

# Palliative care for terminally ill patients in the intensive care unit: Systematic review and metaanalysis

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## ABSTRACT

**Objective:** The purpose of our systematic review was to determine whether the introduction of palliative care (PC) teams reduces length of stay and/or mortality for terminally ill patients (TIPs) in an intensive care unit (ICU).

**Method:** We hoped to examine studies that compared TIPs in an ICU who received end-of-life care following implementation of a PC team (intervention group) to those who received care where PC teams had not yet been introduced (control group). We searched MEDLINE via PubMed, LILACS, Scopus, Embase, and Cochrane CENTRAL (search conducted in December of 2015) without language restrictions. Our outcome measures were length of stay in an ICU, presented as an average difference with a corresponding 95% confidence interval ( $CI_{95\%}$ ), and mortality in the ICU, presented as a risk ratio with a corresponding  $CI_{95\%}$ . Two of our authors independently extracted all of the data.

**Results:** Of the 399 publications identified, 27 were selected for full-text analysis and 19 were excluded, leaving 8 articles for inclusion, which involved a total of 7,846 patients. A metaanalysis of mortality in the ICU was conducted with four studies. Lower mortality was found in the intervention group: risk ratio = 0.78 ( $CI_{95\%} = 0.70-0.87$ ),  $p < 0.00001$ ,  $I^2 = 18\%$ . Length of stay in the ICU was presented as a mean and standard deviation in four studies, and the result was a reduction of ~2.5 days in the length of stay with application of the intervention: mean = -2.44 days ( $CI_{95\%} = -4.41$  to  $-0.48$ ),  $p = 0.01$ ,  $I^2 = 86\%$ .

**Significance of results:** Introduction of palliative care teams can reduce mortality rates in the ICU, and perhaps shorten length of stay in the ICU for terminally ill patients.

**KEYWORDS:** Palliative care, Terminal care, Palliative treatment, End-of-life care, Intensive care units

## INTRODUCTION

Interventions to extend the life process can provide artificial life support for patients with chronic or acute illnesses who are expecting improvement.

However, if applied to terminally ill patients (TIPs), such procedures may merely painfully prolong the process of dying.

The multidisciplinary practice of palliative care (PC) has a number of possibilities for relieving the pain and discomfort experienced by TIPs. It also provides an opportunity for such patients to take an active role in positioning themselves at the end of life, assisted by specialized professionals.

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According to Maciel (2008), the patients eligible for palliative care include those with a life expectancy of weeks to months as well as those with a prognosis ranging from hours to days.

Physicians should be prepared to limit treatment, be it in relation to decision making or to the appropriateness of management for a TIP in an intensive care unit (ICU).

The benefit obtained from medical interventions should be balanced with ethical considerations that lead to better care, according to the available resources and the overriding principles of bioethics: beneficence, non-maleficence, autonomy, and justice.

For Moritz et al. (2008), the fundamental objectives of PC in the ICU are: (1) to accept death as a natural process at the end of life; (2) to prioritize the best interests of the patient; (3) to refute diagnostic and treatment futility; (4) to neither shorten life nor prolong the process of dying; (5) to ensure quality of life as much as quality of death; (6) to relieve pain and other symptoms; (7) to maintain clinical, psychological, social, and spiritual care of both patients and family members; (8) to respect the autonomy of the patient and their legal representatives; (9) to balance the cost and benefit of the medical decision; and (10) to stimulate interdisciplinary practice of care.

Furthermore, the autonomy of the patient must always be respected. Their consent or that of their legal representative should be recorded in the medical record and must precede any decision made by the medical team.

In the current context, believing that TIPs should neither occupy an ICU bed nor die in the ICU, the introduction of palliative care into the ICU may be associated with better quality of life for terminally ill patients.

Our main objective was to evaluate by means of a systematic review whether the introduction of palliative care teams reduces length of stay and mortality for terminally ill patients in intensive care units.

## METHODS

### Types of Studies

As we found only one small randomized clinical trial (RCT), retrospective studies were also considered.

### Participants

Our participants were terminally ill adults in intensive care units.

