

Appendix Table 1. Systematic Reviews and Meta-analyses of Symptoms, Advance Care Planning, Continuity, and Caregiving

Author, Year (Reference)	Domains Addressed	Type of Review	End Date of Search	Intervention	Studies Observational	Overlap With Other Reviews	Description of Subjects Included	Treatments Assessed*	Principal Outcomes Assessed*	Intervention Duration and Timing of Outcomes	Results
Higginson et al., 2000 (25)	Symptom: pain	Systematic review and meta-analysis	February to June 1999	72 citations including 5 systematic reviews, and 67 reports of 43 unique studies; 15 of 30 studies identified through reviews as were randomized and controlled, as were 4 additional studies.	14 of 30 studies identified through systematic reviews were retrospective or observational, as were 10 of the additional studies	Intervention studies and analysis of site of death overlap completely with Gomes and Higginson's (80) update. Gysels and Higginson's (27) review addressed a much broader spectrum of issues within cancer care, unlike this one that focused on end stage, not specific to cancer.	Patients cared for by palliative care services (home care, hospital-based, and hospice in Europe, Australia, and the United States.	Any intervention of more than 1 individual, at least 1 of whom has specialist training, or who spends all their working time in palliative care, in a hospital, home or community setting, or in a combination of these.	Patient and caregiver quality of life and symptoms, site of death, healthcare use and costs.	Short-, intermediate-, and long-term interventions	This review focused uniquely on a meta-analysis and review of the clinical effectiveness of palliative care teams. Outcomes were extracted from all studies considered by the review. Patient outcomes were characterized as pain, other symptoms, quality of life, satisfaction, referral to other services, and therapeutic interventions. Twenty studies evaluated pain as an outcome, and standardized mean differences (SMD) were determined. The mean SMD was 0.41 (95% CI, 0.11 to 0.63) in favor of the effect of palliative care teams in reducing pain.
Carr et al., 2002 (26)	Symptoms: pain and depression	Systematic review	June 2001	34 RCTs of pain interventions	N/A	The pharmacologic and medical therapies for pain and depression are not addressed elsewhere. The findings about the effectiveness of psychosocial and education changes are also addressed within Gysels and Higginson's (27) systematic review of supportive cancer care.	Patients with cancer	Any treatment for cancer-related pain and depression	Pain	Most were intermediate- to short-term.	The review updated a review conducted for the AHRQ 2 y earlier. Thirty-four new studies, 5 of which were studies of chemotherapeutic agents, nonsteroidals, adjuvant analgesics, radiotherapy or radiopharmaceuticals, opioids trials, and bisphosphonates. This update was consistent with the original review that found consistent evidence for the efficacy of these interventions, although study heterogeneity (in intervention design as well as outcome) precluded meta-analysis. The review was also unable to address the preferred route of administration or comparisons among drugs. Eleven controlled trials of the effect of medications on depressive symptoms in cancer patients were identified (6 of which were randomized, 1 of which addressed depression prevention and 1 of which was a pain study that included a depression outcome). All studies of antidepressants for ≥ 6 wk demonstrated efficacy. Two studies that were limited to 4-wk trials did not. Hundreds of studies addressed psychosocial interventions for depression, so the review only summarized meta-analyses. Psychosocial studies, including group or individual counseling, education, and social support strategies were effective. 11 controlled trials of the effect of medications on depressive symptoms in cancer patients were identified, (6 of which were randomized) 1 of which addressed depression prevention, and 1 of which was a pain study that included a depression outcome. All studies of antidepressants for six or more weeks demonstrated efficacy. 2 studies which were limited to 4 week trials did not. Hundreds of studies addressed psychosocial interventions for depression, so the review only summarized meta-analyses. Psychosocial studies, including group or individual counseling, education, and social support strategies were effective.

