	Not eligible study design	Not eligible setting	Not eligible intervention	Not eligible outcomes	Not OECD country	N<20
<b>Study</b>								
Stern, 2012 <sup>140</sup>		X						
Strasser, 2016 <sup>141</sup>					X			
Sun, 2015 <sup>142</sup>			X					
Tattersall, 2014 <sup>143</sup>					X			
Temel, 2007 <sup>144</sup>			X					
The SUPPORT Principal Investigators, 1995 <sup>145</sup>		X						
Thomas, 2016 <sup>146</sup>	X							
Tuca-Rodriguez, 2012 <sup>147</sup>			X					
Uitdehaag, 2014 <sup>148</sup>					X			
Vinciguerra, 1986 <sup>149</sup>	X							
Vinciguerra, 1986 <sup>150</sup>	X							
Vuksanovic, 2016 <sup>151</sup>					X			
Wang, 2011 <sup>152</sup>		X						
Warren, 2011 <sup>153</sup>			X					
Wentlandt, 2012 <sup>154</sup>					X			
Wilkie, 2016 <sup>155</sup>					X			
Yennu, 2014 <sup>156</sup>	X							
Yoong, 2012 <sup>157</sup>								X
Yoong, 2013 <sup>158</sup>								X
Young, 2013 <sup>159</sup>		X						
Zimmermann, 2010 <sup>160</sup>			X					
Zimmermann, 2012 <sup>161</sup>	X							

## References in Appendix Table 4

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**Appendix Table 5. Strength of Evidence for Effects of Integrated Outpatient Palliative Care and Oncology in Symptomatic or Advanced Cancer**

<b>Outcome</b>	<b>Number of RCTs (Patients)</b>	<b>Findings<sup>a</sup></b>	<b>Strength of Evidence (Rationale by Domain)</b>
Quality of life, short-term (follow-up range 1 to 3 months)	9 (1487)	SMD 0.24 higher (0.13 higher to 0.35 higher)	Moderate SOE serious ROB, consistent, precise
Quality of life, long-term (follow-up range 27 weeks to 13 months)	5 (549)	SMD 0.15 higher (0.12 lower to 0.43 higher)	Low SOE serious ROB, consistent, imprecise
Overall symptom burden (follow-up range 1 to 3 months)	5 (837)	SMD 0.25 lower (0.39 lower to 0.11 lower)	Very low SOE serious ROB, inconsistent, imprecise
Mortality (follow-up range 12 to 36 months)	4 (866)	HR 0.77 (0.61 to 0.98) 96 fewer deaths per 1,000 patients (7 to 179 fewer deaths)	High SOE low ROB, consistent, precise

<sup>a</sup> SMD reported is from the sensitivity analyses excluding the single high risk of bias study.

Abbreviations: RCT=randomized controlled trial; ROB=risk of bias; SMD=standardized mean difference;

SOE=strength of evidence

Note: Mortality estimate excludes Groenvold et al. 2017.

**Appendix Table 6. Study Characteristics**

<b>Study Location Total N</b>	<b>Intervention Setting Comparator Time Since Diagnosis</b>	<b>Mean Age in Years % Female Veteran?</b>	<b>% Cancer Type Severity or Prognosis</b>	<b>Outcomes Reported</b>	<b>ROB by Outcome Category</b>
Bakitas, 2009 <sup>13</sup> United States 322	Outpatient Usual care 8-12 weeks	Int: 64.7 Com: 65.4 Int: 40.4% Com: 43.5% Yes	Lung: 36-37% GI: 41-42% Breast: 10-11% GU: 11-12% Stage III or IV	<u>Patient</u> Mental status Quality of life* Disease symptoms* Survival Health services use*	Objective: Low Patient-reported: Low
Bakitas, 2015 <sup>36</sup> United States 207	Home Delayed palliative care Within 30-60 days of diagnosis or recurrence	Int: 64.0 Com: 64.6 Int: 46.2% Com: 48.5% Yes	Lung: 41-44% GI: 23-25% Breast: 10-12% Other: 21-23% Advanced stage	<u>Patient</u> Mental status* Quality of life* Disease symptoms* Survival* Health services use*	Objective: Unclear Patient-reported: Unclear
Clark, 2013 <sup>38</sup> United States 138	Outpatient Usual care Within 12 months	Int: 58.7 Com: 59.9 Int: 37% Com: 32% No	Lung: 11-15%, GI: 36-39% Other: 46-53% Advanced stage ECOG range 0-2	<u>Patient</u> Mental status Quality of life* <u>Caregiver</u> Experience (QOL)	Objective: NR/NA Patient-reported: High
Groenvold, 2017 <sup>41</sup> Denmark 297	Outpatient Usual care 40% < 12 months	Int: 47.6% age 60-79 Com: 44.1% age 60-79 Int: 57% Com: 59% No	Int: Lung: 39% GI: 14% Breast: 21% Other: 26% Com: Lung: 30% GI: 25% Breast: 23% Other: 22%	<u>Patient</u> Survival*	Objective: Unclear

