Economic Evaluation of Palliative Care Interventions: A Review of the Evolution of Methods From 2011 to 2019

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Abstract
Background: End-of-life care is a driver of increasing healthcare costs; however, palliative care interventions may significantly reduce these costs. Economic evaluations that measure the incremental cost per quality adjusted life years (QALY) are warranted to inform cost-effectiveness of the intervention relative to a comparator and permit evaluation of investment against other therapeutic interventions. Evidence from the literature up to 2011 indicates a scarcity of cost-utility studies in palliative care research. Aim: This literature review evaluates economic studies published between 2011 and 2019 to determine whether the methods of economic evaluations have evolved since 2011. Design and Data Sources: A literature search was completed using CENTRAL, OVID MEDLINE, EMBASE and other sources for publications between 2011 and 2019. Study characteristics, methodology and key findings of publications that met the inclusion criteria were reviewed. Quality of studies were assessed using indicators developed by authors of the previous literature review. Results: 46 papers were included for qualitative synthesis. Among them only 6 studies conducted formal cost-effectiveness evaluations-of these 5 measured QALYs and 1 employed probabilistic analyses. In addition, with the exception of 1 costing analysis, all other economic evaluations undertook a healthcare payer perspective. Quality of evidence were comparable to the previous literature review published in 2011. Conclusion: Despite the small increase in the number of cost-utility studies, the methods of palliative care economic evaluations have not evolved significantly since 2011. More probabilistic cost-utility analyses of palliative care interventions from a societal perspective are necessary to truly evaluate the value for money.

Keywords
review literature, palliative care, palliative medicine, cost effectiveness, QALY, costs, economic evaluation

Introduction
Globally, end-of-life care is known to consume a large proportion of healthcare resources. In the United States, Medicare spends 27% to 30% of its total budget on care for people in their last year of life.1 Likewise, estimates from the United Kingdom indicate approximately 20% of hospital bed days to be taken up by end-of-life care.2 Canada is no exception to this observed trend with the cost of dying said to range from $10,000 to $40,000. This is largely due to an end-of-life care approach that focuses on curative treatments or disease focused interventions rather than symptom management.1 Regardless, in Ontario (one of Canada’s most populous provinces) 51.9% of all decedents receive some form of palliative care in the last year of life.3 While families bear substantial caregiving and out-of-pocket costs, a lot of these end-of-life costs are absorbed by the Canadian healthcare system.1 As a result, the sustainability of publicly funded healthcare interventions, especially for terminally ill patients, has been under question.

Fortunately, there is evidence that indicates that palliative care services can significantly reduce the healthcare costs of end-of-life care through reduced hospital admission, length of stay, visits to intensive care unit (ICU) and inappropriate diagnostics or interventions.1,4 Palliative care seeks to prevent and
treat the suffering of both patients with serious medical illness and their families through a multidisciplinary approach. Through services such as better symptom control, coordination of care, and improved communication between healthcare professionals and the patient and family, palliative care aims to enhance the end-of-life journey for terminally ill patients and their caregivers. A palliative care team may consist of specialty-trained clinicians, registered nurses, social workers, chaplains and caregivers. The care can be provided in a variety of settings-hospital and home being the most popular ones. Owing to ageing population, growing demands are being placed on palliative care services. However, due to the highly competitive funding environment, palliative care must compete with other therapeutic interventions for finite resources. Henceforth, policy makers have become increasingly interested in the cost associated with end-of-life care and the cost-effectiveness of palliative care.

Theoretically, economic evaluations in healthcare can be completed in one of 4 ways: cost-utility analysis, cost-effectiveness analysis, cost-benefit analysis or cost-minimization analysis. As recommended by several guidelines, cost-utility analysis is the gold standard for economic evaluations in healthcare decision-making. Its use of Quality-Adjusted-Life-Years (QALYs), which provides a common metric, permits comparative assessment of healthcare interventions across therapeutic areas. However, the appropriateness of using QALYs as the outcome measure of palliative care effectiveness has been debated. QALYs take into account both the quality of life, and the quantity of life generated by the intervention. However, measuring quantity of life generated from palliative care in terminally ill patients is arguably incompatible.

