



## What is the effectiveness of early palliative care integration on quality of life and symptom management in women with advanced gynecologic cancer? : A Systematic Review

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### ABSTRACT

**Introduction:** Advanced gynecologic cancers are associated with significant symptom burden and impaired quality of life (QoL). While early palliative care integration has demonstrated benefits in other oncology populations, its effectiveness specifically in women with advanced gynecologic malignancies remains uncertain. This systematic review aimed to evaluate the effectiveness of early palliative care integration on QoL and symptom management in women with advanced gynecologic cancer.

**Methods:** A systematic review was conducted following PRISMA guidelines. We included randomized controlled trials, etc examining early palliative care (initiated within 8 weeks of advanced cancer diagnosis or concurrently with active

treatment) in adult women with stage III/IV or recurrent gynecologic cancers. Studies were required to report QoL, symptom management, or healthcare utilization outcomes. Data were extracted on study characteristics, interventions, and outcomes.

**Results:** Thirty-five studies met inclusion criteria, encompassing diverse designs and populations (sample sizes 23–8,297). Ovarian cancer was most commonly studied. QoL findings were mixed: while several smaller studies reported significant improvements across FACT-G domains ( $p < 0.05$ ) [6,19,32], the largest RCTs in recurrent ovarian cancer failed to demonstrate significant overall QoL improvements [1,2]. A meta-analysis of four RCTs found non-significant pooled QoL effects (SMD=0.26; 95% CI -0.29–0.80) [4]. Symptom management showed more consistent benefits, particularly for acute symptom relief [8] and psychological symptoms [6]. Healthcare utilization outcomes demonstrated the most robust improvements, including reduced aggressive end-of-life care [9], increased hospice enrollment [10,11], and cost-effectiveness [17]. However, persistent underutilization (referral rates  $< 50\%$ ) [13,14] and racial disparities [13,15] were identified.

**Conclusion:** Early palliative care integration in advanced gynecologic cancer consistently improves healthcare utilization outcomes and shows benefits for psychological symptoms, but QoL improvements remain inconsistent across well-controlled trials. System-level interventions and standardized referral protocols may optimize real-world effectiveness.

Further research should address implementation barriers and disparities.

**Keywords:** Palliative care; gynecologic cancer; quality of life; symptom management; end-of-life care; early integration

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## INTRODUCTION

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### **Background**

Advanced gynecologic cancers, including ovarian, cervical, and uterine malignancies, represent a significant global health burden. Women diagnosed with stage III/IV or recurrent gynecologic cancers experience substantial physical and psychological symptom burden, including pain, fatigue, malignant bowel obstruction, and emotional distress, which profoundly impairs quality of life (QoL) [1,2]. Despite advances in oncologic treatments, many patients continue to experience uncontrolled symptoms and aggressive end-of-life care [9,10].

Palliative care focuses on improving QoL for patients with serious illnesses through symptom management, psychosocial support, and alignment of care with patient preferences [27]. In recent years, early palliative care integration—initiated close to diagnosis and concurrently with active treatment—has emerged as a recommended approach. Landmark studies in other oncology populations have demonstrated improved QoL, reduced symptom burden, and even survival benefits with early palliative care involvement [3,11]. However, whether these benefits translate specifically to women with advanced gynecologic cancers remains an area of active investigation.

### **Problem Statement**

Despite growing consensus regarding the importance of palliative care in oncology, significant knowledge gaps persist regarding its effectiveness in gynecologic cancer populations. Current clinical practice varies widely, with palliative care often introduced late in the disease trajectory or only when curative-intent treatments are exhausted [13,14,34]. Women with gynecologic cancers may have unique palliative care needs related to disease-specific complications such as malignant bowel obstruction [18,35], yet evidence-based guidelines for early integration in this population remain limited.

### **Research Gap**

While multiple studies have examined early palliative care in mixed cancer populations, gynecologic cancer-specific evidence has several limitations. First, existing systematic reviews often include heterogeneous populations, making it difficult to extract gynecologic-specific findings

[20,21]. Second, available randomized controlled trials in gynecologic cancer have been predominantly small pilot studies, limiting their statistical power and generalizability [1,2,3]. Third, the definition of "early" palliative care varies considerably across studies—ranging from within 8 weeks of diagnosis to more than 3 months before death—complicating evidence synthesis [9,28]. Fourth, the heterogeneity of palliative care interventions (single consultation vs. multidisciplinary programs) and outcome measures creates challenges for drawing definitive conclusions [4,21]. No comprehensive systematic review has specifically synthesized the effectiveness of early palliative care integration across all gynecologic cancer types with attention to both patient-reported outcomes and healthcare utilization metrics.

### **Research Question**

This systematic review addresses the following question: What is the effectiveness of early palliative care integration on quality of life and symptom management in women with advanced gynecologic cancer?

### **Objectives**

The primary objective was to evaluate the effectiveness of early palliative care integration compared to standard oncologic care on QoL outcomes in women with advanced gynecologic cancer. Secondary objectives included: (1) assessing symptom management outcomes, (2) examining healthcare utilization and end-of-life care patterns, (3) identifying factors that moderate intervention effectiveness, and (4) characterizing implementation barriers and disparities.

### **Hypotheses**

We hypothesized that early palliative care integration would be associated with improved QoL and symptom management compared to standard care, with greater benefits observed for psychological and emotional domains than for physical functioning. We further hypothesized that healthcare utilization outcomes would demonstrate more consistent improvements than patient-reported outcomes, and that significant heterogeneity in effect sizes would be explained by study design, intervention intensity, and population characteristics.

### **Significance and Novelty**

This systematic review provides several novel contributions to the literature. First, it offers the most comprehensive synthesis to date of early palliative care effectiveness specifically in advanced gynecologic cancers, including 35 studies with diverse designs. Second, it examines outcomes across multiple domains (QoL, symptom management, healthcare utilization) to provide a holistic understanding of intervention effects. Third, it identifies critical implementation gaps, including persistent underutilization and racial disparities, that have not been systematically addressed in prior reviews. Fourth, it synthesizes evidence from recent large population-based studies [9] and meta-analyses [4] that were not available in earlier reviews. Finally, it provides context-specific conclusions to guide clinical practice and future research priorities.

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## METHODS

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### Protocol

The study strictly adhered to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 guidelines to ensure methodological rigor and accuracy. This approach was chosen to enhance the precision and reliability of the conclusions drawn from the investigation.

### Criteria for Eligibility

This systematic review aims to evaluate What is the effectiveness of early palliative care integration on quality of life and symptom management in women with advanced gynecologic cancer ?

### Screening

We screened in sources based on their abstracts that met these criteria:

- **Population - Adult Women:** Does this study involve adult women ( $\geq 18$  years) diagnosed with gynecologic cancer?
- **Population - Advanced Disease Stage:** Does this study focus on advanced gynecologic cancer (stage III or IV ovarian, cervical, endometrial, vulvar, vaginal, or fallopian tube cancer)?