<b>Study Location Total N</b>	<b>Intervention Setting Comparator Time Since Diagnosis</b>	<b>Mean Age in Years % Female Veteran?</b>	<b>% Cancer Type Severity or Prognosis</b>	<b>Outcomes Reported</b>	<b>ROB by Outcome Category</b>
Maltoni, 2016 <sup>34</sup> Europe 207	Outpatient Standard care plus on demand PC Within 8 weeks	Int: 67 (median) Com: 66 (median) Int: 38.5% Com: 47.2% No	Pancreatic: 100% inoperable or metastatic >2 months	<u>Patient</u> Mental status* Quality of life* Disease symptoms* Care experience Health service use	Objective: Unclear Patient-reported: High
McCorkle, 2015 <sup>35</sup> United States 146	Outpatient Enhanced usual care Within 100 days	Int: 51.5% <age 65 Com: 71.3% <age 65 Int: 71.2% Com: 43.7% No	Int: Lung: 56.1% Gyn: 43.9% Comp: GI: 66.2% Head/neck: 33.8% Late-stage	<u>Patient</u> Physical status* Mental status* Quality of life* Disease symptoms*	Objective: Unclear Patient-reported: High
Rummans, 2006 <sup>39</sup> United States 115	Outpatient Usual care Within 12 months	Int: 59.7 Com: 59.4 Int: 40.8% Com: 31.5% No	Lung: 11-18% GI: 36-39%, Other: 45-50% Prognosis > 6 month	<u>Patient</u> Mental status Quality of life* <u>Caregiver:</u> Experience (QOL)	Objective: NR/NA Patient-reported: Unclear
Temel, 2010 <sup>15</sup> United States 151	Outpatient Usual care Within 8 weeks	Int: 65.0 Com: 64.9 Int: 55% Com: 49% No	Lung: 100% Metastatic ECOG range 0-2	<u>Patient</u> Trial Outcome Index* Mental status Quality of life Survival Site of death Health service use	Objective: Low Patient-reported: Unclear

<b>Study Location Total N</b>	<b>Intervention Setting Comparator Time Since Diagnosis</b>	<b>Mean Age in Years % Female Veteran?</b>	<b>% Cancer Type Severity or Prognosis</b>	<b>Outcomes Reported</b>	<b>ROB by Outcome Category</b>
Temel 2017 <sup>40</sup> United States 350	Outpatient Usual care Within 8 weeks	Int: 65.64 Com: 64.03 Int: 48% Com: 44% No	<u>Int</u> Lung: 54.3% GI: 20.6% Pancreatic: 25.1% <u>Com</u> Lung: 54.9% GI: 20.6% Pancreatic: 24.6% NR other than eligibility of "incurable"	<u>Patient</u> Mental status Quality of life*	Objective: NR/NA Patient-reported: Low
Zimmermann, 2014 <sup>37</sup> Canada 461	Outpatient Usual care NR	Int: 61.2 Com: 60.2 Int: 59.6% Com: 53.6% No	Lung: 20-24% GI: 28-33% Gyn/GU: 25-39% Stage III or IV ECOG range 0-2	<u>Patient</u> Quality of life* Disease symptoms Health service use <u>Caregiver</u> Family satisfaction with patient care	Objective: Low Patient-reported: Unclear

Abbreviations: Com=comparator; ECOG=Eastern Cooperative Oncology Group; GI=gastrointestinal; GU=genitourinary; Gyn=gynecologic; Int=intervention; NA=not applicable; NR=not reported; QOL=quality of life; ROB=risk of bias

\*Primary outcome measure identified by study.