Consequently, cost-benefit analysis has been popular in evaluating palliative care. Literature suggests an imperfect overlap between what is measured in QALY scores and what is measured under resource utilization. For example, medical intervention can result in higher QALY score or lower utilization of non-healthcare resources such as leisure and caregiver time or lower utilization of healthcare resources such as ICU, hospitalization and emergency visits. Therefore, cost-benefit analysis has proven to be instrumental in evaluating the economic impact of palliative care by measuring both the benefits and costs of treatment in the same currency. Though cost-benefit analysis is scrutinized for seemingly quantifying the value of human life in monetary terms, it does simplify the difficult nature of measuring the effectiveness of an intervention among terminally ill patients. Subsequently, in the past, vast majority of studies evaluating palliative care have been comparative costing studies based on resource utilization. A literature review published in 2014 identified only 1 formal cost-effectiveness evaluation among 46 economic evaluations published up to 2011 indicating the scarcity of cost-utility analyses in this therapeutic area. Remaining available research consisted of aforementioned costing studies. The review revealed the use of relatively small observational studies and varied methodological approaches to assess the impact of palliative care interventions on costs separately from direct patient important outcomes. However, since then, there have been calls to include QALYs in the economic evaluation of palliative care. Despite criticisms of the limited gain in life years, end-of-life care can generate QALYs from changes in quality of life in the last days of life. Therefore, in order to effectively allocate scarce resources across healthcare, cost-utility analysis is now the recommended method to evaluate the economic implications of palliative care interventions. Additionally, Smith et al (2014) reported direct costs, from the provider or third-party payer perspective, to be the focus of all 46 studies included in the review. Informal caregivers and out-of-pocket costs are central in the care for terminally ill individuals. Therefore, ignoring informal care in economic evaluations can bias cost-effectiveness research.

This paper will update the previous literature review of cost and cost-effectiveness of palliative care by assessing the quality of economic studies published between 2011 and 2019 and evaluating the evolution of methods since 2011 or the lack thereof.

Methods

The inclusion criteria for this review were patients (adult or children) that are terminally ill with any progressive life-limiting disease and is expected to have prognosis of less than 1-year survival. All variations, frequencies and administration (e.g. by clinician, by nurse) of hospice or palliative services in any setting (e.g. hospital-based, home-based) were included in this review. Palliative care comparators are disease focused and target the underlying illness. The term “usual care” is commonly used to capture this type of end-of-life care. Usual care involves acute therapies, and aggressive life-sustaining treatments (e.g. cardiopulmonary resuscitation, intubation and mechanical ventilation support). Studies that compare 2 palliative care services (e.g. early versus late or inpatient versus home-based) were also included in this review. Studies without a comparator were excluded. Costing studies, cost-effectiveness or cost benefit analyses were included. Studies that only looked at resource utilization without costing or clinical outcomes without costs were excluded. Randomized controlled trials, cohort studies (retrospective, prospective, and quasi), before and after studies and modeling studies were included in this review. Case studies, case series, study protocols, reviews, editorials, descriptive or qualitative studies, non-comparative quantitative studies and burden of illness studies were excluded.

Literature search of both electronic databases and grey literature were conducted up to August 31, 2019. Electronic search was completed using Cochrane Central Register of Controlled Trials (CENTRAL) and the OVID interface for MEDLINE Epub Ahead of print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE (R) Daily and Ovid MEDLINE (R) (1946 to present) and EMBASE (1974 to 2019 August 31). The search strategy comprised of controlled vocabulary, such as the National Library of Medicine’s MeSH (Medical Subject Headings), EMTREE and keywords. The search was kept broad in order to capture all publications pertinent to the research question. The main search concepts grouped together were “end of
life care” AND “cost/cost effectiveness.” See Appendix A for the detailed search strategy for this review. The subject headings, keywords and search filter syntax were adjusted for the respective databases. The search was restricted to English language and published year ranging from 2011 to 2019. Searching websites of health technology assessment and related agencies (CADTH, NICE), professional associations (HQO), clinical trial registries (ClinicalTrials.gov) and other specialized databases (Trip, Centre for Review and Dissemination) identified the grey literature. Additionally, papers presented at worldwide meetings and conference proceedings were also searched (Papers First, Proceedings First). Reference list of previous literature reviews and relevant articles were reviewed to identify relevant publications.