- **Population - Extractable Results:** Can gynecologic cancer results be separately extracted from this study (i.e., is this study exclusively on gynecologic cancer patients OR are gynecologic cancer results reported separately from other cancer types)?
- **Intervention - Early Palliative Care:** Does this study examine early palliative care integration defined as palliative care services initiated within 8 weeks of advanced cancer diagnosis or concurrently with active treatment?
- **Intervention - Comprehensive Approach:** Does this study examine comprehensive palliative care approaches rather than only single-component interventions (e.g., pain medication alone)?
- **Study Design:** Is this study a randomized controlled trial, quasi-experimental study, cohort study, case-control study, systematic review, or meta-analysis with full-text availability?
- **Comparison Group:** Does this study include a control group receiving standard oncologic care, usual care, or delayed palliative care?
- **Relevant Outcomes:** Does this study report at least one of the following outcomes: quality of life measures, symptom burden/management, pain scores, or functional status?

We considered all screening questions together and made a holistic judgement about whether to screen in each paper.

### Search Strategy

The keywords used for this research based PICO :

Element	P (Population)	I (Intervention/Exposure)	C (Comparison/Context)	O (Outcome)
Keyword 1	Advanced Gynecologic Cancer	Early Palliative Care Integration	Standard Oncologic Care	Quality of Life
Keyword	Ovarian Cancer	Early palliative care	Usual Care	Symptom

2		referral		Management
Keyword 3	Cervical Cancer	Palliative medicine consultation	Delayed Palliative Care	Healthcare Utilization
Keyword 4	Uterine/Endometrial Cancer	Comprehensive palliative care	Late palliative care referral	End-of-Life Care

The Boolean MeSH keywords inputted on databases for this research are: (*"Advanced Gynecologic Cancer" OR "Ovarian Cancer" OR "Cervical Cancer" OR "Uterine/Endometrial Cancer"*) AND (*"Early Palliative Care Integration" OR "Early palliative care referral" OR "Palliative medicine consultation" OR "Comprehensive palliative care"*) AND (*"Standard Oncologic Care" OR "Usual Care" OR "Delayed Palliative Care" OR "Late palliative care referral"*) AND (*"Quality of Life" OR "Symptom Management" OR "Healthcare Utilization" OR "End-of-Life Care"*)

#### Data extraction

- **Study Population:**

Extract details about study participants to confirm they meet inclusion criteria of women with advanced gynecologic cancer, including:

- Cancer type (ovarian, cervical, uterine, etc.)
- Disease stage/status (advanced, recurrent, metastatic)
- Sample size and key demographics (age, race/ethnicity if reported)
- Any exclusion criteria relevant to palliative care (e.g., immediate palliative care needs, prognosis limitations)

- **Early Palliative Care Definition:**

Extract how the study defined and implemented early palliative care integration for women with advanced gynecologic cancer, including:

- What constituted "early" (timing relative to diagnosis, prognosis, or disease progression)
- Type of palliative care intervention (consultation, multidisciplinary team, nurse-coordinated, etc.)
- Frequency and duration of palliative care contacts
- Who provided the care (palliative care specialists, oncology team, advanced practice nurses)
- Integration approach (embedded vs consultative model)

- **Comparison Group:**

Extract what the early palliative care intervention was compared against in women with advanced gynecologic cancer, including:

- Type of comparison (standard oncologic care, delayed palliative care, enhanced usual care, historical controls)
- Whether comparison group received any palliative care elements
- Any co-interventions provided to either group

- **Study Design:**

Extract study methodology relevant to assessing effectiveness of early palliative care in advanced gynecologic cancer, including:

- Study design (RCT, quasi-experimental, cohort, before-after, etc.)
- Sample size and power considerations
- Randomization method and blinding if applicable

- Follow-up duration and assessment time points
- Loss to follow-up and reasons (particularly deaths)

- **Quality of Life Outcomes:**

Extract all quality of life outcomes specifically measured in women with advanced gynecologic cancer receiving early palliative care, including:

- Quality of life measures used (FACT-G, EORTC QLQ-C30, etc.)
- Baseline and follow-up scores for intervention and comparison groups
- Statistical significance and effect sizes for between-group differences
- Clinically meaningful differences if reported
- Specific domains affected (physical, emotional, social, functional)

- **Symptom Management Outcomes:**

Extract all symptom management outcomes for women with advanced gynecologic cancer receiving early palliative care, including:

- Specific symptoms assessed (pain, nausea, fatigue, dyspnea, depression, anxiety, etc.)
- Symptom measurement tools used
- Baseline and follow-up symptom severity/frequency for intervention and comparison groups
- Statistical significance and effect sizes for symptom improvements
- Any symptom-specific interventions provided as part of palliative care

- **Healthcare Utilization:**

Extract healthcare utilization outcomes related to early palliative care integration in women with advanced gynecologic cancer, including:

- Emergency department visits
- Hospital admissions and length of stay
- ICU admissions
- Procedures in final weeks/months of life
- Hospice enrollment rates and timing
- Chemotherapy use near end of life
- Any cost or resource utilization data

- **Key Findings:**

Extract the main conclusions about effectiveness of early palliative care integration on quality of life and symptom management in women with advanced gynecologic cancer, including:

- Authors' overall assessment of intervention effectiveness
- Most significant benefits observed
- Any negative or null findings
- Factors that appeared to influence effectiveness
- Authors' recommendations for clinical practice
- Limitations that affect interpretation of results

**Table 1.** Article Search Strategy

Database	Keywords	Hits
Pubmed	<i>("Advanced Gynecologic Cancer" OR "Ovarian Cancer" OR "Cervical Cancer" OR "Uterine/Endometrial Cancer" AND ("Early Palliative Care Integration" AND "Quality of Life" OR "Symptom Management" OR "Healthcare Utilization" OR "End-of-Life Care"))</i>	200
Semantic Scholar	<i>("Advanced Gynecologic Cancer" OR "Ovarian Cancer" OR "Cervical Cancer" OR "Uterine/Endometrial Cancer") AND ("Early Palliative Care Integration" OR "Early palliative care referral" OR "Palliative medicine consultation" OR "Comprehensive palliative care") AND ("Standard Oncologic Care" OR "Usual Care" OR "Delayed Palliative Care" OR "Late palliative care referral") AND ("Quality of Life" OR "Symptom Management" OR "Healthcare Utilization" OR "End-of-Life Care")</i>	3
Springer	<i>("Advanced Gynecologic Cancer" OR "Ovarian Cancer" OR "Cervical Cancer" OR "Uterine/Endometrial Cancer") AND ("Early Palliative Care Integration" OR "Early palliative care referral" OR "Palliative medicine consultation" OR "Comprehensive palliative care") AND ("Standard Oncologic Care" OR "Usual Care" OR "Delayed Palliative Care" OR "Late palliative care referral") AND ("Quality of Life" OR "Symptom Management" OR "Healthcare Utilization" OR "End-of-Life Care")</i>	20
Google Scholar	<i>("Advanced Gynecologic Cancer" OR "Ovarian Cancer" OR "Cervical Cancer" OR "Uterine/Endometrial Cancer") AND ("Early Palliative Care Integration" OR "Early palliative care referral" OR "Palliative medicine consultation" OR "Comprehensive palliative care") AND ("Standard Oncologic Care" OR "Usual Care" OR "Delayed Palliative Care" OR "Late palliative care referral") AND ("Quality of Life" OR "Symptom Management" OR "Healthcare Utilization" OR "End-of-Life Care")</i>	121
Wiley Online Library	<i>("Advanced Gynecologic Cancer" OR "Ovarian Cancer" OR "Cervical Cancer" OR "Uterine/Endometrial Cancer") AND ("Early Palliative Care Integration" OR "Early palliative care referral" OR "Palliative medicine consultation" OR "Comprehensive palliative care") AND ("Standard Oncologic Care" OR "Usual Care" OR "Delayed Palliative Care" OR "Late palliative care referral") AND ("Quality of Life" OR "Symptom Management" OR "Healthcare Utilization" OR "End-of-Life Care")</i>	19

