



# Integrated Outpatient Palliative Care in Oncology

September 2017

## Prepared for:

Department of Veterans Affairs  
Veterans Health Administration  
Quality Enhancement Research Initiative  
Health Services Research & Development Service  
Washington, DC 20420

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## PREFACE

The VA Evidence-based Synthesis Program (ESP) was established in 2007 to provide timely and accurate syntheses of targeted healthcare topics of particular importance to clinicians, managers, and policymakers as they work to improve the health and healthcare of Veterans. QUERI provides funding for 4 ESP Centers, and each Center has an active University affiliation. Center Directors are recognized leaders in the field of evidence synthesis with close ties to the AHRQ Evidence-based Practice Centers. The ESP is governed by a Steering Committee comprised of participants from Veterans Health Administration (VHA) Policy, Program, and Operations Offices, VISN leadership, field-based investigators, and others as designated appropriate by QUERI/HSR&D.

The ESP Centers generate evidence syntheses on important clinical practice topics. These reports help:

- Develop clinical policies informed by evidence;
- Implement effective services to improve patient outcomes and to support VA clinical practice guidelines and performance measures; and
- Set the direction for future research to address gaps in clinical knowledge.

The ESP disseminates these reports throughout VA and in the published literature; some evidence syntheses have informed the clinical guidelines of large professional organizations.

The ESP Coordinating Center (ESP CC), located in Portland, Oregon, was created in 2009 to expand the capacity of QUERI/HSR&D and is charged with oversight of national ESP program operations, program development and evaluation, and dissemination efforts. The ESP CC establishes standard operating procedures for the production of evidence synthesis reports; facilitates a national topic nomination, prioritization, and selection process; manages the research portfolio of each Center; facilitates editorial review processes; ensures methodological consistency and quality of products; produces “rapid response evidence briefs” at the request of VHA senior leadership; collaborates with HSR&D Center for Information Dissemination and Education Resources (CIDER) to develop a national dissemination strategy for all ESP products; and interfaces with stakeholders to effectively engage the program.

Comments on this evidence report are welcome and can be sent to Nicole Floyd, ESP CC Program Manager, at [Nicole.Floyd@va.gov](mailto:Nicole.Floyd@va.gov).

**Recommended citation:** Fulton J, LeBlanc T, Porter-Starr K, Kamal A, Ramos K, Cutson T, Freiermuth C, McDuffie J, Adam S, Kosinski A, von Isenburg M, Van Noord M, Williams JW Jr. Integrated Outpatient Palliative Care in Oncology. VA ESP Project #09-009; 2017.

This report is based on research conducted by the Evidence-based Synthesis Program (ESP) Center located at the **Durham VA Medical Center, Durham, NC**, funded by the Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development, Quality Enhancement Research Initiative. The findings and conclusions in this document are those of the author(s) who are responsible for its contents; the findings and conclusions do not necessarily represent the views of the Department of Veterans Affairs or the United States government. Therefore, no statement in this article should be construed as an official position of the Department of Veterans Affairs. No investigators have any affiliations or financial involvement (eg, employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties) that conflict with material presented in the report.



## STAKEHOLDER AND TECHNICAL EXPERT PANEL

In designing the study questions and methodology at the outset of this report, the ESP consulted several technical and content experts. Broad expertise and perspectives were sought. Divergent and conflicting opinions are common and perceived as healthy scientific discourse that results in a thoughtful, relevant systematic review. Therefore, in the end, study questions, design, methodologic approaches, and/or conclusions do not necessarily represent the views of individual technical and content experts.

The list of stakeholders and members of the Technical Expert Panel (TEP) who provided input to this report follows.

### Stakeholders

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## EXECUTIVE SUMMARY

### INTRODUCTION

More than 500,000 Americans, including 40,000 Veterans, are diagnosed with advanced cancer annually in the United States. Palliative care improves quality of life by managing patients' physical symptoms and psychosocial and spiritual distress, often provided concurrently with oncology care. Palliative care occurs across a continuum, beginning at the time of diagnosis of a serious illness and continuing until end of life. Integration of palliative care services with oncology care is now considered standard of care for patients with advanced cancer.