### Interventions

The intervention we employed was introduction of a palliative care team.

### Control

The previous period of care, when there was no palliative care team, was utilized as our control.

### Outcome Measures

Our outcome measures were (1) length of stay in the ICU, (2) mortality in the ICU, and (3) quality of life.

### Search Methods

#### *Electronic Databases*

Our search included the following electronic databases: PubMed (1966 to December of 2015), Embase (1980 to December of 2015), LILACS ([www.bireme.br/](http://www.bireme.br/)) (1982 to December of 2015), and Cochrane Library's Central Register of Controlled Trials (CENTRAL).

We employed the following search strategy: ("end of life care" OR "life care end" OR "life care ends" OR "terminal care") AND ("intensive care unit" OR "intensive care units") AND ("palliative care" OR "palliative treatment" OR "palliative treatments" OR "palliative therapy" OR "palliative surgery").

Our search strategy was specifically adapted for each database. No restrictions were placed on language or publication status.

#### *Searching Other Resources*

The reference lists of relevant publications found in our search were screened for further studies, and experts in the field were contacted.

## Data Collection and Analysis

### *Study Selection*

Studies were grouped and duplicates removed. The titles and abstracts were examined to remove irrelevant items. We then recovered the full text of potentially relevant articles, which were examined by two reviewers to assess eligibility. The final decisions on inclusion into the study and data collection were made. Any disagreements were resolved by discussion. If a consensus was not reached, the opinion of the third author was decisive.

### *Data Extraction and Management*

The details of the eligible studies were extracted independently and summarized. Two reviewers independently extracted all the data relating to the interventions studied. Disagreements were again resolved by discussion.

### *Assessment of Risk of Bias in Included Studies*

If RCTs were recovered, we planned for two of our authors to independently evaluate each paper. As only

one small RCT was found, the included studies were considered as having a high risk of bias, since they were observational retrospective studies covering different time periods.

### Measures of Treatment Effect

Dichotomous outcomes were presented as risk ratios with a corresponding 95% confidence interval ( $CI_{95\%}$ ). For continuous outcomes, the average difference was analyzed with a corresponding  $CI_{95\%}$ .

Statistical heterogeneity was primarily assessed using the  $I^2$  test, which examines the percentage of total variation between studies due to heterogeneity rather than chance. Values of  $I^2 < 40\%$  indicated a low level of heterogeneity and justified the use of a fixed-effect model for metaanalysis; values of  $I^2$  between 30 and 60% were considered moderate, and a random-effects model was used; and values of  $I^2 > 75\%$  indicated a high level of heterogeneity, in which case metaanalysis was not deemed appropriate. We assumed that statistical, methodological, and clinical heterogeneity would be present (Deeks et al., 2008).

### Data Synthesis

For the outcome “mortality in the ICU,” as the heterogeneity was not great ( $I^2 < 40\%$ ), we employed a fixed-effect model according to the Mantel–Haenszel method for metaanalysis (Mantel & Haenszel, 1959).

For “length of stay in the ICU,” as the heterogeneity was high, metaanalysis was not proper. Mean differences were presented between the intervention and control groups in the studies. We utilized the Cochrane program (RevMan 5.3) for the metaanalyses.