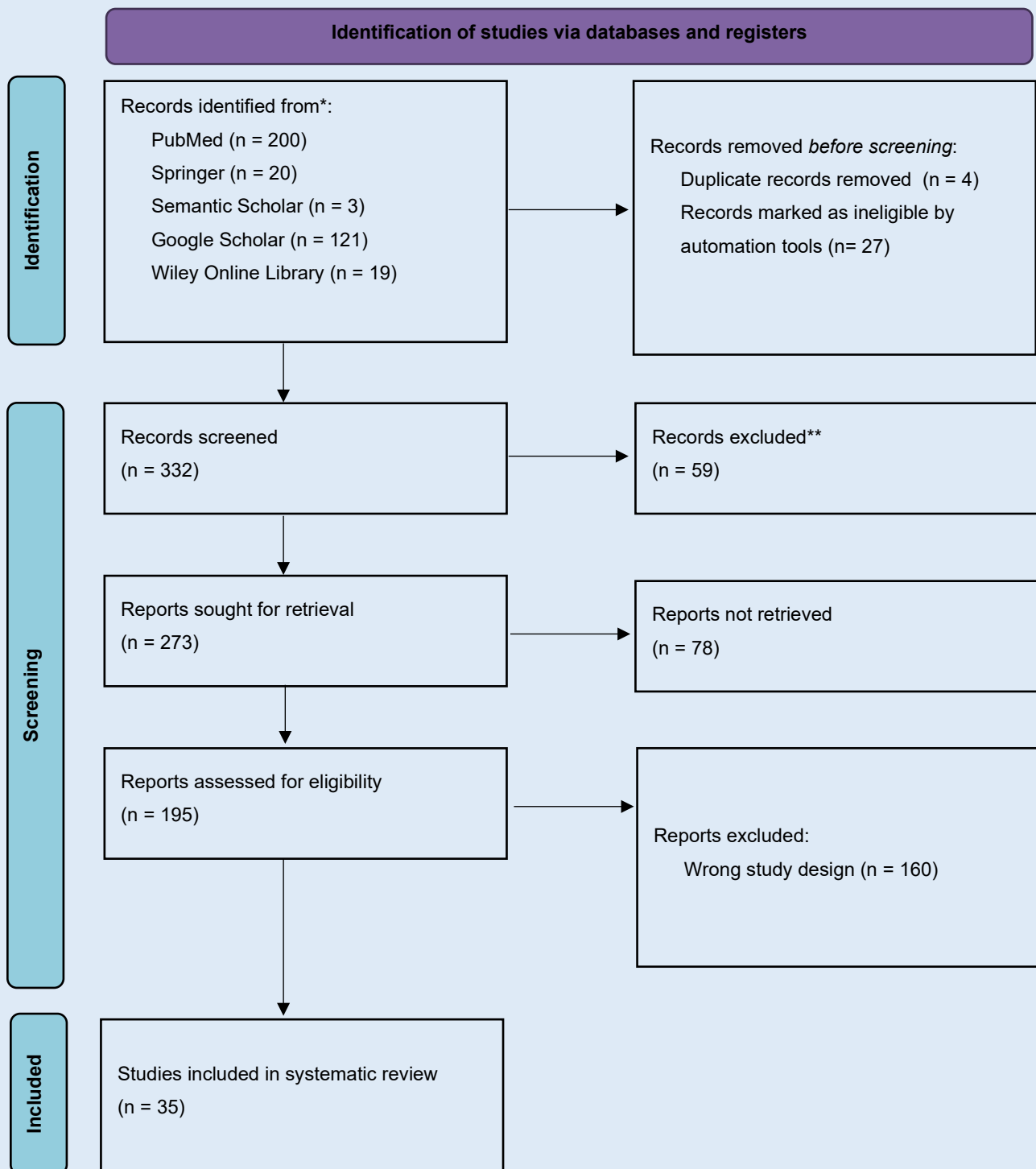


Figure 1. Article search flowchart

## RESULTS

### Characteristics of Included Studies

The 35 included sources encompass a range of study designs, populations, and palliative care intervention models. The majority focused on ovarian cancer, though cervical, uterine, and mixed gynecologic cancer populations were also represented. Study designs included randomized controlled trials, retrospective cohort studies, etc. Sample sizes ranged from 23 to over 8,000 participants.

Study	Cancer Type / Population	Sample Size	Palliative Care Intervention
<b>M. Cusimano et al., 2021</b>	Epithelial ovarian, recurrent/progressed [2]	23 [2]	EPC consultation within 4 weeks of enrollment [2]
<b>B. Davidson et al., 2021</b>	Recurrent ovarian (platinum resistant or sensitive with sentinel events) [1]	54 [1]	Structured PC intervention with gynecologic oncology and PC specialists [1]
<b>Treshita Dey et al., 2023</b>	Locally advanced cervical (IB2–IIIB) [5]	100 (87 analyzed) [5]	Early integration of PC with concurrent chemoradiation [5]
<b>M. Schneider et al., 2021</b>	Ovarian/peritoneal (37%), uterine (32%); 93% advanced/recurrent [15]	152 admissions [15]	Universal inpatient PC consultation protocol [15]

Study	Cancer Type / Population	Sample Size	Palliative Care Intervention
<b>Niyazi Kilic et al., 2021</b>	Ovarian, stage III [16]	111 [16]	PC appointment attendance [16]
<b>Y. Mao et al., 2017</b>	Advanced gynecologic malignancy, elderly [6]	106 [6]	Palliative care nursing [6]
<b>W. Lowery et al., 2013</b>	Recurrent platinum-resistant ovarian [17]	Model-based (no empirical cohort) [17]	Early referral to palliative medicine specialist [17]
<b>Y. C. Lee et al., 2019</b>	Advanced gynecologic, mainly ovarian (73%) [18]	169 [18]	Interprofessional MBO management program [18]
<b>Xiang Zheng et al., 2017</b>	Cervical cancer undergoing radiotherapy [19]	98 [19]	Early nursing intervention [19]
<b>M. Mullen et al., 2017</b>	Ovarian (35.7%), uterine (35.4%); advanced [10]	308 [10]	PC quality improvement initiative (consultation) [10]

Study	Cancer Type / Population	Sample Size	Palliative Care Intervention
<b>A. Zhandos et al., 2025</b>	Gynecologic cancers (general) [20]	32 articles reviewed [20]	Various early PC integration models [20]
<b>Poojani Illangasinghe et al., 2025</b>	Ovarian, cervical, uterine [21]	12 studies reviewed [21]	Coping skills interventions (group therapy, mindfulness, counseling, etc.) [21]
<b>Kusum Kumari et al., 2024</b>	Advanced gynaecological cancers [4]	670 total (289 patients, 381 caregivers) [4]	Palliative care [4]
<b>R. McCorkle et al., 2015</b>	Late-stage cancer including gynecologic [3]	146 [3]	APN-coordinated multidisciplinary intervention over 10 weeks [3]
<b>Y. Segev et al., 2021</b>	Advanced gynecological cancer [22]	189 [22]	Integrative oncology program (>=4 treatments over 6 weeks) [22]

