



# Impact of Early Initiation of Palliative Care Among Cancer Patients in United States of America: Systematic Review and Meta-Analysis of Randomized Control Trials

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**Keywords:** Cancer; Palliative care; Systematic review; Meta-analysis; United States of America.

**Abbreviations:** AJO: African Journals Online, CI: Confidence Interval, ICU: Intensive Care Unit; NOS: Newcastle Ottawa Scale, PC: Palliative Care, PRISMA: Preferred Reporting Items for Systematic Review and Meta-analysis, and USA: United States of America.

## Abstract

**Introduction:** Early initiation of palliative care services is associated with improved end-of-life outcomes, a better quality of life, an increased survival rate, and a longer life expectancy. It helps to decrease intensive medical care, improve quality outcomes, and provide cost savings at the end of life for patients with cancer and their families. There is evidence to suggest early initiation of palliative care improves treatment-related decision-making ability, healthcare utilization, advanced care planning, patient satisfaction, patients' symptoms, and health-related communication skills. Despite recommendations that early palliative care be offered to all patients with cancer, it remains underutilized. Therefore, this study aimed to assess the impact of the early initiation of palliative care among cancer patients in the United States of America.

**Methods:** To find available articles, several databases were searched. The data was extracted and sorted using Microsoft Excel. Then it was exported to STATA/MP 17.0 for analysis. A weighted inverse variance random-effects model with a 95% CI was employed to pool the data. Heterogeneity was assessed using the Galbraith plot and Cochrane I<sup>2</sup> statistics. The possibility of influential studies was examined using a sensitivity analysis test. Furthermore, Egger's test was computed to assess publication bias. Finally, a P-value less than 0.05 was considered statistically significant.

**Result:** This review covered five studies published until May 2023, involving 125,470 study participants. Of these study participants, 62,733 (50%) were in the intervention group, who initiated palliative care early, whereas 62,733 (50%) were in the non-intervention group. The pooled prevalence of early initiation of palliative care among cancer patients in the USA was 30.87% (95% CI: 17.01–44.73). However, the pooled prevalence of death among cancer patients who initiated palliative care later was 37.93% (95% CI: 21.19–54.67). Therefore, 7.06% (95% CI: 4.18–9.94) of cancer patients died due to the delayed initiation of palliative care in the USA.

**Conclusion:** This study showed that a significant number of cancer patients died due to the late initiation of palliative care. Therefore, the early integration of palliative care for cancer patients should be highly emphasized to decrease the impact of late initiation of palliative care.



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## Introduction

Around the globe, the source of distress for cancer patients is often unaddressed, and the data report on cancer patients identifies that their needs are unmet and they need specialized care like palliative care [1]. The utilization of palliative care services helps to improve the survival rate of patients with advanced cancer [2]. Healthcare providers should actively identify and incorporate cancer patients who would benefit from palliative care to increase the utilization of palliative care services and improve their access [3]. The integration of palliative care in the treatment of advanced cancer patients can lead to a significant improvement in quality of life, less aggressive care, an improvement in overall survival status, and longer enrollment in hospice services. These lead to higher satisfaction, fewer unmet needs, and better communication with physicians about medical decision-making [2].

The effectiveness of palliative care increased, but it should be integrated early. Early initiation of palliative care services was associated with improved end-of-life outcomes, a better quality of life, an increased survival rate, and a longer life expectancy. However, the late initiation of palliative care was associated with increased acute care use, an increased possibility of organ failure, and frailty decedents, which suggests potential opportunities for the need for improvement [4]. Early palliative care service is also linked with fewer procedures, a shorter hospital stay, and no immediate effect on mortality [5]. Furthermore, early palliative care service helps to decrease intensive medical care, improve quality outcomes, and provide cost savings at the end of life for patients with cancer and their families [6]. Overall, for adult cancer patients, there is evidence to suggest early initiation of palliative care improves health-related quality of life, mood, treatment-related decision-making ability, health care utilization, advanced care planning, patient satisfaction, patient symptoms, and health-related communication skills [7].

Different studies showed the proportion of early initiation of palliative care services and their effect on the general condition of cancer patients. Accordingly, the proportion of early integration of palliative care was 28% [8], 47%, [9], 32.2% [6], and 28.7% [10]. Patients receiving early palliative care had fewer emergency department visits (2.6 vs. 3.0 visits,  $P=0.004$ ), lower total charges of emergency department care (\$3158 vs. \$3981,  $P<0.001$ ), and lower ICU admissions (0.82 vs. 0.98 visits,  $P = 0.006$ ) [8]. In addition, Early palliative care was predominantly delivered in the outpatient setting (84%), while late palliative care was mostly delivered in the hospital (82%) [6].