Gysels and Higginson, 2004 (27)	Symptoms: pain, dyspnea, and depression	Systematic review	March 2003	317 studies (22 overlapped multiple review domains), many studies addressed symptoms, although the review did not present results specifically by symptoms	317 studies (22 overlapped multiple review domains), many studies addressed symptoms although the review did not present results specifically by symptoms	Partial overlap with other earlier reviews that covered aspects of care planning or support for caregivers of patients with cancer. This review was much more comprehensive and included a discussion of other reviews and meta-analyses relevant to the topic.	Patients with cancer	Any intervention to improve supportive or palliative care. Review examined diverse system interventions to improve aspects of supportive or palliative cancer care. These interventions included care coordination, promoting user involvement, face-to-face communication, improving information, psychological, spiritual, and social support, generalist and specialist palliative care delivery, rehabilitation, complementary and alternative therapies, and caregiver support, including bereavement.	Symptoms; quality of life; patient, caregiver, and provider satisfaction with care; knowledge; place of care and site of death; and utilization	Short-, intermediate-, and long-term interventions	The review covered a broad range of interventions, especially those related to the clinical organization of care to improve supportive care for cancer, although symptoms were not a specific aim of the review.
Pan et al., 2000 (28)	Symptoms: pain and dyspnea	Systematic review	1998	11 RCTs, 2 nonrandomized, controlled trials	8 case reports	Low-quality studies overlapped with Lee et al. (31)	Patients receiving palliative or terminal care.	Complementary and alternative interventions for pain and dyspnea.	Pain and dyspnea	Not reported	The review underscores the relevance of these approaches for improving symptomatic care, although there was mixed evidence in favor of any particular approach with regard to pain or dyspnea. The review examined social support and spiritual care. Two systematic reviews and 15 studies, including 6 high-quality, RCTs addressed social support. These studies all highlighted the importance of bridging professional roles and multidisciplinary efforts to improve social support. Fifteen studies within the overall review examined various interventions with behavioral components that were generally effective for depression. All studies of spiritual support that were identified were low quality, pointing out the need for additional research.
Wilson, 2004 (29)	Symptom: pain	Systematic review	September 2003	24 studies, designs not reported.	Designs not reported.	Intervention studies covered overlap almost completely with previous reviews by Higginson et al. (25) and Gysels and Higginson (27).	Patients with serious, chronic, or terminal illness	Palliative care and hospice service delivery innovations in hospital, home care, nursing home, and hospice settings.	Pain and other symptoms	Short-, intermediate-, and long-term interventions	Most studies identified were observational, but interventions identified were reviewed by Gysels and Higginson (27) and Higginson et al. (25). The review was not organized to address symptom interventions specifically, although pain was frequently reported as an outcome of these studies.
Knols et al., 2005 (30)	Symptoms: pain and depression	Systematic review	June 2004	34 RCTs and controlled, clinical trials	N/A	None	Patients with cancer (16 addressed breast cancer, 22 addressed active treatment, and 12 post-treatment phase)	Physical exercise	Physical function and quality of life, including symptoms	5 wk–12 mo	Approximately half of studies included some measure of quality of life or symptoms. Among these heterogeneous studies, a beneficial effect of exercise was noted on pain in 2 studies, and depression or anxiety in 5 studies.

Lee et al., 2005 (31)	Symptom: pain	Systematic review	February 2004	7 intervention studies	N/A	The 1 high-quality, randomized study was published in 2003. Low-quality studies overlapped with Pan et al. (28)	Patients with cancer	Manual and ear acupuncture, electro-acupuncture	Pain	Immediate to 1 mo	3 RCTs were identified, only 1 of which was high quality (Jadad score 5). This placebo-controlled, 3-arm study of ear acupuncture in 90 patients demonstrated efficacy using the visual analogue scale.
Furlan et al., 2006 (32)	Symptom: pain	Meta-analysis	May 2005	41 randomized trials	N/A	None	6019 patients with chronic noncancer pain, average age 58.1 y (range, 40–71), 63% female, 85% white	Any opioid administered for 7 d or more. Trials were identified for codeine, morphine, tramadol, and propoxyphene	Intensity of pain relief, function, and opioid side effects	1–16 wk	Thirty randomized, placebo-controlled trials identified, of which 28 were meta-analyzed (pain standardized mean difference [SMD], -0.60 [CI -0.69 to -0.050]) Functional status (SMD, -0.31 [CI -0.41 to -0.22]). Side effects that occurred more commonly on opioids included constipation (risk difference [RD], 16%), nausea (RD, 15%), dizziness or vertigo (RD, 8%), somnolence or drowsiness (RD, 9%), vomiting (RD, 5%) and dry skin, itching, or pruritis (RD, 4%). Most trials addressed arthritis or neuropathic pain, and the degree to which they addressed late-stage disease is unclear.