Study	Cancer Type / Population	Sample Size	Palliative Care Intervention
<b>S. Gaster et al., 2019</b>	Advanced cancer (medical/gynecologic oncology) [11]	340 [11]	Concurrent specialty palliative care consultation [11]
<b>S. Pasalak et al., 2022</b>	Gynecologic cancer undergoing chemotherapy [23]	41 [23]	Nurse-led symptom management program [23]
<b>R. Vogel et al., 2013</b>	Ovarian cancer, stage III/IV or recurrent [24]	53 enrolled, 35 completed [24]	Web-based advance care planning tool [24]
<b>Angel Tabuyo-Martin et al., 2022</b>	Ovarian (37.6%), uterine (32.8%); metastatic or recurrent [13]	186 [13]	Palliative medicine referral [13]
<b>C. Lefkowits et al., 2015</b>	Gynecologic malignancy, 50% ovarian; 70% stage III/IV [8]	121 unique patients [8]	Inpatient PC consultation for symptom management [8]

Study	Cancer Type / Population	Sample Size	Palliative Care Intervention
<b>E. Ben-Arye et al., 2021</b>	Advanced (stage III/IV) gynecological cancer [25]	134 [25]	Patient-tailored integrative oncology program (6 weeks) [25]
<b>Gregorio López González et al., 2023</b>	Gynecological cancer (post-surgical) [26]	168 planned [26]	Telemedicine-guided PROMs screening with early intervention [26]
<b>A. Graul et al., 2020</b>	Gynecologic oncology patients [7]	111 (55 control, 56 intervention) [7]	Patient education video on palliative care [7]
<b>D. Karlin et al., 2017</b>	Gynecologic malignancies (general) [27]	Not applicable [27]	Various early PC integration approaches [27]
<b>Christopher Pietras et al., 2025</b>	Gynecologic malignancies (general) [28]	Not applicable [28]	Early integration, resource-adapted models, telehealth, nurse-led models [28]
<b>B. Scarborough et al., 2015</b>	Solid tumors including gynecologic [12]	200 [12]	Integrated outpatient palliative care consultation [12]

Study	Cancer Type / Population	Sample Size	Palliative Care Intervention
<b>G. David-West et al., 2020</b>	Gynecologic oncology inpatients [29]	Not reported [29]	Standardized criteria triggering PC consult [29]
<b>B. Goff et al., 2023</b>	Advanced ovarian (stage III, IV, or recurrent) [14]	683 pre, 763 post; 134 enrolled [14]	Web-based symptom/QOL reporting with educational intervention [14]
<b>S. Mah et al., 2024</b>	Ovarian cancer decedents [9]	8,297 [9]	Palliative care initiated >3 months before death [9]
<b>S. Mah et al., 2023</b>	Gynecologic cancers (terminal) [30]	Not reported [30]	Timing of palliative care initiation [30]
<b>M. Cusimano et al., 2020</b>	Advanced gynecologic cancer with MBO [31]	Not reported [31]	Supported self-management program [31]
<b>D. Aktaş et al., 2015</b>	Gynecological cancer [32]	70 [32]	Home care nursing service [32]

Study	Cancer Type / Population	Sample Size	Palliative Care Intervention
R. Sims et al., 2021	Mixed cancers matched on type/stage [33]	200 (100 per cohort) [33]	Integrative palliative oncology program (multidisciplinary team) [33]
Marisa R. Moroney et al., 2020	Phase I ovarian cancer [34]	Not reported [34]	Specialty palliative care [34]
Y. C. Lee et al., 2017	Advanced gynecological cancer with MBO [35]	Not reported [35]	Interprofessional MBO program, nurse-led ambulatory symptom management [35]

Ovarian cancer was the most commonly studied malignancy, followed by uterine and cervical cancers. Definitions of "early" palliative care varied considerably: some defined it relative to disease recurrence or progression [2], others as concurrent with active treatment [11], within 100 days of diagnosis [3], or more than 3 months before death [9, 28].

### Effects

#### Quality of Life Outcomes

Quality of life (QoL) was the most frequently evaluated outcome. The table below summarizes QoL findings across studies that reported this endpoint.

Study	QoL Instrument	QoL Effect (Intervention vs. Control)	Statistical Significance	Domains Affected
<b>B. Davidson et al., 2021</b>	FACT-O, FACIT-PAL [1]	No difference in overall or subset QoL [1]	p = 0.14 [1]	None significantly different [1]
<b>Treshita Dey et al., 2023</b>	FACT-G [5]	Significant differences in social and emotional well-being between arms; no significant difference in physical/functional [5]	Social and emotional: p < 0.05; physical and functional: NS [5]	Social, emotional [5]
<b>Niyazi Kilic et al., 2021</b>	FACT-G [16]	No overall difference at 3 or 6 months; PC group improved in GP (18 to 20) and GF (16 to 19.8) by 6 months [16]	Overall: p = 0.39 (3 mo), p = 0.66 (6 mo); baseline GP p = 0.02, GF p = 0.003; 6-month GP p = 0.60, GF p = 0.73 [16]	Physical, functional (convergence over time) [16]

Study	QoL Instrument	QoL Effect (Intervention vs. Control)	Statistical Significance	Domains Affected
<b>Y. Mao et al., 2017</b>	FACT-G [6]	All FACT-G domains significantly higher in PC group post-treatment [6]	$p < 0.05$ for all domains [6]	Physical, social/family, emotional, functional [6]
<b>Xiang Zheng et al., 2017</b>	Not specified [19]	Intervention group QoL scores significantly higher [19]	$p < 0.05$ for overall and all function subscales [19]	Physical, role, emotional, cognitive, social [19]
<b>R. McCorkle et al., 2015</b>	FACT-G [3]	No significant between-group differences; symptoms stable or improved in both groups [3]	NS [3]	Physical and emotional symptoms stable [3]

Study	QoL Instrument	QoL Effect (Intervention vs. Control)	Statistical Significance	Domains Affected
<b>S. Pasalak et al., 2022</b>	EORTC QLQ [23]	Higher QoL and lower symptom severity in intervention group at time 2 and time 3 [23]	Not explicitly reported [23]	Not specified [23]
<b>A. Graul et al., 2020</b>	FACT-G [7]	Intervention group had higher total FACT-G (89.2 vs. 75.5); emotional (19.0 vs. 17.0) and functional (22.5 vs. 19.0) subscores higher [7]	FACT-G total p = 0.016; emotional p = 0.032; functional p = 0.030 [7]	Emotional, functional [7]
<b>D. Aktaş et al., 2015</b>	QoL Scale/Cancer Survivors [32]	Intervention group mean 6.01 ± 0.64 vs. control 4.35 ± 0.79 [32]	p < 0.05 [32]	Not specified [32]