Palliative care has undergone increased acceptance and expansion, but understanding of its integration with oncology services is understudied and unclear. While primary care and oncology providers have always provided palliative care, palliative care has only recently become a recognized medicine specialty. Specialty palliative care is delivered in inpatient and outpatient settings and varies significantly in team composition, integration level, patients eligible for consultation, and utilization and cost-saving outcomes. However, which cancer patients may benefit most based on characteristics such as diagnosis, demographics, and stage of disease, as well as which delivery method is most effective, remain open questions.

With increase in availability of clinical palliative care services, health care organizations have tested and implemented degrees and types of integration with oncology care. Leaders have described various integration methods, including co-rounding models for hospitalized patients, embedded or colocated outpatient clinical services, and stand-alone clinics or services. Outpatient settings are where the majority of cancer care is delivered and has been considered the "next frontier" of community-based palliative care services.

This evidence report was commissioned to (1) evaluate the effects of palliative care, initiated "upstream" and integrated with oncology care for patients with cancer, (2) describe intervention characteristics associated with greater patient and caregiver benefits, and (3) describe barriers to implementing integrated palliative care into VA settings. Therefore, we aimed to produce a systematic review to provide actionable information to VA health care providers, leaders, and policymakers regarding the potential benefits of palliative care integration among the diverse population of Veterans with cancer.

### METHODS

The final key questions (KQ) were developed with input from stakeholders and content experts:

KQ 1: In patients with symptomatic or advanced cancer, what are the benefits and harms of integrated outpatient palliative and oncology care compared with usual oncology care?

KQ 2: Which features of integrated palliative and oncology care are associated with greater benefit to patients with symptomatic or advanced cancer?

KQ 3: What are the most common and important barriers to implementing integrated palliative and oncology care in VA settings?

## Data Sources and Searches

We conducted searches of MEDLINE® (via PubMed®), the Cochrane Central Registry of Controlled Trials, and CINAHL through November 21, 2016, for KQ 1 and KQ 2; through January 19, 2017, for KQ 3. We examined the bibliographies of recent reviews and contacted content experts for additional relevant studies.

## Study Selection

Using prespecified eligibility criteria, 2 reviewers evaluated titles and abstracts to identify potentially eligible studies, which then underwent full-text screening by 2 independent reviewers. Key eligibility criteria were trial or quasi-experimental design, adults with advanced cancer, interventions delivered in outpatient settings, evidence of integration between palliative care and oncology services, and specific outcomes: quality of life, survival, and health care utilization. Because details of integrated care were routinely absent from the published literature, we provisionally included all studies meeting other eligibility criteria and attempted to contact all authors for missing information. Studies addressing KQ 3, barriers to implementation, had to be conducted in the VHA or be related to a study included for KQ 1, and both quantitative and qualitative study designs were included. Disagreements about study eligibility were resolved by discussion or by a third investigator.

## Data Abstraction, Categorization of Interventions, and Quality Assessment

Study characteristics including patient characteristics, intervention/comparator details, and outcomes at 2 timepoints—postintervention and at least 6 months postintervention—were abstracted into a custom database. Review and reconciliation were conducted as done for full-text screening. We categorized interventions along 2 dimensions: clinical elements of palliative care (eg, physical, psychological) and levels of integrated care (from minimal to full collaboration). For studies addressing implementation, we abstracted data on study design and implementation barriers and facilitators. Quality assessment was completed independently by 2 investigators; disagreements were resolved by consensus or by arbitration from a third reviewer. We used the Cochrane risk of bias (ROB) tool for randomized controlled trials (RCTs) and the revised Newcastle Ottawa Scale for cohort studies; we adapted the Critical Appraisal Checklist for qualitative studies. We assigned a summary ROB score (low, moderate, or high) to individual studies.