Even though the burden of cancer is increasing worldwide, the concept of palliative care is not well addressed around the globe. It is important to have global evidence on the impact of early versus late initiation of palliative care. Despite recommendations that early palliative care be offered to all patients with metastatic cancer, palliative care services remain underutilized. Thus, it is very necessary to investigate the impact of early initiation of palliative care since it improves the quality of life for cancer patients and their families. Therefore, the purpose of this systematic review and meta-analysis was to assess the impact of early initiation of palliative care among cancer patients in the United States of America.

## Methods

### Study protocol

The Preferred Reporting Items for Systematic Review and

Meta-analysis (PRISMA) checklist for reporting findings is used to identify the impact of early initiation of palliative care among cancer patients in the USA [11].

### Databases and searching strategies

In this systematic review and meta-analysis, randomized control trial studies were searched using the following databases: Google Scholar, Web of Science, African Journals Online (AJOL), HINARI, PubMed/MEDLINE, and EMBASE. To retrieve the available articles on the impact of early initiation of palliative care for cancer patients, the following search engines were used: "impact," "effect," "proportion," "relation," "early," "late," "utilization," "initiation," "integration," "palliative care," "end-of-life care," "cancer patients," "advanced cancer patients," "cancer," "patients," "randomized control trial," "trials," "United States of America," "USA,". The study utilized the "AND" and "OR" Boolean operators' strings (Table 1).

### Screening and eligibility of the studies

All available randomized control trials were investigated and exported to the citation manager of EndNote Reference software version 8 (Thomson Reuters, Stamford, CT, USA) to sort and avoid possible duplications. The author AG selects each article based on its title and abstract using the predetermined inclusion criteria. Using a Microsoft Excel sheet, the author extracted the first name of the researcher, the year of publication, the nation where the studies were done, the study design, the sample size, the mortality rate of patients who initiated palliative care early, and the mortality rate of patients who initiated palliative care later. All randomized control trials that reported the impact of early initiation of palliative care by cancer patients in the USA and were published until May 25, 2024, were included. However, articles that did not report outcome variables, qualitative studies, case reports, news, studies without full text after repeated emailing of the correspondence author, and studies of poor quality were excluded from the final analysis.

### Outcome measurement of the study

In this study, there are two outcomes: the proportion of death among cancer patients who initiated palliative care early and the proportion of death among cancer patients who initiated palliative care later. Early initiation of palliative care is defined as those cancer patients who initiated palliative care within 30 days of admission, whereas late initiation of palliative care is defined as those palliative care patients who initiated palliative care service after 30 days of admission.

### Quality assessment

The qualities of the articles were assessed using the Newcastle-Ottawa Scale (NOS) for cross-sectional studies [12]. The methodological quality, comparability, outcomes, and statistical analysis of the studies were the assessment tools used to declare the quality of the studies. Studies scored on a scale of  $\geq 7$  out of 10 were considered to have high quality. The author critically evaluated and assessed the articles for consideration and inclusion in the final analysis.

### Data processing and analysis

In this study, the data was extracted and cleaned using a Microsoft Excel spreadsheet. Then, the data were exported to STATA version 17 for analysis. The effect of early and late initiation of palliative care for cancer patients was examined using a

weighted inverse variance random-effects model at 95% CI [13]. The Cochrane Q-test and  $I^2$  with the correspondence p-value and Galbraith plot, were used to evaluate the studies' heterogeneity [14]. Sensitivity analysis was also performed to detect the presence or absence of influential studies. Furthermore, Egger's test was performed to investigate publication bias, and a funnel plot was displayed [15]. Finally, a statistical test with a P-value of  $< 0.05$  was considered statistically significant.

### Patient and public involvement

It was not appropriate or possible to involve patients or the public in the design, or conduct, or reporting, or dissemination plans of our research.

### Result

A total of 255 articles were found in different databases after utilizing the search keyword. After critically evaluating each article, a substantial number of articles were excluded from the analysis due to the presence of duplication, being unable to get the full text, being unable to report the outcome of interest, and failing to fulfill the inclusion criteria. Furthermore, some articles were removed after carefully reviewing the study's title and abstract. Finally 5, articles that fulfilled the inclusion criteria were included (Figure 1).