A single reviewer independently screened the titles and abstracts of studies generated by the indicated search strategy. Duplicates were removed and studies were excluded based on following criteria: wrong population (e.g. not terminally ill, diabetes), wrong study type (e.g. qualitative, non-comparative), wrong intervention (e.g. radiotherapy, chemotherapy) and wrong outcomes (e.g. no costs). Corresponding abstracts that seemed eligible or required further evaluation was included for full-text review. Full texts were also screened independently to select studies that met the inclusion criteria. Using a standard data extraction form, the reviewer independently extracted data from the included studies which were randomly spot checked by a second reviewer. Only studies published between 2011 and 2019 were included in this literature review.

For the purpose of this review, the quality indicators reported in the literature review by Smith et al (2014) was used to assess the quality of the included studies.6 This checklist was adapted from existing evaluation guidelines.14-19 Drawing on the Cochrane Handbook, Drummond’s guidelines for economic submissions, the CONSORT statement, and the Delphi list, a set of 31 indicators suitable for evaluating diverse set of papers was customized. Refer to publication by Smith et al. (2014) for complete details of the criteria.6 Briefly, the 31 indicators cover core 6 categories: study description, sample selection and size, measurement, reporting, analysis and conclusion. Microsoft excel spreadsheet was used to evaluate the studies with 3 possible scores: 0 (poor), 2 (incomplete or unclear) or 4 (good). In cases where the indicators were not applicable, it was excluded from the final calculation. An overall mark, ranging from 0 (lowest quality) to 1 (highest quality) was calculated for each of the 6 core categories.

Results
Study Selection
A total of 3284 unique records were returned from the initial database search. After 936 duplicates were removed, a total of 2348 unique records were screened and 2187 were excluded. The full text of 161 papers were assessed and 46 papers were selected for qualitative analysis. Details of the screening process and reasons for exclusion are shown Figure 1.

Study Characteristics
The key characteristics of the 46 included papers are outlined in Table 1.20-66 The publications can be categorized into 6
Table 1. Characteristics of Included Studies (n = 46).

| Study            | Country     | Study type       | Diagnosis                        | Prognosis | Intervention                                      | Control                                      | Perspective | Type of EE | Key results                                                                                                                                                                                                 |
|------------------|-------------|------------------|----------------------------------|-----------|--------------------------------------------------|----------------------------------------------|-------------|------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Baker et al, 2012 | Scotland    | Prospective cohort | Multiple Comorbidities           |           | 96 patients who received anticipatory care planning | 96 Patients with access to similar inpatient facilities including a community hospital | Healthcare payer | Costing analysis | Survivors from the ACP (anticipatory care plan) had 510 fewer days in the hospital than in 12 months pre-intervention-reduction of 52% Similar mortality rates but number who died in hospital and hospital bed use in last 3 months of life were significantly lower for decedents with an ACP than in control |
| Balboni et al, 2011 | United States | Prospective cohort | Cancer                           | ≤5 years  | 87 High spiritual support                        | 252 low spiritual support                   | Healthcare payer | Costing analysis | Patients reporting their R/S needs were inadequately supported by clinic staff and were less likely to receive a week or more of hospice (54% vs. 72.8%; p = .01) and more likely to die in an ICU. EOL costs were higher when patients reported that their spiritual needs were inadequately supported ($4947 vs. $2833, p = 0.03) |
| Bentur et al, 2014 | Israel      | Retrospective cohort | Cancer                           | ≤6 months | 40 home-hospice care & hospital based usual care | 153 hospital based usual care only          | Healthcare payer | Costing analysis | The average cost of care for the last 6 months of life, for patients with Home Hospice Unit (HHU) care, was US$13,648 compared to US$18,503 for patients without HHU care. |
| Bleeker et al, 2011 | United States | Cross Sectional Study | Heart Failure                    | >6 Months | 6436 Hospice                                      | 10177 Non-hospice                             | Healthcare payer | Costing analysis | 6,436 (38.7%) received hospice care during the last 6 months of life. Mean total medical expenditures were $31,793 (SD 25,691) among decedents with hospice care, in comparison to $34,067 (SD 40,561) among decedents without hospice care. Hospice care wasn't associated with reduced expenditures in heart failure |
| Bond et al, 2018  | United States | Retrospective cohort | Any                              |           | 3146 palliative care                              | 3146 usual care                              | Healthcare payer | Costing analysis | Overall adjusted costs were $9,500 lower in the palliative group (95% CI-$16,207 to-$2,793). The program spent $1.15 million in intervention and execution costs in the community and generated $3,087,500 savings in Medicare expenditure in our sample. The net cost saving was $1,572,330 and resulted in a 104% return on investment. |
| Carey et al, 2017  | Australia    | Before and after  | Any                              |           | 17 palliative care                                | 17 usual care                                | Healthcare payer | Incremental cost per life years saved | The mean cost per hospital admission episode expressed in NWAUs reduced by $1802.50. A saving of $1802.50 per hospital admission for 276 admissions over the 10-month period of the study amounted to a total savings of $519,570.00 |
| Cassel et al, 2016 | United States | Retrospective cohort | Cancer, COPD, HF, Dementia       |           | 368 palliative care & usual care                  | 1075 usual care alone                        | Healthcare payer | Costing analysis | Intervention participants in all 4 disease groups had less hospital use and lower hospital costs than non-intervention participants, which drove lower overall healthcare costs. In the final 6 months of life, healthcare costs for the intervention groups stayed largely the same from month to month, whereas costs for comparison participants increased dramatically. |
| Chen et al, 2015  | Taiwan       | Retrospective cohort | End stage renal disease (ESRD) & cancer |           | 19,942 palliative care                            | 131,547 usual care                           | Healthcare payer | Costing analysis | The expanded hospice benefit policy for ESRD patients was associated with an additional reduction of 7.3% in costs. This translates into a reduction of approximately US$497 (NTS16,052 at US$1 = NT$32.28). |