Study	QoL Instrument	QoL Effect (Intervention vs. Control)	Statistical Significance	Domains Affected
<b>Kusum Kumari et al., 2024 (meta-analysis)</b>	Not specified [4]	Pooled SMD = 0.26 (95% CI: -0.29 to 0.80; I2 = 76%) [4]	CI crosses zero [4]	Not specified [4]
<b>Poojani Illangasinghe et al., 2025 (systematic review)</b>	FACT-G and others [21]	Majority of RCTs showed significant improvement (p < 0.05) [21]	p < 0.05 in most included RCTs [21]	Mental, emotional well-being [21]

Among the RCTs directly comparing early palliative care with standard care, QoL results were mixed. The two largest RCTs focused on recurrent ovarian cancer—Davidson et al. (n = 54) and Cusimano et al. (n = 23)—both failed to demonstrate statistically significant overall QoL improvements [1, 2]. The cluster RCT by McCorkle et al. (n = 146) similarly found no between-group differences in primary patient-reported outcomes, though both arms showed symptom stability or improvement [3]. By contrast, smaller or non-randomized studies reported significant QoL improvements: Mao et al. found significant gains across all FACT-G domains in elderly patients with advanced gynecologic cancers (p < 0.05) [6], and Aktaş et al. reported substantially higher QoL in patients receiving home care services (6.01 vs. 4.35, p < 0.05) [32]. Zheng et al. also showed significant QoL improvements in cervical cancer patients receiving early nursing intervention (p < 0.05 across all domains) [19].

Notably, the meta-analysis by Kumari et al. pooling four RCTs found a non-significant pooled effect on QoL (SMD = 0.26; 95% CI: -0.29 to 0.80) with substantial heterogeneity (I2 = 76%) [4],

while the systematic review by Illangasinghe et al. concluded that the majority of included RCTs demonstrated significant QoL improvements [21]. The Graul et al. RCT reported significantly higher FACT-G total scores and emotional and functional subscores in the intervention group at baseline, but these represented baseline differences between groups rather than longitudinal change [7]. The Kilic et al. longitudinal analysis found no significant overall QoL change over time, but did observe convergence between PC and no-PC groups in physical and functional well-being by 6 months, with the PC group improving from GF 16 to 19.8 and GP 18 to 20 [16].

Domain-specific findings suggest that emotional and social well-being may be more responsive to palliative care than physical functioning. Dey et al. found significant improvements in social and emotional well-being but not in physical or functional domains [5]. Similarly, Graul et al. found significant differences in emotional and functional subscores [7], and Mao et al. reported broad improvements across all psychosocial dimensions [6].

#### Symptom Management Outcomes

Study	Symptoms Assessed	Assessment Tool	Key Findings	Statistical Significance
C. Lefkowitz et al., 2015	Pain, fatigue, anorexia, depression, anxiety, nausea, dyspnea [8]	Modified ESAS [8]	Significant improvement in pain, anorexia, fatigue, and dyspnea within 1 day of PC consult [8]	p < 0.05 for pain, anorexia, fatigue, dyspnea [8]

Study	Symptoms Assessed	Assessment Tool	Key Findings	Statistical Significance
<b>Y. Mao et al., 2017</b>	Somatization, depression, anxiety, hostility, phobic symptoms, interpersonal sensitivity [6]	SCL-90 [6]	All SCL-90 domains significantly improved in PC group [6]	$p < 0.05$ [6]
<b>B. Scarborough et al., 2015</b>	Pain [12]	Not specified [12]	Pain significantly better addressed in intervention group [12]	$p < 0.001$ [12]
<b>S. Pasalak et al., 2022</b>	Multiple symptoms including sexual function [23]	ESAS, EORTC QoL, Modified Brief Sexual Symptom Checklist [23]	Lower symptom severity in intervention group; preserved sexual function [23]	Not separately reported [23]

Study	Symptoms Assessed	Assessment Tool	Key Findings	Statistical Significance
<b>Kusum Kumari et al., 2024</b>	Symptom burden, depression [4]	Not specified [4]	Symptom burden reduced (SMD = -0.75; 95% CI: -1.75 to 0.25; I2 = 89%); depression reduced (SMD = 0.08; 95% CI: -0.19 to 0.34; I2 = 0%) [4]	CI's cross zero for both [4]
<b>E. Ben-Arye et al., 2021</b>	Fatigue, pain, appetite, nausea/vomiting, sleep [25]	ESAS, EORTC QLQ-C30 [25]	Better maintained RDI in consistent IO group; lower neuropathy and pain [25]	RDI difference p = 0.005; taxane-specific p = 0.012 [25]
<b>A. Zhandos et al., 2025 (review)</b>	Pain, fatigue, depression, anxiety [20]	Not specified [20]	Early PC integration promotes improved symptom control [20]	Not reported [20]

The evidence on symptom management shows more consistent directional benefits than the QoL literature, particularly for acute symptom relief. Lefkowitz et al. demonstrated that inpatient PC

consultation was associated with statistically significant improvements in moderate-to-severe pain, anorexia, fatigue, and dyspnea within a single day, with the prevalence of moderate-to-severe pain dropping from a baseline of 52% [8]. Scarborough et al. found that integrated palliative care significantly improved pain management ( $p < 0.001$ ) [12]. Mao et al. reported significant improvements across multiple psychological symptom dimensions including depression, anxiety, somatization, and hostility (all  $p < 0.05$ ) [6].

The meta-analysis by Kumari et al. found a trend toward reduced symptom burden (SMD = -0.75) and depression (SMD = 0.08), but both confidence intervals crossed zero and heterogeneity was very high for symptom burden ( $I^2 = 89\%$ ) [4]. Ben-Arye et al. found that consistent integrative oncology treatment preserved chemotherapy adherence (relative dose intensity), with particular benefit during taxane-based regimens (RDI 0.93 vs. 0.87,  $p = 0.012$ ), though the effect was not observed with platinum-based cycles [25]. The nurse-led symptom management program by Pasalak et al. reported lower symptom severity in the intervention group at mid- and end-of-treatment time points, along with preserved sexual function [23].

#### Healthcare Utilization and End-of-Life Care Outcomes

Study	Outcome Measured	Key Findings	Statistical Significance
S. Mah et al., 2024	Hospital death, late chemotherapy, ICU admission, aggressive EOL care [9]	Early PC (>3 months before death) associated with lower rates of all aggressive EOL metrics [9]	Significant (specific p-values not extracted) [9]

Study	Outcome Measured	Key Findings	Statistical Significance
<p><b>M. Mullen et al., 2017</b></p>	<p>Procedures in last 30 days, hospice enrollment, time on hospice [10]</p>	<p>Fewer procedures (44% to 31%, <math>p = 0.01</math>); inpatient hospice doubled (12.5% to 25.7%, <math>p = 0.02</math>); time on inpatient hospice increased (1.9 to 6.0 days, <math>p = 0.02</math>) [10]</p>	<p><math>p = 0.01</math> (procedures); <math>p = 0.02</math> (inpatient hospice rate and duration) [10]</p>
<p><b>S. Gaster et al., 2019</b></p>	<p>Hospice enrollment, ACP, chemotherapy in last 14 days, ED visits, hospitalizations, cost [11]</p>	<p>Higher hospice enrollment (78% vs. 50%, <math>p &lt; 0.05</math>); earlier enrollment by 14 days; more ACP (57% vs. 16%); lower ED visits (50% vs. 67%) and hospitalizations (20% vs. 59%) [11]</p>	<p>Hospice and ACP: <math>p &lt; 0.05</math>; ED and hospitalization trends NS [11]</p>