## Appendix Table 7. Clinical Elements of Palliative Care and Definitions

Below are the definitions for the 8 clinical elements of palliative care interventions. The table that follows shows which elements were present in each included study and the frequency of the intervention. For full study citations, please refer to the report's main reference list.

- **Structural** and processes of care: interdisciplinary team engagement (engagement with patients or families, coordinated assessment and continuity of care across healthcare settings)
- **Physical** aspects of care: what is being done to decrease symptoms (assessment and pharmacological, interventional, behavioral and/or complementary treatments)
- **Psychological** or psychiatric aspects of care: what is being done to address mental health issues (assessment and treatment of psychological and/or psychiatric concerns for patient or caregiver)
- **Social** aspects of care: interdisciplinary engagement and collaboration with patients and families (identify, support or capitalize on their strengths; facilitate patient-family understanding of illness; perform social assessment including caregiving or adaptive equipment needs, or need/access to community resources)
- **Spiritual**, religious, and existential aspects of care: support of spiritual belief system, if present (practices or rituals for comfort/relief; this ideally involves a trained chaplain on the palliative care team)
- **Cultural** aspects of care: identification of and respect for cultural differences (tailored communication to literacy level and language spoken; accommodation of cultural practices and traditions)
- **End of life** care of patient: guidance through the dying process (information on what to expect at end of life, suggestions of coping strategies; *eg*, the stages of grief: denial through acceptance)
- **Ethical and legal** aspects of care: goals of care (discussions about impact of treatment decisions, determination of patient's decision-making capacity, advance care planning completion; *eg*, Do Not Resuscitate [DNR])

<b>Study Impact Rating</b>	<b>Frequency and Duration of Intervention</b>	<b>Structural</b>	<b>Physical</b>	<b>Psychological</b>	<b>Social</b>	<b>Spiritual</b>	<b>Cultural</b>	<b>End of Life</b>	<b>Ethical/Legal</b>
Bakitas, 2009 <sup>13</sup> Moderate	Four 30-40 minute weekly education sessions via telephone; monthly follow-up calls averaging 12 minutes; dyads invited to attend monthly group	No	Physical symptom management; <i>eg</i> , self-care	Psychological symptom management; <i>eg</i> , problem-solving	Attention to communication and coordination of resources	No	No	Advance care planning	Decision making about advance care planning
Bakitas, 2015 <sup>36</sup> Low	Six 30-45 minute weekly coaching sessions via telephone; 10 monthly follow-up calls	No	Physical symptom management; <i>eg</i> , self-care	Psychological symptom management; <i>eg</i> , problem-solving	Attention to communication and coordination of resources	Framing advanced illness challenges as personal growth opportunities	No	Life review as applies to advance care planning	Decision making about advance care planning
Clark, 2013 <sup>38</sup> Low	Six 90-minute sessions in-person over 2 weeks; 10 phone calls over 6 months	No	Physical therapy exercises and management of health behavior, substance use, symptoms	Psychological symptom and mood management	Social needs & communication strategies	Exploration of meaning, purpose, grief, and loss	No	No	Writing advance directives
Groenvold, 2017 <sup>41</sup> Low	Individualized frequency and intensity; 95% of patients had at least one face-to-face visit with team and 80% had at	No	Yes, but no details	Yes, but no details	No	No	No	No	No



<b>Study Impact Rating</b>	<b>Frequency and Duration of Intervention</b>	<b>Structural</b>	<b>Physical</b>	<b>Psychological</b>	<b>Social</b>	<b>Spiritual</b>	<b>Cultural</b>	<b>End of Life</b>	<b>Ethical/Legal</b>
	least one telephone contact over the 8-week trial								
Maltoni, 2016 <sup>34</sup> Low	Every 2-4 weeks from enrollment until death	Yes, but no details	Yes, but no details	Yes, but no details	No	Yes, but no details	No	No	No
McCorkle, 2015 <sup>35</sup> None	10 weekly visits	Coordinated interdisciplinary team that collaborates with other providers to teach patients and families	Physical symptom management: executing care procedures and addressing adverse events	Counseling to clarify illness experience and enhance quality of life	Enhancing self-efficacy for decision making and problem solving about family and caregivers	No	No	No	Goals for advance care discussed
Rummans, 2006 <sup>39</sup> Low	Eight 90 minutes sessions over 3 weeks	No	Physical therapy exercises and discussion of healthy lifestyle	Cognitive behavioral therapy for mood; stress management and irrational thinking	Sources and use of support, communication, interpersonal relationships and coping	Explore grief, guilt, hope, purpose, meaning, rituals, beliefs, death	No	Explore end of life, death, and afterlife; other "spiritual aspects"	No
Temel, 2010 <sup>15</sup> Moderate	Once within 3 weeks from randomization, and monthly thereafter	Yes, but no details	Yes, but no details	Yes, but no details	Yes, but no details	Yes, but no details	No	Yes, but no details	Yes, but no details
Temel,	Visit with	Regular	Helping to	Addressed	Addressed	Addressed	No	Discussed	Discussed