(continued)
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| Study            | Country      | Study type    | Diagnosis                  | Prognosis       | Intervention                           | Control                        | Perspective       | Type of EE         | Key results                                                                                     |
|------------------|--------------|---------------|----------------------------|-----------------|----------------------------------------|--------------------------------|-------------------|-------------------|-----------------------------------------------------------------------------------------------|
| Chen et al 2018  | United States| Retrospective | Any                        | –               | 50 palliative care                     | 95 propensity matched controls | Healthcare payer  | Costing analysis | 12 months after program enrollment, mean annual payment was $5783 per patient among participants and $22,031 per patient among the matched controls. In the second year, the intervention group had a decrease of $106,46 per patient; the control group had an increase of $7604 per patient. |
| Chiang et al 2016| Taiwan       | Retrospective | Cancer                     | –               | 238 inpatient and home hospice (IH) care | 330 inpatient hospice (IH) care only | Healthcare payer  | Costing analysis | The mean health care costs in the last month of life were significantly less for patients in the IH group than for those in the IH group (U.S. $1,385.00-$1,370.00 versus U.S. $2,155.00-$1,739.00, p < 0.001). |
| Chou et al 2013  | Taiwan       | Retrospective | COPD                       | ≤2 years        | 43 lung cancer                         | 103 COPD                      | Healthcare payer  | Costing analysis | COPD patients receive more care aimed at prolonging life than aimed at relieving symptoms and providing end of life support. |
| DesRosiers et al2014| South Africa| Retrospective | Advanced neurological illness, pulmonary disease, cardiac disease, end-stage hepatic disease, end-stage renal disease | ≤2.5 months | 56 hospital-based palliative care | 48 usual care | Healthcare payer and societal perspective | Costing analysis (direct and indirect costs) | For the intervention group patients, a total of 253 admission days were recorded at a mean of 4.52 days per patient, for a formal cost of R4696 per patient. For the control patients, a total of 447 admission days were recorded, resulting in a formal cost of R9673 per patient. The admission bed day costs per patient over the study period were, therefore, a mean of R4977 lower per patient for the intervention compared with the controls. |
| Enomoto et al 2015| United States| Retrospective | Cancer                     | ≤1 year         | 2719 hospice care                      | 4664 usual care               | Healthcare payer  | Costing analysis | Patients who used hospice services had $7035 (95% CI, $6040-$8160) lower mean Medicare costs for oral cavity cancer and $7730 (95% CI, $6340-$9100) lower mean Medicare costs for pharyngeal cancer than patients who did not use hospice services in the last month of life. Hospital charges were moderately lower for patients managed directly by a palliative medicine attending (OR: 1.14, 95% CI 0.505, 95% CI 0.299-0.852). Median charges were lower in the PCU than in the medical surgical units (P < .0001). |
| Eti et al 2014  | United States| Before and after | Any                        | ≤6 months       | 230 hospital-based palliative care     | 230 hospital-based usual care  | Healthcare payer  | Costing analysis | The average contribution margin was $3246 in the early intervention group as opposed to a $1416 loss in the late intervention group. In aggregate, there was a profit of $695,069 with early intervention versus $223,483 loss with the late intervention group. |
| Fitzpatrick et al 2018 | United States| Retrospective | Any                        | –               | 228 early palliative care              | 221 late palliative care       | Healthcare payer  | Costing analysis | Total cost of investigations for PCU patients was $1,180,29 (4 of 50 patients), compared with $8,440.26 (29 of 50 patients) in the tertiary hospital. Expenditure was less if palliative care were the primary caregivers. |
| Gogna et al 2018 | Australia     | Retrospective | Any                        | –               | 4 inpatient palliative care            | 29 usual care                 | Healthcare payer  | Costing analysis | Total cost of investigations for PCU patients was $1,180,29 (4 of 50 patients), compared with $8,440.26 (29 of 50 patients) in the tertiary hospital. Expenditure was less if palliative care were the primary caregivers. |
### Table 1. (continued)