## RESULTS

### Description of Studies

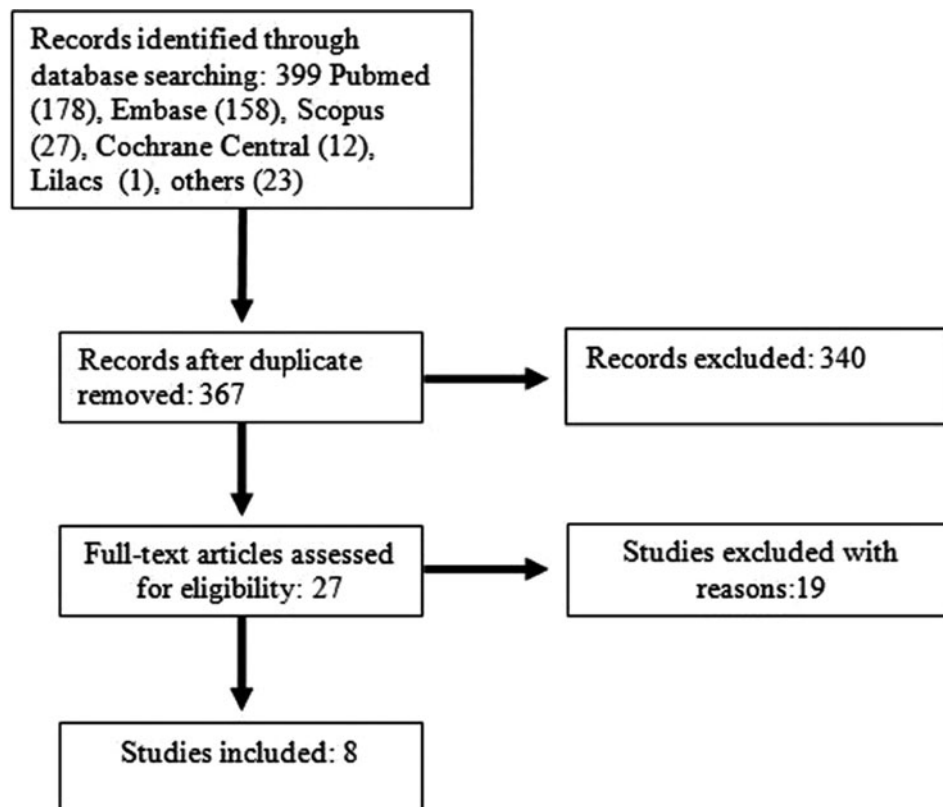
#### Results of the Search

Conducted in December of 2015, the search recovered 399 papers. After exclusion of duplicates and analysis of titles and abstracts, 27 articles were selected, all of which were completely examined, and 8 which were selected for our review (Figure 1).

The main characteristics of the selected studies are summarized in Table 1. The 8 included studies involved 7,846 participants. Seven of the studies were observational in nature and compared retrospective data before and after implementation of a palliative care team. Only one small study with 20 participants (Cheung et al., 2010) was randomized.

### Types of Interventions

The interventions implemented by a PC team can be summarized as follows: offering family support,



**Fig. 1.** Flowchart for selection of included studies.

**Table 1.** Characteristics of the included studies

Study	Type of study/period	Method	Study site	n (before)	n (after)
Campbell & Guzman (2003)	Cohorts comparison, retrospective and prospective (07/01/1998 to 06/30/1999).	Retrospective: historic control group (07/01/1998 to 06/30/1999); analyses of patients' records for GCI and MOSF in ICU. Prospective: intervention group (07/01/1999 to 06/30/2000), interventions of palliative care team in ICU.	Detroit Receiving Hospital. Detroit, Michigan, USA	MOSF = 22 GCI = 18	MOSF = 21 GCI = 20
Elsayem et al. (2006)	Retrospective review: 1999 (before), 2004 (after)	Review in hospital database from 1999 to 2004, compared to the period before September 1999, when the palliative care team was implemented, to the period subsequent to it, until 2004. The palliative care unit was created in 2002.	University of Texas MD Anderson Cancer Center Houston, Texas, USA	One year ICU deaths = 280. Does not provide number of admissions.	One year ICU deaths = 258. Does not provide number of admissions.
Norton et al. (2007)	Observational prospective: 03/26/2004 to 03/03/2005.	Conducted from 03/26/2004 to 03/03/2005 for all patients admitted to ICU among those identified with severe disease and high death risk. Phase of regular care (03/26/2004 to 07/23/2004); proactive phase with palliative care (07/26/2004 to 03/03/2005).	University of Rochester Medical Center, Rochester, New York, USA	65	126
Curtis et al. (2008)	Retrospective review (07/2003–10/2005).	Records review of patients who died before (07/2003 to 03/2004) and after (12/2004 to 10/2005) intervention; on improvement in quality of palliative care in ICU.	Harborview Medical Center, University of Washington, Seattle, Washington, USA	253	337
Cheung et al. (2010)	Randomized controlled trial (05/2006–10/2008).	Conducted from 05/2006 to 10/2008, for terminally ill or pre-terminal patients for whom improvement of clinical situation was considered unlikely. Assessment period from 05/2006 to 10/2008.	Concord Repatriation General Hospital. Sydney, New South Wales, Australia	10	10
Digwood et al. (2011)	Retrospective review (01/01/2006–12/31/2009).	Review of electronic data of all discharges from the medical ICU from 01/01/2006 to 12/31/2009; 5,035 cases. The two years that preceded the opening of the palliative care unit (10/01/2008) were compared to the two following years.	North Shore University Hospital. New York, New York, USA	2319	2716
Lustbader et al. (2011)	Two retrospective cohorts (01/01/2003–06/01/2009).	Comparison of two cohorts. Historical control group (those who died in ICU between 01/01/2003 and 06/30/2004) compared to those who died from 01/01/2005 to 01/06/2009, when palliative care had already been introduced into the ICU.	North Shore University Hospital. Manhasset, New York, USA	515	693
Lamba et al. (2012)	Observational prospective (03/2003–05/2005).	Patients from the Liver Transplantation Service in the surgical ICU before (03/2003–03/2004) and after (03/2004–05/2005) the palliative care intervention.	University of Medicine and Dentistry of New Jersey, University Hospital, Newark, New Jersey, USA	79	104