Tremont-Lukats et al., 2005 (33)	Symptom: pain	Meta-analysis	December 2002	27 randomized, double-blind, controlled trials	N/A	None	Patients with neuropathic pain, average age 51.7 y, median size for trials was 28	Systematically administered local anesthetic-type drugs (mexilitine, lidocaine, and tocainamide)	Pain intensity (100 mm VAS most common)	Immediate-to short-term	19 trials evaluated lidocaine or mexilitine for chronic, neuropathic pain and found they were effective vs. placebo (weighted mean difference [WMD], -10.60 mm [CI, -14.52 to -6.68, <i>P</i> < 0.001), 5 trials compared lidocaine, mexilitine, or tocainamide vs. other analgesics and found no difference (WMD, -0.60 mm [CI -6.96 to 5.75 mm]). The degree to which these trials addressed late-stage disease is unclear.
Jennings et al., 2002 (61)	Symptom: dyspnea	Meta-analysis	May 1999	18 double-blind, RCTs	N/A	None	Patients with dyspnea from any disease. Two studies addressed cancer and 1 heart failure.	Any opioid given to relieve dyspnea	Dyspnea (most studies used visual analogue scale)	Immediate (single-dose studies) to short-term, (multiple-dose duration not described.)	16 of 18 studies had Jadad scores of 4, all of them only failing to describe randomization procedures. All studies were small with the total sample in the 18 studies of 293 and the largest study of 79 patients. Results across these studies were consistent, and 12 studies showed a pooled SMD, -0.31 (CI -0.50 to -0.13). No clinically significant adverse effects of opioids on respiratory function were noted in these studies.
Salman et al., 2003 (62)	Symptom: dyspnea	Meta-analysis	September 2000	20 randomized trials	N/A	None	Patients with COPD (FEV1 < 70% or FEV1/FVC < 70%). Almost all studies addressed patients in their mid-60s.	Any type of rehabilitation (upper-extremity, lower-extremity, or respiratory muscle exercise)	Exercise capacity and dyspnea (12 studies used the CRQD)	6–12 wk for patients with mild or moderate COPD (15 studies); 10 wk–2 mo for patients with severe COPD (6 studies)	Both walking distance and dyspnea outcomes were strongly related. Among all 12 studies that used the CRQD, 11 that included at least lower extremity training (vs. 1 that did not) demonstrated a pooled benefit. Of 3 studies of severe COPD, 2 that included at least 6 mo (vs. 1 of < 3 mo) did not demonstrate benefit. Short- and longer-term trials were both effective in mild to moderate COPD.
Booth et al., 2004 (63)	Symptom: dyspnea	Meta-analysis	End date not reported (most recent trial 2001)	37 studies, including 29 randomized designs	N/A	None	Patients with advanced cancer, heart failure, and COPD	Intermittent, ambulatory, and long-term oxygen therapy	All studies reported some measure of dyspnea (most commonly Borg or visual analogue scale)	Immediate, longer-term trials up to 12 wks	Most studies (22) were conducted to evaluate intermittent oxygen use during exertion for COPD. Of these, 13 demonstrated a benefit on dyspnea. Only 2 were negative, and others indicated increased endurance with equivalent dyspnea. Fewer studies evaluated COPD patients at rest, patients with cancer, or heart failure. With the exception of oxygen for exercise, evidence was mixed for all these conditions. 2 of 3 studies in advanced cancer showed benefit in crossover trials comparing room air.
Ram et al., 2005 (64)	Symptom: dyspnea	Meta-analysis	April 2004	20 RCTs	N/A	None	Patients with stable COPD	Theophylline treatment for ≥ 7	Dyspnea, patient preference, and walk distance	Not reported	Only 2 studies reported dyspnea and wheezing using similar numerical scale. Together, they found nonsignificant improvements in symptoms. Five other studies reported disparate measures of symptoms, all of which reported improvement in the intervention group.