### Characteristics of the studies and study participants

This review covered five studies published until May 2023, involving 125,470 study participants. Of these study participants, 62,733 (50%) were in the intervention group, who initiated palliative care early, whereas 62,733 (50%) were cancer patients who initiated palliative care later which is the non-intervention group. All the studies are done in the USA (4, 16-19). All the included studies are randomized control trials in design. The sample size of the included studies ranged from 122 to 124697 Table 2).

### Impact of early versus late initiation of palliative care

This systematic review and meta-analysis showed the impact of early versus late initiation of palliative care on the mortality rate among cancer patients in the USA. Accordingly, the pooled prevalence of death among cancer patients who initiated palliative care early was 30.87% (95% CI: 17.01–44.73) (Figure 2). However, the pooled prevalence of death among cancer patients who initiated palliative care later was 37.93% (95% CI: 21.19–54.67) (Figure 3). Therefore, 7.06% (95% CI: 4.18–9.94) of cancer patients died due to the delayed initiation of palliative care in the USA.

### Heterogeneity and publication bias

The asymmetrical distribution of the included articles was visible in the funnel plot indicating the presence of publication bias (Figure 3). In addition, the visual examination of the Galbraith plot reveals the presence of significant heterogeneity ( $I^2$  100%,  $p < 0.001$ ) (Figure 4).

### Sensitivity analysis

A leave-one-point sensitivity analysis employing the random-effects model in this systematic review and meta-analysis revealed that all point estimates were within the overall 95% confidence interval (17.01–44.73), indicating the absence of any influential studies (Table 3).

### Discussion

Palliative care is the active, all-encompassing treatment of a patient's body, mind, and soul. It is a potent complement to the patient's overall psychosocial care. It promotes managing symptoms and quality of life throughout a serious illness. Palliative care is a relatively well-accepted idea in the developed world today, addressing the needs of patients facing the inevitable end of their lives due to a life-limiting illness [20]. Palliative care integration can result in a markedly improved quality of life, less aggressive treatment, and an improved overall survival status for patients with advanced cancer [21]. These outcomes can lead to a greater degree of satisfaction, fewer unmet needs, and improved communication with physicians regarding medical decision-making. Palliative care services started early have been linked to greater quality of life, higher survival rates, longer life expectancies, and better end-of-life outcomes. However, there may be room for improvement given that delayed palliative care beginning was linked to higher rates of acute care utilization, an increased risk of organ failure, and frailty decedents [4].

The result of this systematic review and meta-analysis showed that the pooled prevalence of death among cancer patients who initiated palliative care early was 30.87% (95% CI: 17.01–44.7), whereas the pooled prevalence of death among cancer patients who delayed initiating palliative care was 37.93% (95% CI: 21.19–54.67). Thus, 7.06% (95% CI: 4.18–9.94) of cancer patients died due to the delayed initiation of palliative care in the USA.

This may be because patients with advanced cancer who had palliative care in addition to normal treatment reported feeling better and having an improved standard of life than those who did not receive early palliative care [22].

Furthermore, an abundance of studies has demonstrated that early palliative care can enhance overall cancer outcomes, including psychological comfort, pain and symptom control, patient satisfaction, and even survival. Numerous early palliative care integration and incorporation models in clinics, hospitals, and home settings have been examined; the results unequivocally demonstrate the advantages of providing palliative care at the time of cancer diagnosis [23].

In this study, significant heterogeneity ( $I^2$  100%,  $< 0.001$ ) was identified. The possible source for this heterogeneity might be due to a huge variation in sample size within the included studies, where the sample size of one included study was 124697, whereas the remaining four studies' sample size was below 300. This is supported by Heterogeneity is to be expected in a meta-analysis. It could be surprising, if not impossible if multiple studies performed by different researchers in different places with different methods all ended up establishing the same underlying parameter. For this study, the impact of heterogeneity in the sample sizes resulted in differences in the results of the primary researchers. In research work, therefore, a standardized sample size is recommended to be assigned to published articles, and the unpublished articles should also be within a given range of sample sizes [24]. Furthermore, a leave-one-point sensitivity analysis revealed that all point estimates were within the overall 95% confidence interval (17.01–44.73). This is because none of the included studies are influential over the others.

**Table 1:** Search of databases on the impact of early initiation of palliative care among cancer patients in United States of America.