collecting perceptions of family members, encouraging family involvement in decision making, offering palliative care consultations in the ICU, and, when possible, transferring the patient to a PC unit. Only one study intended to improve medical care and quality of life with their intervention (Curtis et al., 2008).

## Outcomes Measured

Campbell and Guzman (2003): in-hospital mortality; length of stay in the ICU; time interval from ICU admission to do-not-resuscitate (DNR); time between identification of critical condition and establishment of PC; time between identification of critical condition and death.

Elsayem et al. (2006): mortality in the ICU and hospital wards in relation to global mortality in the hospital; length of stay in the ICU and hospital wards.

Norton et al. (2007): length of stay in the hospital and in the ICU; in-hospital and ICU mortality rate.

Curtis et al. (2008): length of stay in the ICU; evaluation of quality of death; assessment of satisfaction experienced by family members and nurses.

Cheung et al. (2010): mortality in the ICU and hospital; number of consultations by the PC team; mean length of hospital and ICU stays; satisfaction of patients, family members, and care team.

Digwood et al. (2011): mortality and length of stay in the ICU.

Lustbader et al. (2011): length of stay in the ICU; hospital length of stay; number of patients with DNR status; number of patients with respiratory failure along with mechanical ventilation.

Lamba et al. (2012): mortality in the ICU; rate of designation of DNR; duration of such determination; length of stay in the ICU.

A description of the included studies is provided in Table 1.

## Excluded Studies

A total of 19 studies were excluded: 5 had conflicting objectives for the PC intervention in the ICU (Lin et al., 2009; Lim et al., 2013; Obermeyer et al., 2014; Kross et al., 2014; Binney et al., 2014), and 14 employed an inappropriate methodology (Lonberger

et al., 1997; Nelson & Danis, 2001; Mularski & Osborne, 2003; Paice et al., 2004; Lloyd et al., 2004; Sprung et al., 2008; Klein et al., 2012; Strand & Billings, 2012; Aslakson et al., 2014; Hui et al., 2014; Naib et al., 2015; Barnato et al., 2014; Jang et al., 2015; Kim et al., 2015).

## Effects of Interventions

### Length of Stay in the ICU

Length of stay in the ICU was presented as a mean and standard deviation in four studies. Two types of patients were evaluated in the study by Campbell and Guzman (2003): those with multiple organ system failure (MOSF) and those with global cerebral ischemia (GCI), with averages and standard deviations provided separately. A total of 81 patients were analyzed (43 with MOSF, 38 with GCI). Some 191 patients were presented by Norton et al. (2007), 590 by Curtis et al. (2008), and 52 by Lamba et al. (2012), for a total of 914 patients. There was a significant reduction of ~2.5 days in length of stay with application of the PC team intervention (average = -2.44 days,  $CI_{95\%} = -4/41$  to  $-0.48$ ,  $p = 0.01$ ). However, since there was considerable between-study heterogeneity ( $I^2 = 86\%$ ), a metaanalysis was not appropriate (Figure 2).