| Study                  | Country          | Study type       | Diagnosis                          | Prognosis | Intervention                                      | Control                  | Perspective       | Type of EE              | Key results                                                                 |
|------------------------|------------------|------------------|------------------------------------|-----------|--------------------------------------------------|--------------------------|-------------------|------------------------|-----------------------------------------------------------------------------|
| Goldhagen et al., 2016 | United States    | Before and after | Any                                | ≥1 year   | 48 community based pediatric palliative care     | 48 usual care            | Healthcare payer  | Costing analysis       | Following enrollment in the program, hospital charges declined by $1201 for total charges per quarter for hospital services and $1047 for diagnostic charges per quarter. Although the total charges decreased, the decline did not reach statistical significance ($p = 0.34$). |
| Gozalo et al, 2015     | United States    | Retrospective    | Any                                | ≤1 year   | 144,782 nursing home hospice care                | 433,316 usual care       | Healthcare payer  | Costing analysis       | Hospice use was associated with a reduction in aggressive end-of-life care, but it was also associated with a net increase of $6,761 in Medicare expenditures per decedent in the last year of life. |
| Greer et al., 2016     | United States    | Randomized       | Cancer                             | ≥1 year   | 68 palliative care (PC) with standard oncology care | 70 standard oncology care alone | Healthcare payer  | Incremental cost per life years saved | Patients in the standard care group had a total mean cost that was $11,260 less expensive than the early PC group (between-group median difference = $13,664). However, given that participants in the early PC group on average lived 98 days longer than patients in the standard care group, the mean total cost per day for the early PC group was $117 less expensive than the standard care group ($p = 0.13$). We found that randomization to PC was associated with a cost-effectiveness ratio of $41,938/life year saved, compared to standard care. |
| Hollingsworth et al., 2016 | Australia        | Before and after | End stage heart failure or non-malignant lung disease | ≥1 year   | 35 palliative care (PC)                          | 35 usual care            | Healthcare payer and societal perspective | The annualised total cost per patient was AUD$90,060 before PC and AUD$11,841 after PC. Cost savings was calculated using the mean time in study after PC and cost saving per day inclusive of cost per case to be AUD$41,023 per patient after deducting the cost of palliative care per patient. |
| Hopp et al, 2015       | United States    | Before and after | Any                                | ≤6 months | 148 hospice care                                | 148 usual care           | Healthcare payer  | Costing analysis       | Total costs per month declined US$3416 per month, from an average of US$9294 per month at baseline to US$3878 at 6 months. |
| Hung et al., 2018      | Taiwan           | Retrospective    | Cancer                             | ≤1 year   | 97,614 hospice care                              | 97,614 usual care        | Healthcare payer  | Costing analysis       | Hospice care accounted for savings in raw health care expenditures up to the last 6 months before death, with average cost savings of US $566.34 to US $300.16, but total costs for the entire last year of life were higher for hospice users than for hospice nonusers (mean cost difference of US $1473.10). |
| Hwang et al., 2013     | Taiwan           | Cross Sectional  | Terminal hepatocellular carcinoma   | ≤4 years  | 729 HCC patients                                 | 729 controls with usual care | Healthcare payer  | Costing analysis       | HCC patients in hospital wards received more narcotic palliative care whereas length of stay (8 ± 7.7 days versus 14.1 ± 14.3 days, $P < 0.001$), and medical costs were significantly less in the hospice care group ($141/day versus $326/day). |
| Isenberg et al., 2017  | United States    | Modeling         | Any                                | ≤1 year   | Palliative care                                  | Usual care               | Healthcare payer  | Cost utility            | Combining the QALYs generated from patient encounters (0.05 QALY) and caregivers (0.06 QALYs), the PCU could yield 3.11 QALYs. PCU produced $353,645 in savings, accounting for the money saved by treating patients in the PCU versus other functional units. |