Study	Outcome Measured	Key Findings	Statistical Significance
<p><b>M. Schneider et al., 2021</b></p>	<p>Inpatient PCA completion, outpatient PCA referrals [15]</p>	<p>PCA increased from 38% to 63% (RR 1.95, 95% CI 1.26–3.02); outpatient referrals from 5% to 20% (p = 0.005) [15]</p>	<p>PCA: RR 1.95; outpatient referrals: p = 0.005 [15]</p>
<p><b>Y. C. Lee et al., 2019</b></p>	<p>Hospital LOS, surgery rate, palliative chemo rate, survival [18]</p>	<p>Shorter cumulative LOS (13 vs. 22 days, adjusted p = 0.006); more palliative chemo (83% vs. 56%); less surgery (11% vs. 21%); longer median OS (243 vs. 99 days, adjusted p = 0.002) [18]</p>	<p>Adjusted p = 0.006 (LOS); p = 0.002 (OS) [18]</p>
<p><b>W. Lowery et al., 2013</b></p>	<p>Cost modeling: hospitalization, ED, chemo, QALYs [17]</p>	<p>Modeled savings of \$1,285/patient; ICER &lt; \$50,000/QALY unless outpatient EPC cost exceeds \$2,400 [17]</p>	<p>Sensitivity analysis: dominant or cost-effective [17]</p>

Study	Outcome Measured	Key Findings	Statistical Significance
<b>B. Scarborough et al., 2015</b>	Hospice enrollment, hospital/ICU deaths [12]	Higher hospice enrollment ( $p < 0.001$ ); lower death in hospital/ICU ( $p = 0.04$ ) [12]	$p < 0.001$ (hospice); $p = 0.04$ (death location) [12]
<b>B. Davidson et al., 2021</b>	Hospital admissions, hospice timing, place of death [1]	No differences in admissions ( $p = 0.96$ ), hospice timing ( $p = 0.41$ ), or place of death ( $p = 0.68$ ) [1]	All NS [1]
<b>R. Sims et al., 2021</b>	ED visits, ICU stays, inpatient admissions, hospice referrals, ACP [33]	No differences in ED, ICU, admissions, hospice; significantly more ACP documents ( $p = 0.000132$ ) [33]	ACP: $p = 0.000132$ ; all others NS [33]

Study	Outcome Measured	Key Findings	Statistical Significance
<b>Angel Tabuyo-Martin et al., 2022</b>	PM referral patterns, ED visits, chemotherapy near EOL by race [13]	Only 44.2% referred to PM; Black patients had more ED visits (26.1% with $\geq 7$ vs. 10.7% White, $p = 0.035$ ) and more chemo in last 30 days (15.2% vs. 4.3%, $p = 0.049$ ) [13]	Racial differences: $p = 0.035$ (ED), $p = 0.049$ (chemo) [13]
<b>B. Goff et al., 2023</b>	PC referral and visit rates [14]	Referrals increased from 8.64% to 12.84%; visits from 6.73% to 7.34% [14]	Not reported as statistically significant [14]

Healthcare utilization outcomes demonstrated the most consistently positive results. The largest and methodologically strongest study in this review—the population-based cohort by Mah et al. ( $n = 8,297$  ovarian cancer decedents)—found that initiating palliative care earlier than 3 months before death was associated with significantly lower rates of hospital death, late chemotherapy, ICU admission, and aggressive end-of-life care [9]. This finding aligns with the Pietras et al. review conclusion that early palliative care involvement, particularly more than 3 months before death, is associated with less aggressive end-of-life care and better alignment with patient preferences [28].

Multiple before-after and retrospective studies showed improvements in hospice utilization. Mullen et al. found that a PC initiative doubled inpatient hospice enrollment and reduced procedures in the last 30 days of life from 44% to 31% [10]. Gaster et al. reported that palliative care consultation

was associated with higher hospice enrollment (78% vs. 50%), earlier enrollment by 14 days, and substantially greater advance care planning documentation (57% vs. 16%) [11]. Scarborough et al. similarly found significantly higher hospice enrollment and fewer hospital/ICU deaths [12].

However, not all studies found utilization benefits. Davidson et al. found no differences in hospital admissions, hospice timing, or place of death between intervention and control arms [1], and Sims et al. found no differences in ED visits, ICU stays, or hospice referrals, though advance care planning documents were significantly increased [33]. The cost-effectiveness decision model by Lowery et al. estimated savings of \$1,285 per patient with early palliative care referral, and found the intervention cost-effective (ICER < \$50,000/QALY) unless outpatient costs exceeded \$2,400 [17, 17].

A concerning finding across several studies was the persistent underutilization of palliative care. Tabuyo-Martin et al. found that only 44.2% of patients with advanced or recurrent gynecologic cancers were referred to palliative medicine, and 30% died without any referral [13]. Goff et al. found that despite a web-based intervention, palliative care referral rates increased only modestly (8.64% to 12.84%), with visit rates barely changing [14]. Moroney et al. similarly documented underutilization of specialty palliative care in a phase I ovarian cancer population [34]. Racial disparities were identified by multiple studies: Schneiter et al. found that all inpatient deaths occurred among Black patients ( $p = 0.03$ ) [15], and Tabuyo-Martin et al. found Black patients had more ED visits and higher rates of chemotherapy in the last 30 days of life compared to White patients [13].

### **Survival Outcomes**

Three studies reported survival data. The interprofessional MBO program by Lee et al. found significantly longer median overall survival in the program group compared to historical controls (243 vs. 99 days, adjusted  $p = 0.002$ ) [18]. Segev et al. found that adherence to an integrative oncology program was associated with greater 3-year survival compared to non-adherent patients (HR 2.18, 95% CI 1.2–3.9) and controls (HR 2.23, 95% CI 1.35–3.7) [22]. Davidson et al., by contrast, found no overall survival difference between structured PC and usual care arms (9.3 vs. 10.1 months,  $p = 0.21$ ) [1]. Given the non-randomized designs of the positive survival studies and the potential for selection bias (healthier or more motivated patients may be more likely to adhere to integrative

programs or be referred to comprehensive programs), these survival associations should be interpreted cautiously.

### **Synthesis**

The apparent contradiction—several studies reporting significant QoL and symptom benefits while others find null effects—can be substantially explained by examining three dimensions of heterogeneity: study design and rigor, intervention type and intensity, and population and context.

The type and intensity of palliative care intervention also appears to moderate outcomes. Interventions involving structured, nurse-led, or multidisciplinary programs with sustained contact—such as Pasalak et al.'s nurse-led symptom management program [23] and McCorkle et al.'s 10-week APN-coordinated intervention [3]—tended to stabilize or improve symptoms even when between-group differences were non-significant, because comparator arms also improved. By contrast, single-consultation models (e.g., Lefkowitz et al. [8]) showed acute symptom relief but did not measure sustained QoL outcomes. The enhanced usual care comparators in several trials (e.g., both arms in McCorkle et al. received a Symptom Management Toolkit [3]) likely attenuated between-group differences, as multidisciplinary oncology teams inherently provide some palliative care elements.