<b>Study Impact Rating</b>	<b>Frequency and Duration of Intervention</b>	<b>Structural</b>	<b>Physical</b>	<b>Psychological</b>	<b>Social</b>	<b>Spiritual</b>	<b>Cultural</b>	<b>End of Life</b>	<b>Ethical/Legal</b>
2017 <sup>40</sup> Low	palliative care team member $\geq$ 1 time/month until death	palliative care appointments; oncologist could schedule extra palliative care visits; inpatient palliative care team followed if admitted	understand prognosis, treatment options; then making treatment goals, communicate care preferences	coping, depression, and anxiety	coping with family, familial understanding of illness, and family caregiver referral	spiritual coping, rituals, and belief systems		end-of-life care preferences and life review	advance care planning
Zimmermann, 2014 <sup>37</sup> Low	Initial consult, 1 week follow-up via phone; Monthly outpatient visits; On-demand telephone management for urgent issues for 4 months	Multi-disciplinary assessment	Assessment of symptoms; urgent care if necessary	Assessed psychological distress	Assessed social support	No	No	No	No

## Appendix Table 8. IMPACT Ratings Table and Definitions Used

The table that follows contains details related to how the impact rating was determined for each study comparing integrated palliative and oncology care interventions to a comparator or control. Table cells show what was measured, the timepoint of measurement, and an indication of the effect size. All comparisons are in the direction of intervention versus control. For full study citations, please refer to the report's main reference list.

Definitions of the impact ratings:

- **High**—Pattern of positive effects across all patient-centered outcomes; may also have positive effects on end-of-life care and/or utilization. Magnitude of effects include at least 1 primary outcome with summary or median SMD/effect size of 0.8 or greater; mean difference that substantially exceeds the minimum clinically important difference; or risk ratio (RR) or hazard ratio (HR)  $\geq 2$  or odds ratio (OR)  $\geq 3$ .
- **Moderate**—Pattern of mostly positive effects across patient-centered outcomes; may also have positive effects on end-of-life care and/or utilization. Magnitude of effects include at least 1 primary outcome with summary or median SMD/effect size of  $\geq 0.5$ ; mean difference that meets or exceeds the minimum clinically important difference; or RR or HR  $\geq 1.5$  or  $\geq 2$ .
- **Low**—Inconsistent pattern of statistically positive and negative effects across patient-centered outcomes; may also have inconsistent effects on end-of-life care and/or utilization. Magnitude of effects include at least 1 primary outcome with summary or median SMD/effect size of  $\geq 0.25$ ; mean difference that is statistically significant but does not meet the minimum clinically important difference; or RR or HR  $\geq 1.25$  or  $\geq 1.5$ .
- **No impact**—Pattern of statistically nonsignificant effects or inconsistent pattern of statistically positive and negative effects but all patient centered outcomes are statistically nonsignificant.