## Data Synthesis and Analysis

We described the included studies using summary tables and graphical displays. We computed summary effects (*ie*, meta-analysis) when studies were conceptually homogeneous and there were at least 3 studies with the same outcome. When quantitative synthesis was possible, we combined dichotomous outcomes using random-effects models and computed summary risk ratios or hazard ratios. Continuous outcomes were summarized using the standardized mean difference. We adjusted analyses for small numbers of studies, performed sensitivity analyses as appropriate, and evaluated for statistical heterogeneity using visual inspection and Cochran's  $Q$  and  $I^2$  statistics. When quantitative synthesis was not feasible, we synthesized intervention effects qualitatively. We gave more weight to the evidence from higher quality studies with more precise estimates of effect. Publication bias could not be assessed statistically because there were fewer than 10 studies in all analyses.

To identify intervention and integration elements associated with greater effects, we used quantitative (*ie*, subgroup analyses of moderator variables) and qualitative cross-case impact analysis. To carry out the analyses, we ranked studies by impact level. We then analyzed the relationship of intervention and integration elements with intervention impacts using tables and graphical displays. To derive the impact measure, we randomly ordered the studies on a spreadsheet and listed each study's set of outcomes, without any identifiers. Two authors considered the outcomes reported for each study and independently rated the intervention impact on a 4-point scale. Disagreements were resolved by consensus. The studies were rated high, moderate, low, or no impact.

The strength of evidence (SOE) for each key question was assessed using the GRADE approach, which considers study design, ROB, consistency, directness, and precision. These domains were evaluated using GRADEpro software ([grade.pro.org](http://grade.pro.org)).

## RESULTS

### Results of Literature Search

The literature search identified 1,916 unique citations from a combined search of MEDLINE (via PubMed), CINAHL, and the Cochrane Central Register of Controlled Trials. An additional 71 articles were identified from manual searches of bibliographies and current literature published after the search date for a total of 1,988 unique citations. After screening at both the abstract and full-text level, 24 articles were retained for data abstraction (13 primary papers and 11 companion papers).

### Summary of Results for Key Questions

Nine trials addressed KQ 1. Integrated palliative care was delivered by multidisciplinary teams in outpatient settings, but the intensity of interventions varied considerably. Most studies enrolled mostly white men and women with multiple types of advanced cancer at a median of 8 to 12 weeks following diagnosis or recurrence. There were several benefits of palliative care. Integrated palliative care improved short-term (SMD 0.24; 95% CI 0.13 to 0.43) but not longer-term patient quality of life (SMD 0.15; 95% CI -0.12 to 0.43). Over the 4 studies reporting this outcome, integrated palliative care decreased overall mortality (HR 0.77; 95% CI 0.61 to 0.98). When an outlier study was excluded, overall symptom burden improved modestly, but there was no effect when evaluating all studies. Psychological symptoms did not improve with palliative care, but only a subset of studies reported this outcome. Palliative care that included a specific caregiver intervention improved short-term depressive symptoms in caregivers. Caregiver experience and quality of life were not improved, but few studies reported this outcome. In those studies that assessed utilization, palliative care increased the likelihood of dying at home but did not reduce overall patterns of health care utilization. However, confidence intervals were wide, suggesting low statistical power. Adverse effects of integrated palliative care were not specified as an outcome and were not reported in any trials.

The same 9 trials addressed KQ 2. We found that published trials of palliative care do not routinely describe elements of integration with oncology care. Classifying integration required author queries for additional data. When these data were obtained, 2 were classified as having basic collaboration onsite and 4 as having close collaboration onsite with some systems integration. Three studies could not be classified due to missing information. We did not identify

an association between the integration level and overall intervention effects or effects on short-term quality of life. However, these analyses were limited by the small number of studies and the limited range of integration levels.

Few studies (n=4) directly addressed KQ3 – common and important barriers to implementing integrated palliative and oncological care in the VHA. Common barriers to implementation included low participation rates in interventions using shared appointments, perceptions that palliative care is meant to be used later in the disease trajectory, and poor communication and coordination among providers and patients. Facilitators to implementation were shared decision-making aids, greater collaboration among local leaders within a health care system, improved patient-centered care, performance measures for patient-centered care, and patient-provider education about roles and responsibilities of care both in oncology and palliative care services.