In the study by Cheung et al. (2010), length of stay in the ICU was given as a median and interquartile range (IQR): control with no intervention ( $n = 10$ ), median = 5 (8) days; intervention group ( $n = 10$ ), median = 3 (7) days. Digwood et al. (2011) presented length of stay as an average but did not provide a standard deviation: before ( $n = 2,319$ , average = 4.6 days) and after ( $n = 2,716$ , average = 4 days). Elsayem et al. (2006) presented their results as a median and as a minimum and maximum value for each patient who died in the ICU: for the year 1999 (before),  $n = 280$ , median = 12 days (1–75); for 2004 (after),  $n = 258$ , median = 11 days (1–156). Lustbader et al. (2011) presented their results as a median: 4 days both before ( $n = 515$ ) and after ( $n = 693$ ).

### ICU Mortality

It was possible to conduct metaanalysis on mortality in the ICU for four studies: Norton et al. (2007),

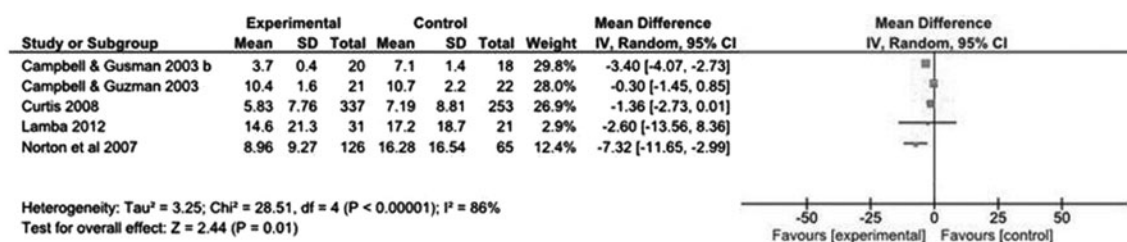
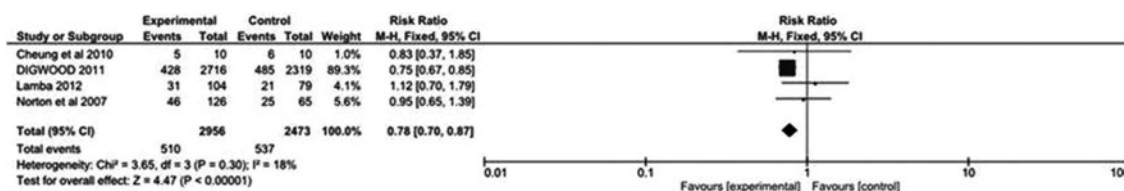


Fig. 2. Length of stay in the ICU before and after implementation of a palliative care team.



**Fig. 3.** Metaanalysis of mortality rates in the ICU before and after implementation of a palliative care team.

Cheung et al. (2010), Digwood et al. (2011), and Lamba et al. (2012) (comprising a total of 5,429 patients). Mortality was significantly lower in the intervention groups: risk ratio = 0.78,  $CI_{95\%} = 0.70-0.87$ ,  $p < 0.00001$ , with little heterogeneity between studies ( $I^2 = 18\%$ ). The number needed to treat to prevent one death in the ICU was 23 (Figure 3).

In the study by Elsayem et al. (2006), the ICU mortality rate was given in relation to global mortality in the hospital, while the other studies—Campbell and Guzman (2003), Curtis et al. (2008), and Lustbader et al. (2011)—did not present this outcome.

#### Quality of Life in the ICU

The study conducted by Curtis et al. (2008) was the only one that considered quality of life in the ICU as an outcome. They utilized an instrument called the Quality of Dying and Death Questionnaire, which was administered to family members. However, they found no significant difference for this outcome before and after the intervention.