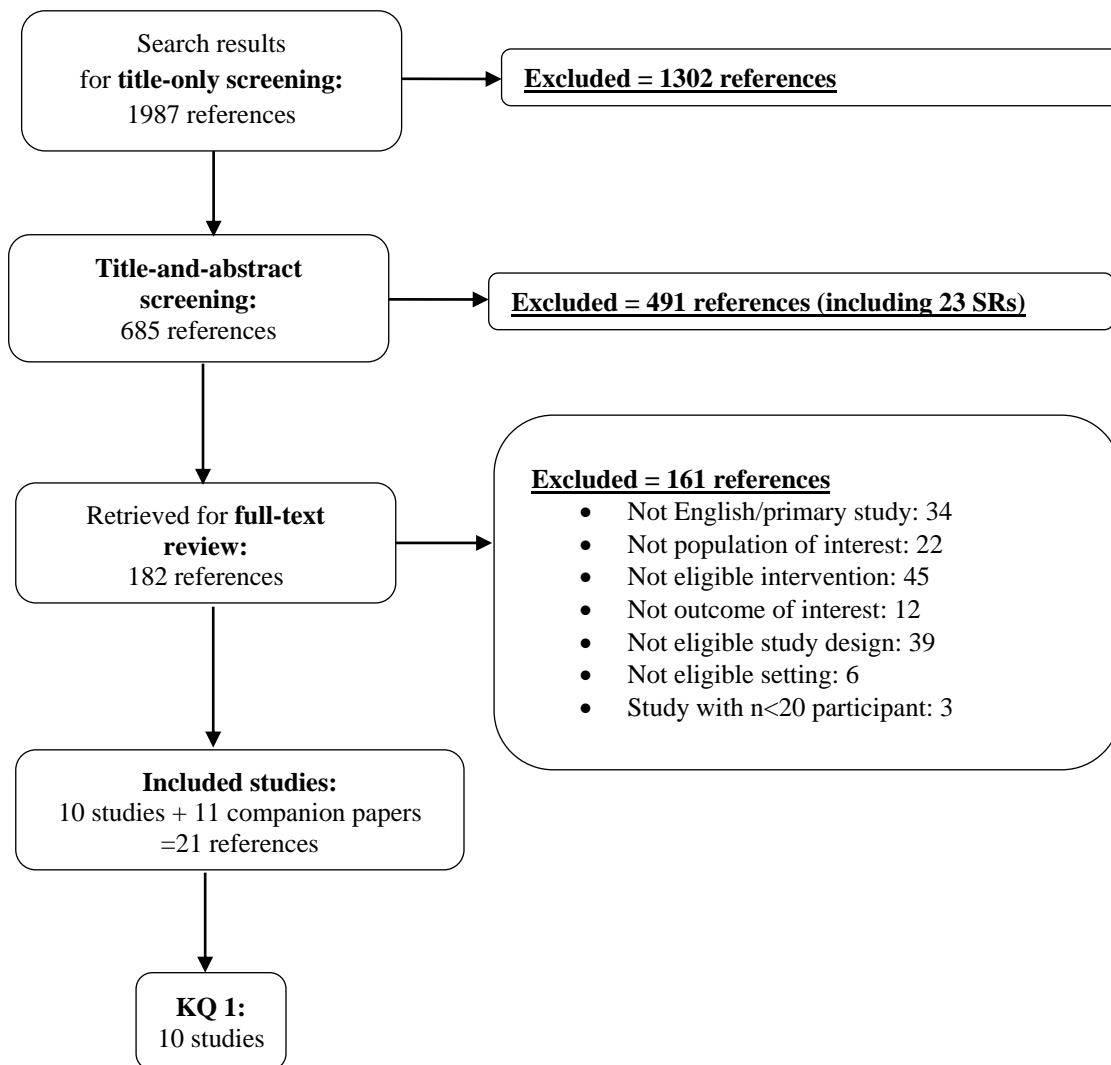
Study	QOL	Symptom Burden	Mortality	Site of Death	End of Life Treatment	HC Utilization	Final Impact Rating
Bakitas, 2009 <sup>13</sup>	<u>At 13 months</u> FACT-PC mean difference: 4.6 (SE 2.0), p=0.02	<u>At 13 months</u> CES-D mean difference: -1.8 (SE 0.81), p=0.02  ESAS mean difference: -27.8 (SE 15), p=0.06	Survival at longest follow-up: 49/161 vs 42/161, p=0.14  Median survival time: 14 months vs 8.5 months, p=NR	NR	NR	<u>At 13 months</u> Hospital days (range 0 to 25), p=0.14  ICU days (range 0 to 2), p>0.99  ER visits (range 0 to 4), p=0.53	Moderate
Bakitas, 2015 <sup>36</sup>	<u>At 3 months</u> TOI Cohen's d: 0.11, p=0.24  <u>At 12 months</u> Cohen's d: 0.11, p=0.24;	<u>At 3 months</u> QUAL-E Cohen's d: -0.21, CES-D Cohen's d: 0.04,  <u>At 12 months</u> QUAL-E Cohen's d: -0.31, CES-D Cohen's d: 0.1,  <u>Significance over all timepoints (3,6,9,12)-</u> QUAL-E, p=0.09 CES-D, p=0.33	1 year survival rate: 66/104 vs 49/103, p=0.038  Average length of survival: 18.3 vs 11.8 months	Died at home: 27/50 vs 28/59, p=0.60	In decedents, chemotherapy during last 2 weeks of life measured at end of study RR=1.57 (95% CI 0.37 to 6.7)	In decedents, hospital days at end of study: RR=0.73 (95% CI 0.41 to 1.27), p=0.26  ICU days at end of study: RR=0.68 (95% CI 0.23 to 2.02), p=0.49  ED visits at end of study: RR=0.73 (95% CI 0.45 to 1.19), p=0.21	Low
Clark, 2013 <sup>38</sup>	<u>At 4 weeks</u> FACT-G mean difference: 5.5 (no SD), p=0.02  <u>At 27 weeks</u> mean difference: 0.1, p=0.88	<u>Exact timepoints unknown</u> POMS: p=NS  FACT Spiritual Well-being Scale: p=NS	NR	NR	NR	NR	Low
Groenvold, 2017 <sup>41</sup>	NR	NR	Overall median survival: 323 days vs. 364 days, p=0.16	NR	NR	NR	Low
Maltoni, 2016 <sup>34</sup>	<u>At 12±3 weeks</u> TOI mean difference: 6.3 (95% CI 0.75 to 11.95)	<u>Overall</u> HCS mean difference: 3.78 (95% CI 0.86 to 6.71), p=0.008  <u>At 12±3 weeks</u> HADS-A: p=0.06 HADS-D: p=0.28, NS	Survival probability at study end: 22.4% vs 12.3%, NS	At home vs hospice: p=0.138, NS  At nursing home: p=0.702, NS	Chemotherapy last 30 days: p=0.192, NS  Admission 30 days before death: p=0.539, NS  ER visits 30 days before death: p=0.729, NS	Primary care visits at 12±3 weeks and at study end: p=0.0001  Hospitalizations, timeframe unclear: p=0.417, NS  ER visits to study end: p=0.891, NS	Low
McCorkle, 2015 <sup>35</sup>	<u>At 3 months</u> FACT-G: p=0.371	<u>At 3 months</u> SDS: p=0.610 for	NR	NR	NR	NR	None