## DISCUSSION

### Key Findings and Strength of Evidence

We identified 7 RCTs and 2 cluster-randomized trials addressing benefits and harms of integrated palliative care, all of which were comparative effectiveness trials and examined palliative care services that were moderately integrated with oncology care. All interventions were colocated in the same facility and classified as moderately integrated. All interventions included physical and psychological aspects of care; none included cultural aspects of care. We found a pattern of positive effects, including lower mortality and improved short-term quality of life. Other outcomes were reported less frequently (*eg*, caregiver outcomes, utilization), and intervention effects for these outcomes could not be determined definitively. SOE was rated for primary outcomes (quality of life and symptom burden) and mortality.

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

Outcome	Number of RCTs (Patients)	Findings <sup>a</sup>	Strength of Evidence (Rationale by Domain)
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

We qualitatively examined associations between integration elements, palliative care intervention domains, and intervention impact (based on cross-case impact analyses). There was no clear association between level of integration and intervention effects, but these analyses were limited by the small number of studies and limited variability in integration elements.

Separately, we identified 4 articles studying Veteran populations that addressed barriers to and facilitators of integrated palliative and oncology care. Common barriers to implementation included cost of personnel, limited staffing and space, low participation by patients in shared medical appointments, and perceptions that palliative care is limited to end stages of disease. The facilitators to implementation identified by VA leaders were relevant palliative care performance measures, communication and collaboration between health care leaders, and patient-provider education about roles and responsibilities of palliative and oncology teams.

### **Clinical Policy Implications and Applicability**

The VA does not have current guidelines that address provisions for standard integration of outpatient palliative care into routine oncology care. Current guidelines from medical professional societies all recommend routine integration of palliative care. Our results and the findings of recent systematic reviews and meta-analyses support these recommendations in demonstrating quality of life improvements with integrated care. Our analysis is unique in focusing only on outpatient integration of palliative care with oncology practice, compared to a recent high-quality meta-analysis that assessed outcome improvements across multiple conditions and care locations. We are among the first to find an aggregate improvement in survival across multiple trials in the oncology setting, which may be in part due to our more narrow focus. All studies were conducted in economically developed countries; 2 trials enrolled Veterans, but samples were predominantly Caucasian. It is unclear whether the findings generalize to individuals from other ethnic and racial groups. Regardless, our findings suggest an important role for consistent integration of palliative care into routine outpatient oncology care, which should be considered in applicable policies and clinical practices in VA.

### **Research Gaps/Future Research**

Although it would be possible to generate an extensive list of gaps in evidence, we restricted this list to the areas judged to be highest priority, given the current state of evidence. First, research is needed with ethnically, racially, and socioeconomically diverse groups of people. Trials should report more clearly the intervention elements, dose, and integration elements. A study comparing inpatient palliative care to integrated palliative and oncology care in outpatient settings could provide invaluable comparative effectiveness data. Studies are also needed in community settings. Outcome measures should be standardized and include input on barriers and facilitators to implementation as well as the outcomes most valued by patients. As it pertains to the VHA, a key component of the Quality Enhancement Research Initiative (QUERI) program is to advance implementation science and identify effective strategies for implementing effective interventions. However, palliative care does not appear to be a particularly good fit into any of the 15 existing QUERI Centers, so to pursue this, it is likely a new QUERI Center would need to be formed that focuses on this issue.



## Conclusions

There is a small but growing literature about integrated palliative and oncology care interventions for patients with symptomatic or advanced cancer. Overall, we identified a diverse set of interventions that showed moderate levels of integration. These interventions demonstrated a pattern of small-to-moderate, positive short-term effects on mortality and on outcomes that are important to patients. Effects on other outcomes such as health care utilization and caregiver outcomes are less well studied. However, considerable gaps remain in the evidence for some policy-relevant outcomes and critical intervention elements. More clearly defined palliative care intervention characteristics and integration elements would allow for a more precise understanding of the impact of integrated palliative and oncology care on outcomes. New studies should report both intervention elements and integration elements more carefully, adopt a standard set of outcomes, and attend to recruiting a more racially and ethnically diverse population.