Shukla et al., 2006 (65)	Symptom: dyspnea	Meta-analysis	December 2005	54 RCTs of crossover or parallel design from 33 unique studies	N/A	None	Patients with symptoms, stable airflow obstruction (FEV1 <75%). Patients could be receiving inhaled steroids. Trials were included if FEV1/FVC was <70% at baseline.	Long-acting β -agonists (fomoterol or salmeterol) vs. anticholinergics (ipatropium or tiotropium) or placebo with or without rescue β -agonists	Dyspnea-free days, rescue medication use and exacerbations, and dyspnea self-report	4–16 wk	Few studies reported symptom-free days and nights, and measures were heterogeneous. Twelve studies comparing long-acting β -agonists to placebo reduced exacerbations (odds ratio [OR], 0.74 [CI, 0.64 to 0.87]). Four studies reported hospitalization and the pooled effect indicated reduced risk of hospitalization. No difference was noted vs. anticholinergics. Two studies comparing long acting β -agonists to placebo reported dyspnea using the Transitional Dyspnea Index and the pooled effect for the odds ratio of clinically meaningful improvement in dyspnea was 1.70 (CI 1.25 to 2.31, $P < 0.001$). No difference in TDI was noted in 2 studies that compared long acting β -agonists to anticholinergics.
Roffe et al., 2005 (71)	Symptom: depression	Systematic review	Search termination not reported but most recent citation 2002	6 RCTs	N/A	None	Patients with mixed-stage cancer	Guided imagery, imagery, or visualization as the sole adjuvant to patients undergoing therapy, or sole palliative therapy	Depression, anxiety	Immediate to 3 wks	Only 4 of 6 studies were published and all were small and of low quality. No conclusions could be drawn about the effectiveness of guided imagery.
Walsh et al., 1998 (75)	Advance care planning	Systematic review	August 1997	10 RCTs	N/A	Four of 10 studies also cited by Gysels and Higginson (27)	Cancer outpatients	Communication interventions to improve breaking bad news, including written summaries and audiotapes	Knowledge recall, understanding, satisfaction, psychological well-being	5 d–5 mo	Inconsistent effects on knowledge and satisfaction noted, and few studies addressed psychological adjustment.
Hanson et al., 1997 (76)	Advance care planning	Systematic review	March 1996	16 studies, 7 of which were randomized trials	N/A	This review and its conclusions overlap almost entirely with Guo and Harstall (79)	Healthy and chronically ill outpatients	Interventions to improve end-of-life care	Advance directive completion	Not reported	All the studies addressed end-of-life discussions and advance directive completion.
Baggs, 2002 (77)	Advance care planning	Systematic review	2000	86 reports of some overlapping studies, including multiple reports from 4 intervention trials, 3 of which were randomized	Mostly observational studies.	Interventions covered by Higginson et al. (25)	Patients with advanced or terminal illness, age >45 y	Interventions addressed hospital-based, end-of-life care	Diverse	Not reported	The few and diverse nature of the interventions precludes conclusions about effective practices to improve care.
Song, 2004 (78)	Advance care planning	Systematic review	December 2002	7 studies, including 5 RCTs	2 observational studies	No other review aimed to characterize effective outcomes.	Healthy or chronically ill, mostly elderly outpatients. One study addressed inpatients.	Discussions about end-of-life care	Satisfaction, emotional well-being	Not reported.	Few studies have evaluated effective outcomes of advance care planning. Three studies, 2 of which were randomized, showed improved satisfaction or emotional well-being following discussions. No study demonstrated a worsening of satisfaction or emotional well-being following care planning discussions.

Guo and Harstall, 2004 (79)	Advance care planning	Systematic review	March 2004	1 systematic review [Rofee et al. (71)] and 10 RCTs	N/A	This report subsumed Hanson et al. (76)	Mostly elderly patients, including those in nursing homes (2 studies), hospitals, and outpatient settings	Interventions to improve advance directive implementation	Advance directive completion rates, understanding, satisfaction	Not reported	The review was intended to identify studies supporting advance directive implementation. Six of the RCTs, as well as studies addressed in the review, support the effectiveness various communication interventions (prompts to physicians, physician-patient communication, education) to improve advance directive completion rates in outpatient and nursing home settings.
Gomes and Higginson, 2006 (80)	Advance care planning	Meta-analysis	September 2004	58 studies, including 3 RCTs and 1 quasi-experimental study	54 observational studies	Studies through 1999 were addressed in a previous report (4)	Terminally ill patients with cancer	Intervention studies included various palliative care or hospice services	Site of death	Not reported	The review identified a limited number of interventional studies. 17 factors were associated with home death in the observational literature, including low functional status, preferences, previous receipt of home care and its intensity, living with relatives, and extended family support.