Study	QOL	Symptom Burden	Mortality	Site of Death	End of Life Treatment	HC Utilization	Final Impact Rating
		time*group  HADS-A: p=0.1173  PHQ-9: p=0.927 for time*group					
Rummans, 2006 <sup>39</sup>	<u>At 4 weeks</u> Spitzer Uniscale mean difference: 8.7 (no SD), p=0.047, % of people improved by 8 points, p=0.025  <u>At 27 weeks</u> mean difference: 0, p>.99, improved by 8 points NR	<u>At 4 weeks</u> SDS: p=NS  POMS: p=NS  FACIT-SP mean difference: 9, p=0.003	NR	NR	NR	NR	Low
Temel, 2010 <sup>15</sup>	<u>At 12 weeks</u> TOI mean difference: 6.0 (95% CI 1.5 to 10.4), Cohen's d 0.52, p=0.009  FACT-L: mean difference 6.5 (95% CI 0.5 to 12.4), Cohen's d 0.42, p=0.03	<u>At 12 weeks</u> overall LCS mean difference: 1.7 (95% CI 0.1 to 3.2), p=0.04  Specific diagnosis, % meeting threshold- PHQ-9: p=0.04  HADS-D: p=0.0  HADS-A: p=0.66, NS	Overall median survival: 11.6 months (95% CI 6.4 to 16.9) vs 8.9 (95% CI 6.3 to 11.4), p=0.02	<u>At 18 mo follow-up</u> Place of death (home vs other): 40/61 vs 36/66, p=0.28	Aggressive care: 16/49 vs 30/56, p=0.05  Hospitalization (30 days before death): 18/49 vs 30/56, p=NR; Chemotherapy (last 60 days of life): 32/61 vs 47/67, p=0.05  ED (30 days before death): 11/49 vs 17/56, p=NR	Hospitalizations from enrollment to death: 36/49 vs 43/56, p=NR  ED days during entire study: 26/49 vs 32/56, p=NR  Cost savings mean difference: \$117 (\$74)	Moderate
Temel, 2017 <sup>40</sup>	<u>At 12 weeks</u> FACT-G mean difference: 2.40 (95% CI -0.38 to 5.18), p=0.09  <u>At 24 weeks</u> mean difference: 5.36 (95% CI 2.04 to 8.69), p=0.02	<u>At 12 weeks</u> PHQ-9 mean difference: -0.78 (95% CI -1.76 to 0.21), p=0.12  <u>At 24 weeks</u> mean difference: -1.17 (95% CI -2.33 to -0.01), p=0.048	NR	NR	NR	NR	Low
Zimmermann, 2014 <sup>37</sup>	<u>At 3 months</u> FACIT-SP mean difference: 3.56 (95% CI, -0.27 to 7.40), p=0.07	<u>At 3 months</u> ESAS mean difference: -1.70 (95% CI, -5.26 to 1.87), p=NS	Raw data for number of deaths: 44/228 vs 26/233, p=NR	NR	NR	NR	Low