Databases	Searching terms	Number of studies
MEDLINE/ PubMed	"Impact," OR "effect," OR "proportion," OR "relation," AND "early," OR "late," AND "utilization," OR "initiation," OR "integration," AND "palliative care," OR "end-of-life care," AND "cancer patients," OR "advanced cancer patients," OR "cancer," OR "patients," AND "randomized control trial," OR "trials," AND "United States of America," OR "USA,".	240
Google Scholar	"Impact," OR "effect," OR "proportion," OR "relation," AND "early," OR "late," AND "utilization," OR "initiation," OR "integration," AND "palliative care," OR "end-of-life care," AND "cancer patients," OR "advanced cancer patients," OR "cancer," OR "patients," AND "randomized control trial," OR "trials," AND "United States of America," OR "USA,".	13
Other databases	"Impact," OR "effect," OR "proportion," OR "relation," AND "early," OR "late," AND "utilization," OR "initiation," OR "integration," AND "palliative care," OR "end-of-life care," AND "cancer patients," OR "advanced cancer patients," OR "cancer," OR "patients," AND "randomized control trial," OR "trials," AND "United States of America," OR "USA,".	2
Total retrieved articles		255
Included studies		5

**Table 2:** Characteristics of studies and study participants on the impact of early initiation of palliative care among cancer patients in United States of America.

Author	Country	Stud design	Sample size	Early initiation of PC		Late initiation of PC		Death of cancer patients after early initiation of PC		Death of cancer patients after late initiation of PC	
				No.	%	No.	%	No.	%	No.	%
Marie A et al, 2015	USA	Randomized control trial	207	104	50.2	103	49.8	52	25.1	62	30.0
Joseph A. et al, 2012	USA	Randomized control trial	151	77	51.0	74	49.0	60	39.7	65	43.0
Jennifer S. et al, 2017	USA	Randomized control trial	293	145	49.5	150	51.2	41	14.0	50	17.1
J. Nicholas et al, 2015	USA	Randomized control trial	122	61	50.0	61	50.0	27	22.1	39	32.0
Danial Q. et al, 2018	USA	Randomized control trial	124697	62349	50.0	62348	50	33045	53.0	41773	67.0

PC: Palliative Care

**Table 3:** Sensitivity analysis on the impact of early initiation of palliative care among cancer patients in United States of America.

Study omitted	Estimate	95% CI	
		Lower	Upper
Marie A et al, 2015	32.26	19.25	46.02
Joseph A. et al, 2012	28.64	14.44	53.05
Jennifer S. et al, 2017	35.14	10.08	53.20
J. Nicholas Dionne-Odom et al, 2015	32.98	22.71	55.98
Danial Qureshi et al, 2018	35.37	14.32	35.53
<b>Combined</b>	<b>30.87</b>	<b>17.01</b>	<b>44.73</b>

### Conclusion

In the USA, there was a difference between the early and late initiation of palliative care for cancer patients and their outcomes. This study showed that a significant number of cancer patients died due to the late initiation of palliative care as compared to early initiation. Therefore, the early integration of palliative care services for cancer patients should be highly emphasized to decrease the impact of late initiation of palliative care.

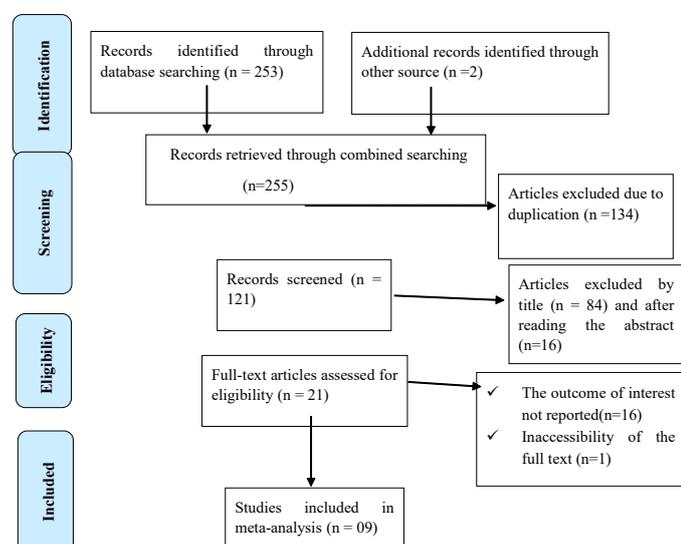
### Contribution of the paper

#### What is already known

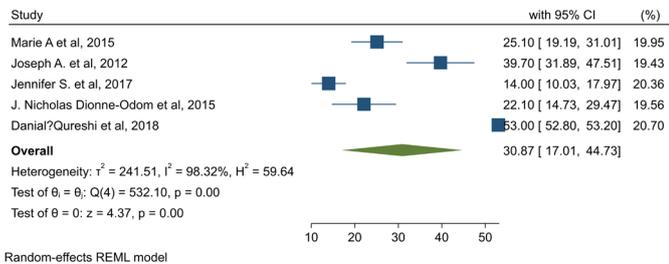
- Utilization of palliative care by cancer patients
- Mortality rate of cancer patients who did not receive palliative care
- Benefit of palliative care for cancer patients