Healthcare utilization outcomes are more consistently positive than QoL outcomes, and this divergence may reflect that process-level changes (referral patterns, documentation, hospice enrollment) are more directly responsive to system-level interventions than patient-reported subjective outcomes. The Mah et al. population-based study (n = 8,297) provides the strongest evidence that initiating palliative care more than 3 months before death reduces aggressive end-of-life care [9], a finding reinforced by the Pietras et al. review [28] and consistent with the before-after studies by Mullen et al. [10] and Gaster et al. [11]. The null findings from Davidson et al. on utilization [1] and Sims et al. on ED/ICU metrics [33] may reflect that these were smaller studies with insufficient power to detect utilization differences, or that their palliative care interventions were not sufficiently differentiated from the control condition.

Taken together, the evidence supports the following context-specific conclusions: (1) early palliative care integration consistently improves healthcare process outcomes—palliative care referral rates, hospice enrollment, advance care planning, and fewer aggressive interventions near

death—particularly when implemented as system-level protocols more than 3 months before death [9–11]; (2) QoL and symptom benefits are more reliably observed for psychological and emotional domains than for physical functioning [5–7], and acute inpatient symptom relief following PC consultation is well-supported [8]; (3) the magnitude of QoL improvement attributable specifically to early palliative care above standard multidisciplinary oncology care remains uncertain, as the best-controlled RCTs in gynecologic cancer populations have been underpowered and have not demonstrated significant between-group differences [1, 3]; and (4) persistent underutilization of palliative care, with referral rates below 50% even at specialized centers [13, 14], and racial disparities in end-of-life care intensity [13, 15], represent critical implementation gaps that may limit the real-world effectiveness of early integration strategies.

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## DISCUSSION

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This systematic review of 35 studies provides a comprehensive evaluation of early palliative care integration in women with advanced gynecologic cancer. The findings reveal a complex picture: while healthcare utilization outcomes demonstrate consistent improvements, patient-reported QoL benefits are more variable and context-dependent. This discussion synthesizes the key findings, explores explanations for heterogeneous results, examines implementation challenges, and considers implications for clinical practice and future research.

### **Quality of Life: Heterogeneity and Contextual Factors**

The most striking finding regarding QoL outcomes is the apparent contradiction between studies reporting significant improvements and those finding null effects. Several factors may explain this heterogeneity.

First, study design and methodological rigor substantially influence findings. The two largest randomized controlled trials specifically in recurrent ovarian cancer—Davidson et al. (n=54) and Cusimano et al. (n=23)—both failed to demonstrate statistically significant overall QoL improvements [1,2]. Similarly, the cluster RCT by McCorkle et al. found no between-group differences in primary outcomes [3]. These well-controlled studies suggest that when early palliative care is compared against enhanced usual care (where oncology teams may already provide substantial supportive care), the incremental benefit may be smaller than suggested by less rigorous designs. By

contrast, non-randomized studies and those with usual care comparators that lacked palliative care elements reported larger effect sizes [6,19,32], raising the possibility of confounding and selection bias.

Second, intervention type and intensity appear to moderate outcomes. Structured, nurse-led, or multidisciplinary programs with sustained contact—such as Pasalak et al.'s nurse-led symptom management program [23] and McCorkle et al.'s 10-week APN-coordinated intervention [3]—tended to stabilize or improve symptoms even when between-group differences were non-significant. These findings suggest that ongoing, relationship-based palliative care may be more effective than single consultations. However, single-consultation models demonstrated acute benefits for symptom relief [8], indicating that different intervention types may serve different purposes along the disease trajectory.

Third, domain-specific effects are noteworthy. Several studies found that emotional and social well-being were more responsive to palliative care than physical functioning [5,7,21]. Dey et al. reported significant improvements in social and emotional well-being but not in physical or functional domains [5]. Graul et al. found significant differences in emotional and functional subscores [7]. These patterns suggest that palliative care's primary mechanism for QoL improvement may be through psychological support and coping enhancement rather than direct modification of physical symptoms. This interpretation is consistent with the systematic review by Illangasinghe et al., which found that coping skills interventions significantly improved mental and emotional well-being [21].

The meta-analysis by Kumari et al. pooling four RCTs found a non-significant pooled effect on QoL (SMD=0.26; 95% CI -0.29–0.80) with substantial heterogeneity ( $I^2=76%$ ) [4]. This finding underscores that the overall evidence does not support a large, consistent QoL benefit across all gynecologic cancer populations, and that effect sizes vary considerably based on context and intervention characteristics.

### **Symptom Management: Consistent Benefits with Caveats**

The evidence on symptom management showed more consistent directional benefits than the QoL literature, particularly for acute symptom relief. Lefkowitz et al. demonstrated clinically meaningful improvements in moderate-to-severe pain, anorexia, fatigue, and dyspnea within one day

of inpatient palliative care consultation [8]. This rapid improvement highlights the value of palliative care expertise in managing complex symptoms even when overall QoL effects are less certain.

Psychological symptoms showed particularly robust improvements. Mao et al. reported significant improvements across multiple dimensions including depression, anxiety, somatization, and hostility [6]. These findings align with the domain-specific QoL results and suggest that palliative care's psychosocial components may be especially valuable. The nurse-led program by Pasalak et al. also reported preserved sexual function, an often-overlooked aspect of quality of life in gynecologic cancer patients [23].

However, the meta-analysis by Kumari et al. found that while symptom burden trended toward reduction (SMD=-0.75), the confidence interval crossed zero and heterogeneity was very high ( $I^2=89\%$ ) [4]. This suggests that while many individual studies show benefits, the overall evidence remains inconsistent, and factors moderating symptom improvement require further investigation.

An innovative finding from Ben-Arye et al. was that integrative oncology treatment preserved chemotherapy adherence, with particular benefit during taxane-based regimens [25]. This suggests that early palliative care may have indirect benefits on treatment delivery, potentially affecting disease outcomes.

### **Healthcare Utilization: The Most Consistent Benefits**

Healthcare utilization outcomes demonstrated the most robust and consistent improvements across studies. The population-based cohort by Mah et al. ( $n=8,297$  ovarian cancer decedents) provides the strongest evidence that initiating palliative care more than 3 months before death is associated with significantly lower rates of hospital death, late chemotherapy, ICU admission, and aggressive end-of-life care [9]. This finding is reinforced by the Pietras et al. review [28] and consistent with multiple before-after studies [10,11].

Several mechanisms may explain why utilization outcomes are more consistently positive than patient-reported outcomes. First, process-level changes (referral patterns, documentation, hospice enrollment) are directly responsive to system-level interventions, whereas patient-reported outcomes are influenced by numerous factors including disease progression and psychosocial variables. Second, utilization outcomes may be less susceptible to measurement error and recall bias

than QoL assessments. Third, the large sample sizes in utilization studies (e.g., Mah et al. n=8,297 [9]) provide greater statistical power to detect differences compared to smaller RCTs.

The improvements in hospice utilization are particularly noteworthy. Mullen et al. found that a palliative care initiative doubled inpatient hospice enrollment and reduced procedures in the last 30 days [10]. Gaster et al. reported higher hospice enrollment (78% vs. 50%), earlier enrollment by 14 days, and substantially greater advance care planning documentation (57% vs. 16%) [11]. These findings suggest that early palliative care facilitates more goal-concordant care at the end of life.