Higginson et al., 2000 (25)	Advance care planning	Systematic review and meta-analysis	February to June 1999	72 citations, including 5 systematic reviews and 67 reports of 43 unique studies. 15 of 30 studies identified through reviews were randomized and controlled, as were 4 additional studies.	14 of 30 studies identified through systematic reviews were retrospective or observational, as were 10 of the additional studies	Changes and analysis of site of death overlap completely with Gomes and Higginson's (80) update.	Patients cared for by palliative care services (home care, hospital-based, and hospice in Europe, Australia, and the United States	Any intervention of more than 1 individual, at least 1 who has specialist training or spends all their working time in palliative care, in a hospital, home or community setting, or in a combination of these.	Patient and caregiver quality of life and symptoms, site of death, healthcare utilization, and costs.	Short-, intermediate-, and long-term interventions	This review focused uniquely on a meta-analysis and review of the clinical effectiveness of palliative care teams. Many of the palliative interventions are included in a later update focused specifically on cancer Gysels and Higginson (27). Outcomes were extracted from all studies considered by the review. 9 studies included information on home death rate. Although the SMD was significant (0.28), excluding 1, large, outlier study (National Hospice Study) reduced the estimate of effect and its significance 0.18 (CI -0.07 to 0.33).
Shalowitz et al., 2006 (81)	Advance care planning	Systematic review	December 2004	16 studies, including 2 interventions	14 observational studies	None	Unclear	The 2 intervention trials addressed whether discussing patient preferences improved surrogate accuracy	Patient-surrogate concordance	Not reported	Only 2 of 16 studies evaluated interventions. Observational studies indicated that surrogates often understood patient preferences (68% concordance for 19 526 paired responses); however, the 2 intervention studies were ineffective in improving surrogate concordance.
Wilson, 2004 (29)	Advance care planning	Systematic review	September 2003	11 studies, design not reported	Design not reported	Intervention studies covered in Wilson overlap almost completely with previous reviews by Higginson et al. (25) and Gysels and Higginson (27)	Patients with serious, chronic, or terminal illness	Palliative care and hospice service delivery innovations in hospital, home care, nursing home, and hospice settings.	Advance directive completion	Short, intermediate, and long-term interventions	Most studies identified were observational, but interventions identified were reviewed by Gysels and Higginson (27) and Higginson et al. (25).

Gysels and Higginson, 2004 (27)	Continuity	Systematic review	March 2003	317 studies (22 overlapped multiple review domains), 13 studies on coordination of care, including 11 RCTs.	317 studies (22 overlapped multiple review domains), 2 observational studies address coordination, 5 addressed information enhancement	Wilson (29) overlapped but was much less extensive	Patients with cancer	Any intervention to improve supportive or palliative care. Review examined diverse system interventions to improve aspects of supportive or palliative cancer care. These interventions included care coordination, promoting user involvement, face-to-face communication, improving information, psychological, spiritual, and social support, generalist and specialist palliative care delivery, rehabilitation, complementary and alternative therapies, and caregiver support including bereavement.	Symptoms, quality of life, patient, caregiver, and provider satisfaction with care, knowledge, place of care and site of death, utilization	Short-, intermediate-, and long-term interventions	The review covered a broad range of interventions, especially those related to the clinical organization of care, to improve supportive care for cancer.
				2 meta-analyses (discussing 23 RCTs) and 11 RCTs addressed face-to-face communication.							The review addressed several areas with specific implications for continuity— coordination of care, information, and communication. A key aspect of studies that improved coordination and was associated with successful home-based care was enhanced communication between professional providers and caregivers.
				2 meta-analyses, 1 of which included 10 RCTs and 17 additional RCTs on information enhancement							With respect to face-to-face communication, the review suggested that a few high-quality studies support training strategies to improve physician communication. Mixed evidence supports a relationship between improved physician communication and patient outcomes.
											Regarding information enhancement strategies, effective approaches stressed processes that included listening to, recording, and responding to patients' needs and priorities.