Study	QOL	Symptom Burden	Mortality	Site of Death	End of Life Treatment	HC Utilization	Final Impact Rating
	At 4 months mean difference: 6.44 (95% CI, 2.13 to 10.76), p=0.006	At 4 months mean difference: -4.41 (95% CI, -8.76 to -0.06), p=0.05					

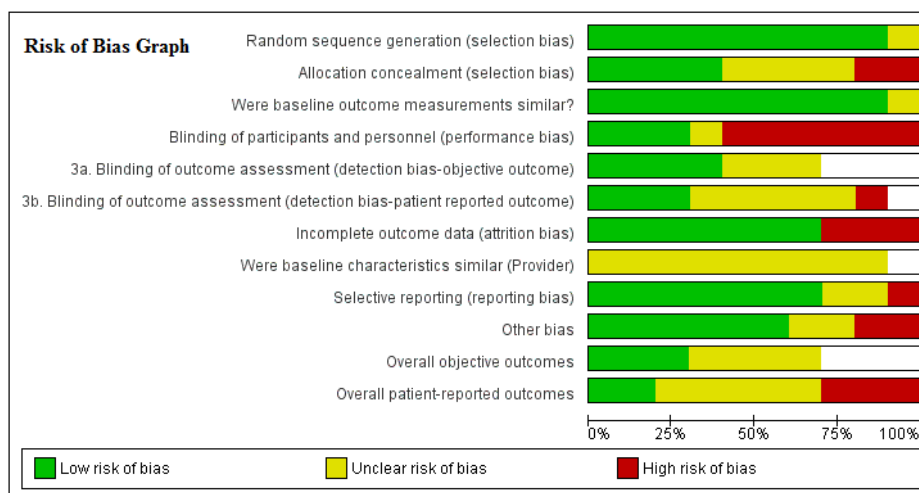
Abbreviations: CES-D=Center for Epidemiologic Studies Depression Scale; CI=confidence interval; ED=emergency department; ER=emergency room; ESAS=Edmonton Symptom Assessment Scale; FACIT-SP=Functional Assessment of Chronic Illness Therapy-Spiritual Well-Being; FACT-G=Functional Assessment of Cancer Therapy-General; FACT-L=Functional Assessment of Cancer Therapy-Lung; HADS=Hospital Anxiety and Depression Scale; HCS=Hepatobiliary Cancer Subscale; LCS=Lung cancer subscale; NR=not reported; PHQ=Patient Health Questionnaire; POMS=Profile of Mood States; QOL=quality of life; QUAL-E=Quality of life at end of life symptom impact subscale; SDS=Symptom Distress Scale; TOI=Trial Outcome Index