Cost-effectiveness analyses support these utilization benefits. Lowery et al.'s decision model estimated savings of \$1,285 per patient with early palliative care referral and found the intervention cost-effective unless outpatient costs exceeded \$2,400 [17]. This economic evidence is crucial for advocating for palliative care program implementation.

However, not all studies found utilization benefits. Davidson et al. found no differences in hospital admissions, hospice timing, or place of death [1], and Sims et al. found no differences in ED visits, ICU stays, or hospice referrals, though advance care planning documents were significantly increased [33]. These null findings may reflect insufficient statistical power or interventions that were not sufficiently differentiated from control conditions.

### **Implementation Gaps and Disparities**

A concerning finding across multiple studies was the persistent underutilization of palliative care. Tabuyo-Martin et al. found that only 44.2% of patients with advanced or recurrent gynecologic cancers were referred to palliative medicine, and 30% died without any referral [13]. Goff et al. found that despite a web-based intervention, palliative care referral rates increased only modestly (8.64% to 12.84%) [14]. Moroney et al. similarly documented underutilization in a phase I ovarian cancer population [34]. These findings suggest that even when evidence supports early palliative care, implementation barriers remain substantial.

Racial disparities in end-of-life care represent another critical implementation gap. Schneiter et al. found that all inpatient deaths occurred among Black patients (p=0.03) [15]. Tabuyo-Martin et al. found that Black patients had more ED visits (26.1% with  $\geq 7$  vs. 10.7% White, p=0.035) and higher rates of chemotherapy in the last 30 days (15.2% vs. 4.3%, p=0.049) compared to White

patients [13]. These disparities demand targeted interventions to ensure equitable access to palliative care.

### **Survival Outcomes: Cautious Interpretation**

Three studies reported survival data with conflicting results. Lee et al. found significantly longer median overall survival in an interprofessional malignant bowel obstruction program compared to historical controls (243 vs. 99 days, adjusted  $p=0.002$ ) [18]. Segev et al. found that adherence to an integrative oncology program was associated with greater 3-year survival [22]. However, Davidson et al. found no overall survival difference (9.3 vs. 10.1 months,  $p=0.21$ ) [1].

The positive survival findings must be interpreted cautiously given the non-randomized designs and potential for selection bias. Patients who adhere to integrative programs or are referred to comprehensive palliative care may be healthier, more motivated, or have better social support—factors that independently predict improved survival. Until randomized trials confirm survival benefits, claims that early palliative care extends survival in gynecologic cancers remain speculative.

### **Synthesis and Interpretation**

The apparent contradictions in this evidence base can be reconciled by considering the following context-specific conclusions:

First, early palliative care integration consistently improves healthcare process outcomes—palliative care referral rates, hospice enrollment, advance care planning, and fewer aggressive interventions near death—particularly when implemented as system-level protocols more than 3 months before death [9,10,11]. These benefits are robust across study designs and populations.

Second, QoL and symptom benefits are more reliably observed for psychological and emotional domains than for physical functioning [5,6,7,21]. Acute inpatient symptom relief following palliative care consultation is well-supported [8], but sustained QoL improvements above standard multidisciplinary oncology care remain uncertain, as the best-controlled RCTs have been underpowered and have not demonstrated significant between-group differences [1,3].

Third, the magnitude of benefit attributable specifically to early palliative care depends heavily on comparator conditions. In settings where usual care already includes substantial supportive

care elements, the incremental benefit of formal palliative care integration may be smaller. This "contamination" of control groups may explain null findings in some RCTs.

Fourth, persistent underutilization and racial disparities represent critical implementation gaps that limit real-world effectiveness [13,14,15]. Even when early palliative care is efficacious in research settings, its population-level impact will be constrained if most eligible patients never receive it.

### **Implications for Clinical Practice**

Despite these limitations, several practice recommendations emerge. First, healthcare systems should implement standardized referral criteria for palliative care in advanced gynecologic cancers, with the goal of initiating palliative care at least 3 months before anticipated death [9,28]. Second, interdisciplinary models integrating palliative care specialists with gynecologic oncology teams may optimize outcomes [18,23]. Third, routine screening for psychological distress and symptom burden should trigger palliative care involvement. Fourth, efforts to address racial disparities must be prioritized, including culturally tailored interventions and systematic monitoring of referral patterns [13,15]. Fifth, advance care planning should be initiated early and revisited regularly [11,33].

### **Implications for Future Research**

Future research priorities should include: (1) adequately powered randomized controlled trials in homogenous gynecologic cancer populations; (2) studies identifying optimal timing, intensity, and duration of palliative care interventions; (3) research on implementation strategies to increase referral rates and address disparities; (4) development and validation of gynecologic cancer-specific palliative care outcome measures; (5) cost-effectiveness analyses using real-world data; and (6) studies examining novel delivery models including telehealth and nurse-led interventions.

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## **CONCLUSION**

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This systematic review of 35 studies evaluating early palliative care integration in women with advanced gynecologic cancer reveals that while healthcare utilization outcomes consistently improve—including reduced aggressive end-of-life care, increased hospice enrollment, and cost-effectiveness—patient-reported quality of life benefits are more variable and context-dependent. The strongest evidence supports early palliative care initiated more than 3 months before death to optimize

end-of-life care quality. Psychological and emotional well-being appear more responsive to palliative care interventions than physical functioning, suggesting that psychosocial support mechanisms may drive quality of life improvements.

However, several critical gaps limit definitive conclusions. Well-controlled randomized trials in gynecologic-specific populations remain underpowered and have not consistently demonstrated significant quality of life benefits above enhanced usual care. The heterogeneity of intervention models, outcome measures, and definitions of "early" integration complicates evidence synthesis. Most importantly, persistent underutilization of palliative care—with referral rates below 50% even at specialized centers—and racial disparities in end-of-life care intensity represent fundamental implementation failures that must be addressed.

### **Recommendations**

**For clinical practice:** Healthcare institutions should implement standardized referral protocols for early palliative care in advanced gynecologic cancers, targeting initiation at least 3 months before anticipated death. Interdisciplinary models integrating palliative care specialists with gynecologic oncology teams should be prioritized. Routine screening for psychological distress and culturally tailored interventions to address racial disparities are essential.

**For health policy:** Policymakers should support reimbursement models that incentivize early palliative care integration and remove barriers to concurrent palliative and oncologic care. Quality metrics should include palliative care referral rates, timing of hospice enrollment, and monitoring of disparities.

**For future research:** Adequately powered randomized trials in homogenous gynecologic cancer populations are needed, with attention to optimal timing, intensity, and duration of interventions. Implementation science research should identify strategies to increase referral rates and address disparities. Development of gynecologic cancer-specific palliative care outcome measures would facilitate evidence synthesis. Finally, studies examining novel delivery models—including telehealth, nurse-led interventions, and embedded palliative care—may identify approaches that maximize benefit while addressing underutilization.

In conclusion, early palliative care integration in advanced gynecologic cancer holds promise for improving end-of-life care quality and addressing psychological symptoms, but real-world effectiveness will depend on overcoming persistent implementation barriers and ensuring equitable access for all women.

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