Higginson et al., 2000 (25)	Continuity	Systematic review and meta-analysis	February to June 1999	72 citations including 5 systematic reviews, and 67 reports of 43 unique studies; 15 / 30 studies identified through reviews were randomized and controlled, as were 4 additional studies.	14 / 30 studies identified through systematic reviews were retrospective or observational, as were 10 of the additional studies	Changes and analysis of site of death overlap completely with Gomes and Higginson's (80) update	Patients cared for by palliative care services (home care, hospital-based, and hospice) in Europe, Australia, and the United States	Any intervention of more than one individual, at least one of whom has specialist training, or who spends all their working time in palliative care, in a hospital, home / community setting or in a combination of these.	Patient and caregiver quality of life and symptoms, site of death, healthcare utilization, costs.	Short, intermediate, and long term interventions	This review focused uniquely on a meta-analysis and review of the clinical effectiveness of palliative care teams. Many of the palliative interventions are included in a later update focused specifically on cancer (27). Outcomes were extracted from all studies considered by the review. 9 studies included information on home death rate. Although the SMD was significant (0.28), excluding one, large outlier study (National Hospice Study) reduced the estimate of effect and its significance (0.18, 95% CI -0.07 to 0.33).
McAlister et al., 2004 (116)	Continuity	Meta-analysis	2003	29 randomized trials	N/A	Focused on outpatient heart failure care and broad inclusion criteria.	5039 patients with heart failure	Outpatient-based multidisciplinary management strategies	Mortality, readmission	3–12 mo	Based on a priori decision and confirmed by tests of homogeneity, studies were evaluated based on whether they were multidisciplinary team oriented, focused on enhancing patient self care, or used telephone coordination. Multidisciplinary teams demonstrated the most impact on mortality risk (risk ratio [RR] 0.75, 95% CI 0.59 to 0.96), heart failure (RR 0.74, 95% CI 0.63 to 0.87) and all-cause hospitalizations (RR 0.81, 95% CI 0.71 to 0.92). Other strategies were beneficial, but less so.
Phillips et al., 2004 (117)	Continuity	Meta-analysis	October 2003	18 randomized controlled studies	N/A	Narrowly construed to evaluate high-quality studies of readmission, the study overlaps partially with McAlister (24) and Windham (29) which was broader in aims and design inclusion criteria.	Older (>55 y) patients discharged from the hospital with heart failure. 3304 patients in the included studies were 62% male and 14% nonwhite. Mean participant age was >70 y in 16/18 trials and mean left ventricular ejection fraction <40% in 8 trials.	Interventions targeting heart failure with components for inpatient care and post-discharge support.	Readmission and mortality	3–12 mo	Patients in these trials had a high mortality rate (10-30% over 6-12 mo of follow-up). During a pooled mean observation period of 8 mo, there were less readmissions in 18 studies among intervention than control patients (relative risk [RR] 0.75, 95% CI 0.64 to 0.88). In 14 studies, there was a trend toward lower mortality among intervention patients, and in 6 studies a greater percentage improvement in quality of life scores.
Ram et al., 2004 (114)	Continuity	Meta-analysis	May 2003	7 randomized trials	N/A	None	744 patients presenting to the emergency department with an acute exacerbation of COPD, considered for admission, elderly (mean age in 6 trials 66–71 y), balanced gender except for 1 study	Hospital at home versus hospitalization	Mortality (6 studies) and readmission (7 studies)	2–3 mo	Mortality (relative risk 0.89, 95% CI 0.72 to 1.12) and hospital re-admission (relative risk 0.61, 95% CI 0.36-1.05) were not significantly different compared with inpatient care. Costs were significantly lower in four studies (1 Spanish, 1 Australian) that reported it favoring hospital at home.

Smeenk et al., 1998 (115)	Continuity	Systematic review	1997	9 studies, including 5 randomized	Not reported	Complete overlap of intervention studies with Higginson et al. (25)	Patients with terminal cancer	Intervention aimed at more than 1 aspect of care with the main goal of improving home support	Quality of life, readmission	Immediate to 6 mos	Heterogeneity and limited outcomes did not allow for synthesis, but there were no benefits to special home care services for patients with cancer. Very few high quality studies were identified.