**Appendix Figure 1. PRISMA Literature Flow**



**Appendix Figure 2. Risk of Bias Elements**

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Were baseline outcome measurements similar?	Blinding of participants and personnel (performance bias)	3a. Blinding of outcome assessment (detection bias-objective outcome)	3b. Blinding of outcome assessment (detection bias-patient reported outcome)	Incomplete outcome data (attrition bias)	Were baseline characteristics similar (Provider)	Selective reporting (reporting bias)	Other bias	Overall objective outcomes	Overall patient-reported outcomes
Bakitas,2009	+	?	+	-	+	-	+	?	+	+	+	+
Bakitas,2015	+	?	+	?	+	+	+	?	+	?	?	?
Clark,2013	?	?	+	-		?	-	?	-	-		-
Groenvold,2017	+	+	+	+	?		+		+	+	?	?
Maltoni,2016	+	-	?	-	?	?	-	?	?	?	?	-
McCorkle,2015	+	+	+	+	+	?	-	?	+	-	?	-
Rummans,2006	+	?	+	-		+	+	?	+	+		?
Temel,2010	+	-	+	-	?	?	+	?	+	+	+	?
Temel 2017	+	+	+	-		+	+	?	?	+		+
Zimmermann,2014	+	+	+	+	+	?	+	?	+	+	+	?

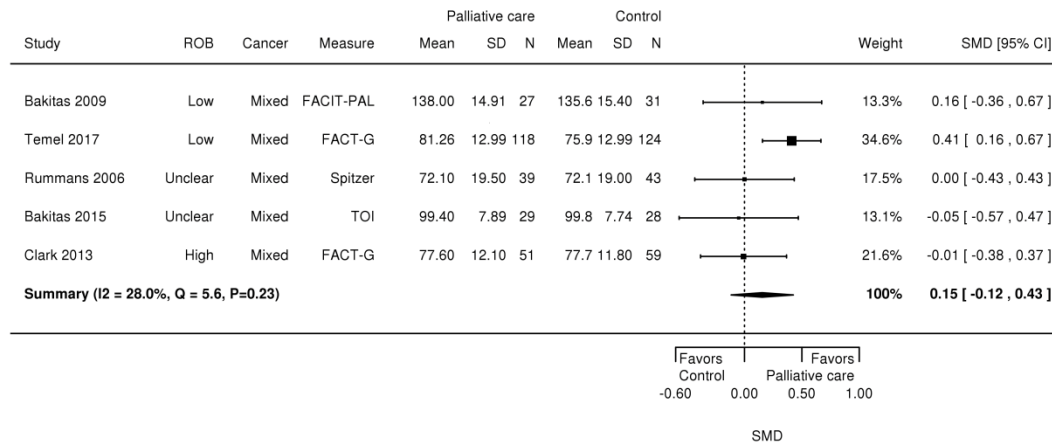


<sup>a</sup>White space indicates items that were not applicable.

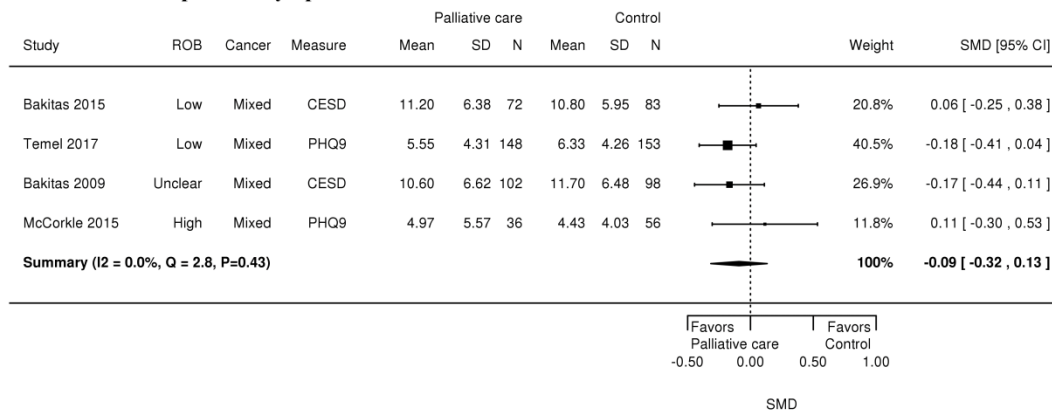


## Appendix Figure 3. Integrated Palliative Care Outcomes

### 3A: Long-term (6-12 months) Effects on Quality of Life



### 3B: Effects on Depressive Symptoms



### 3C: Risk of Dying at Home