#### What this paper adds

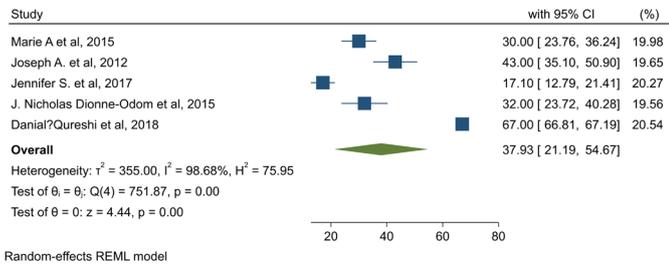
- A comprehensive review of the literature with a clear focus on specific populations, which gives strong evidence on pooled prevalence of early initiation of palliative care among cancer patients (30.87% (95% CI: 17.01–44.73)).
- The use of robust statistical methods to analyze pooled data, detailed meta-regression and subgroup analysis to identify sources of heterogeneity, which helps to report reliable evidence on the impact of late initiation of palliative care for cancer patients (37.93% (95% CI: 21.19–54.67)).
- It will provide an insight to improve the quality of life for cancer patients and their families by early integration of palliative care.



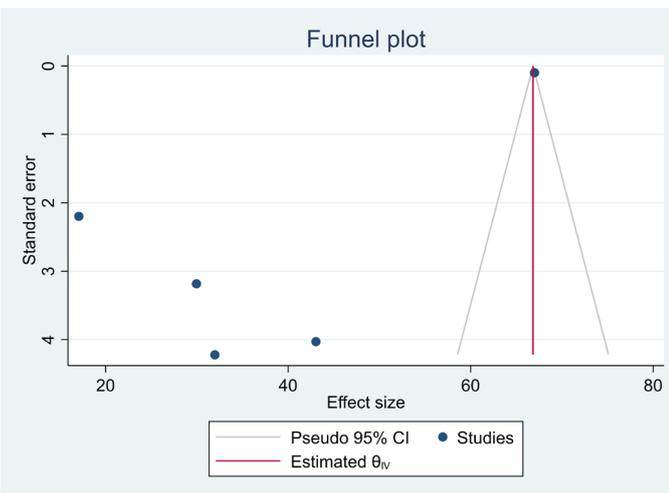
**Figure 1:** PRISMA flow chart diagram on selection of articles done on the impact of early initiation of palliative care among cancer patients in United States of America.



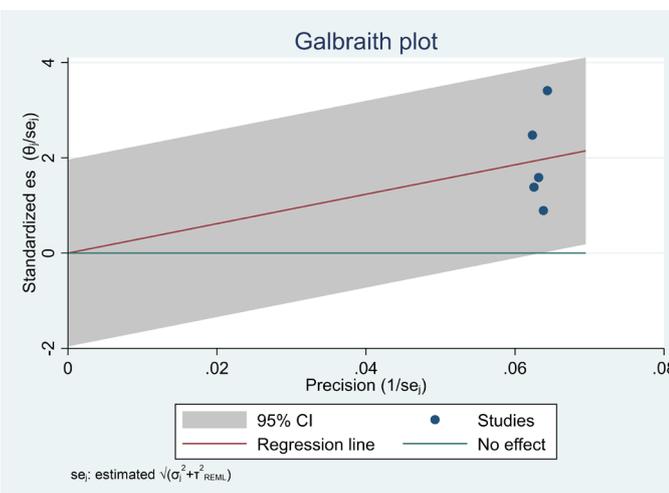
**Figure 2:** Frost plot on the pooled prevalence of death among cancer patients who initiated palliative care early at USA.



**Figure 3:** Frost plot on the pooled prevalence of death among cancer patients who initiated palliative care later at USA.



**Figure 4:** Funnel plot with 95% confidence limits on the pooled prevalence of death among cancer patients who initiated palliative care early at USA.



**Figure 5:** Galbraith plot with 95% confidence limits on the pooled prevalence of death among cancer patients who initiated palliative care early at USA.

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