Taylor et al., 2005 (113)	Continuity	Meta-analysis	January 2005	9 RCTs	N/A	None	Patients with moderate to severe chronic obstructive pulmonary disease (COPD)	Nurse led or coordinated case management	Mortality, readmission, and quality of life (7 studies) and disability (5 studies)	3–12 mo	2 studies evaluated interventions of only 1 mo with little evidence of benefit. Meta-analysis of longer term interventions indicated no difference in mortality (odds ratio 0.85, 95% CI 0.58 to 1.26), as well as quality of life, disability, or emotional well-being. Mixed evidence was found (2 trials favoring, 3 not favoring) with respect to reducing readmission.
Wilson 2004 (29)	Continuity	Systematic review	September 2003	11 studies, design not reported	Design not reported	Intervention studies covered in Wilson overlap almost completely with prior reviews by Higginson et al. (25) and Gysels and Higginson (27)	Patients with serious, chronic, or terminal illness	Palliative care and hospice service delivery innovations in hospital, home care, nursing home, and hospice settings.	Communication and site of care	Short-, intermediate-, and long-term interventions	Most studies identified were observational, but interventions identified were reviewed by Gysels and Higginson (27) and Higginson et al. (25). One summary covered nurse case management, finding mixed evidence, although only 4 relevant RCTs were cited.
Windham et al., 2003 (118)	Continuity	Systematic review	March 2002	32 studies including 15 RCTs, 16 controlled designs	1 descriptive study	Focused on older heart failure patients regardless of setting.	Older patients with heart failure (median study size, 63)	Interventions to reduce utilization	Hospital admissions (29 studies), hospital days, and other utilization measures	Not reported	More effective studies used a variety of interventions including close monitoring of symptoms by nurses or care managers. Education was common component of effective programs, and they often included a multidisciplinary team component (e.g., physician, nurse, and case managers).
Acton and Kang, 2001 (132)	Caregiving burden	Meta-analysis	1999	24 reports, including 13 experimental studies and 14 quasi-experimental or before and after evaluations	N/A	The study was dementia-specific, so narrower than Sorenson (133) and more stringent designs than Yin (130)	1254 caregivers of patients with dementia (mean 51 participants per study).	Interventions designed to reduce burden for caregivers of patients with dementia	Caregiver burden	Immediate to 8 mo	Weighted pooled effect of 21 homogenous interventions was insignificant (-0.08, 95% CI -0.19 to 0.02). Examining specific intervention types, 3 multi-component studies showed a small effect on burden (0.46, 95% CI 0.14 to 0.78), although other intervention types did not.
Acton and Winter, 2002 (131)	Caregiving burden	Systematic review	2001	73 published and unpublished reports, all of which had either control group or pre-post design	N/A	This review overlaps with Acton's other review, and discusses a wider range of study designs using a qualitative synthesis	Caregivers of patients with dementia	Interventions designed to reduce burden for caregivers of patients with dementia	Caregiver burden, knowledge, psychosocial wellbeing	Immediate to 1 year	The findings of this review were similar to those of Acton and Winter's (131) methodologically more stringent and quantitative review.

Gysels and Higginson, 2004 (27)	Caregiver burdens	Systematic review	March 2003	317 studies (22 overlapped multiple review domains). The review based its conclusions regarding caregivers on a previous review conducted by the authors. They identified 5 randomized controlled trials	317 studies (22 overlapped multiple review domains)	None. The higher quality studies identified were either palliative care focused, or dealt with support groups.	Patients with cancer	Any intervention to improve supportive or palliative care. Review examined diverse system interventions to improve aspects of supportive or palliative cancer care. These interventions included care coordination, promoting user involvement, face to face communication, improving information, psychological, spiritual, and social support, generalist and specialist palliative care delivery, rehabilitation, complementary and alternative therapies, and caregiver support including bereavement.	Symptoms, quality of life, patient, caregiver, and provider satisfaction with care, knowledge, place of care and site of death, utilization	Short, intermediate, and long term interventions	The review covered a broad range of interventions, especially those related to the clinical organization of care, to improve supportive care for cancer, With respect to services for caregivers, studies were too diverse to draw conclusions related to specific supportive strategies.