## DISCUSSION

### Summary of Main Results

From the studies analyzed, there is evidence that the introduction of palliative care teams can reduce mortality in the intensive care unit, as well as decrease length of stay. However, the great heterogeneity among our studies renders the evidence for the second outcome very weak.

### Completeness and General Applicability of the Evidence

Most of the included studies examined length of stay, but some presented this outcome as a median or average without a standard deviation, which made inclusion in the metaanalysis impossible. Although the metaanalysis demonstrated a significant reduction in length of stay in the ICU, the heterogeneity among studies was very high, thus affecting the credibility of the metaanalysis.

Mortality in the ICU was analyzed in five studies (Elsayem et al., 2006; Norton et al., 2007; Cheung et al., 2010; Digwood et al., 2011; Lamba et al.,

2012), but one of them presented the percentage of all hospital deaths (Elsayem et al., 2006), so that it was not possible to include this study in the metaanalysis. Since mortality in the ICU was reduced in the metaanalysis due to the results of only a single study (Digwood et al., 2011), the general applicability of this evidence that implementation of a palliative care team can reduce mortality in the ICU is weakened.

In addition, four studies included a retrospective review of the data gathered from medical records, another compared two cohorts (retrospective and prospective), one was a randomized controlled trial, and one was a prospective observational study, which weakens our evidence even further.

### Quality of the Evidence

The included studies were considered to have a high risk of bias, since most presented retrospective data in their analysis, thus lowering the quality of their evidence.

### Potential Bias in the Review Process

We are confident that the comprehensive survey of the literature employed in our review captured most of the relevant studies published and minimized the likelihood that we missed any relevant publications.

However, there is the possibility that the included studies are the ones that show the effects of the intervention in a weak manner, which constitutes another potential source for weakening of the evidence.

### Agreements and Disagreements with Other Studies or Reviews

No reviews on the subject were found, and nearly all of the articles that studied the outcomes evaluated in our review showed a trend toward reduction in length of stay in the ICU, as well as lower mortality. The one exception was the research by Lamba et al. (2012), which found a trend toward higher mortality in the intervention group.

The study by Kim et al. (2015) at first appeared to be dissonant with the findings of our review. This is a retrospective analysis of patients admitted to the ICU from July to October 2010 who received a PC

consultation, compared to those who did not. Some 41 palliative care patients were considered, and 80 patients not in PC were chosen for comparison. The PC patients had longer ICU stays (8 days,  $IQR = 4-15$  vs. 4 days,  $IQR = 2-7$  days,  $p < 0.001$ ) and higher mortality rates (64.3 vs. 12.5%,  $p < 0.001$ ). These results appear to disagree with our review, but one must take into consideration that the PC patients were older ( $64 \pm 19.2$  vs.  $55.6 \pm 14.5$  years,  $p = 0.021$ ) and had more comorbidities than the non-PC patients. Palliative care patients usually stay longer in the ICU and tend to have higher mortality rates than less seriously ill individuals.

## CONCLUSIONS

The studies analyzed suggest that implementation of PC teams can reduce the suffering of patients receiving end-of-life care in an ICU and that of their family members, as this intervention leads to reduced mortality rates in the ICU and perhaps shorter lengths of stay. Transferring patients in end-of-life care from ICUs to palliative care units seems to generate a reduction in the use of costly procedures and intensive monitoring, and thus leads to overall cost savings, making effective management of the pain and suffering of patients and family members at the end of life more possible.

## Implications for Practice

The examined studies point toward decreased mortality and perhaps reduced length of stay in an ICU via implementation of palliative care. This may represent a reduction in the use of nonbeneficial resources and concomitantly represent savings in treatment costs, aside from fostering the possibility of making more ICU beds available for patients whose needs are greater.

## Implications for Research

The literature is still scarce when it comes to quantitative studies that analyze family satisfaction, quality of life, length of stay, and mortality with the use of a palliative care team for terminally ill patients in an intensive care unit. Further high-quality studies are needed to adequately address this issue.

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## CONFLICTS OF INTEREST

The authors hereby declare that they have no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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