Higginson et al., 2000 (25)	Caregiver burdens	Systematic review and meta-analysis	February to June 1999	72 citations including 5 systematic reviews, and 67 reports of 43 unique studies; 15 / 30 studies identified through reviews were randomized and controlled, as were 4 additional studies.	14 / 30 studies identified through systematic reviews were retrospective or observational, as were 10 of the additional studies	Interventions and analysis of site of death overlap completely with Gomes and Higginson's (80) update	Patients cared for by palliative care services (home care, hospital-based, and hospice in Europe, Australia, and the United States	Any intervention of more than one individual, at least one of whom has specialist training, or who spends all their working time in palliative care, in a hospital, home / community setting or in a combination of these.	Patient and caregiver quality of life and symptoms, site of death, healthcare utilization, costs.	Short, intermediate, and long term interventions	This review focused uniquely on a meta-analysis and review of the clinical effectiveness of palliative care teams. Many of the palliative interventions are included in a later update focused specifically on cancer (4).
Sorensen et al., 2002 (133)	Caregiving burden	Meta-analysis	Not reported but most recent studies 2001	78 studies, designs not reported. (other than at least 45 randomized designs)	Not reported	Accepted a wider variety of designs and not specific to dementia. Partial overlap with Yin (130) and Acton and Winter (131)	2 268 caregivers of patients > 60, mean age 62 y, mean female 69%, 14% nonwhite, providing 30 hours / wk of care for an average of 4 y	Interventions to reduce burden among caregivers for the elderly	Caregiver burden, depression, wellbeing, knowledge, and symptoms of the care recipient	Immediate to 1 year.	Outcomes were extracted from all studies considered by the review.13 studies reported caregiver outcomes and a standardized mean difference was 0.15 (95% CI -0.14 to 0.48) consistent with a nonsignificant positive effect Pooled effect demonstrated an immediate benefit on burden (75 studies), depression (53 studies), wellbeing (28 studies) knowledge (48 studies), and symptoms in the care recipient (41 studies). These effects were maintained in follow-up for burden, depression, wellbeing, and knowledge. Among randomized studies, effects were diminished but benefits maintained for burden (45 studies, -0.12, 95% CI -0.16 to -0.07), depression (40 studies, -0.06, 95% CI -0.11 to -0.01), knowledge (34 studies, 0.37, 95% CI 0.27 to 0.46), and the symptoms among the care recipient (34 studies, -0.12, 95% CI -0.20 to -0.03).

Wilkinson et al., 1999 (129)	Caregiving burden	Systematic review	June 1998	83 studies identified, 22 'key papers' highlighted in the paper, of which 3 are randomized designs	Not reported	Intervention trials discussed in 'key papers' also identified in Higginson et al. (25)	Terminally ill patients	Palliative care services including hospice	Patient and caregiver satisfaction	Not reported	The small, methodologically limited studies identified suggested an association between palliative care and improved satisfaction.
Wilson, 2004 (29)	Caregiving burdens	Systematic review	September 2003	3 reviews and 8 studies, design not reported	Design not reported	Intervention studies covered in Wilson overlap almost completely with prior reviews by Higginson et al. (25) and Gysels and Higginson (27)	Patients with serious chronic or terminal illness	Palliative care and hospice service delivery innovations in hospital, home care, nursing home, and hospice settings.	Diverse 'family needs'	Short, intermediate, and long term interventions	Most studies identified were observational, but interventions identified were reviewed by Gysels and Higginson (27) and Higginson et al. (25).
Yin et al., 2002 (130)	Caregiving burden	Meta-analysis	2000	26 studies included 17 randomized designs	N/A	Similar review aim to Sorenson (133) but narrower methodological criteria. About half of studies overlap.	1970 caregivers of elderly adults, mean study size 109, mean caregiver age 60.1 y, 79% women	Interventions to reduce burden for caregivers of elderly adults	Caregiver burden	2 wk to 1 year	Both group and individual interventions demonstrated a positive, beneficial effect. Weighted mean effect for all studies was 0.41 (95% CI 0.32 to 0.51) indicating a moderate positive treatment effect. That effect was maintained but diminished among the 11 randomized studies.

* Reviews may have had broader aims or the studies may have included other outcomes, but those that are most relevant to this review are highlighted. Three reviews addressed multiple domains and each of these reviews is described in each section to which it was relevant. AHRQ = Agency for Healthcare Research and Quality; COPD = CRQD = Chronic Respiratory Disease Questionnaire; OR = odds ratio; RCT = randomized controlled trial; RD = risk difference; SMD = standardized mean differences; WMD = weighted mean difference.