(continued)
| Study | Country       | Study type            | Diagnosis        | Prognosis       | Intervention | Control         | Perspective | Type of EE                             | Key results                                                                                                                                                                                                 |
|-------|---------------|-----------------------|------------------|-----------------|--------------|-----------------|-------------|----------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| John- | United        | Prospective cohort    | Heart Failure    | –               | 43 palliative | 34 usual care   | Healthcare payer | Costing analysis                       | Estimated differences in costs show that the average healthcare costs reduced by £785 in palliative care group. This is statistically insignificant and subject to considerable uncertainty. |
| et al. | Kingdom       |                       |                  |                 |              |                 |             |                                        |                                                                                                  |
| Kel-  | United        | Retrospective cohort  | –                |                 | 1064 Any hospice prior to death | 2005 No hospice | Healthcare payer | Costing analysis                       | $2561 saving in Medicare for each patient enrolled in hospice 53-105 days before death compared to non-hospice Higher savings with shorter enrollment periods-$2650, $5040, $6430 per patient enrolled 1-7, 8-14, 15-30 days prior to death respectively Hospice patients had lower rates of hospital service use and in hospital death compared to control. |
| et al.| States        |                       |                  |                 |              |                 |             |                                        | With project CARE-per residence cost savings of SGD $7129 over last 3 months of life and SGD $3707 over last month.                                                                                                                                 |
| Kelvin| Singapore     | Quasi-experimental    | –                | ≤6 months to 1 year | 48 with hospice care-Project Care at the End of Life for Residence in homes for the Elderly (CARE) | 197 without any end of life care program | Healthcare payer | Costing analysis                       | With project CARE-per residence cost savings of SGD $7129 over last 3 months of life and SGD $3707 over last month.                                                                                           |
| et al.| Taiwan        | Retrospective cohort  | Cancer           | ≤1 year         | 37,080 hospice shared care program | 83,131 hospice palliative care | Healthcare payer | Costing analysis                       | Total medical expenditure per person was US$4,664 and US$3,939 for non-HSC and HSC groups, respectively. The medical expenditure savings per person among those who received various combinations of hospital care ranged between 15.4% and 44.9%. |
| et al.| Korea         | Retrospective cohort  | Terminal Cancer  | 12 months       | 32 Hospice Ward | 72 General ward | Healthcare payer | Costing analysis                       | Daily total average expenditure for each inpatient was $1193.930 and $266.161 in hospice and general ward respectively Hospice ward type in palliative hospice therapy may contribute to reduce economic medical costs and to more specific total care for terminally ill patients. |
| et al.| United        | Modeling              | Ovarian cancer   | 6 months        | Early referral to palliative care | Usual care | Healthcare payer | Incremental Cost Effectiveness Ratio Quality Adjusted Life Year | With early palliative care (EPC) compared to usual care there was a cost saving of $1285/patient over routine care. EPC was either dominant or cost-effective with an incremental cost effectiveness ratio <$50,000/QALY. With no clinical benefit other than QoL, EPC remained cost-effective with ICER $37,440/QALY. |
| et al.| States        | Prospective cohort    | Cancer           | –               | 288 inpatient palliative care (PC) | 735 usual care | Healthcare payer | Costing analysis                       | Preliminary results suggest that costs were lower for the intervention group (p < 0.01). EPC reduces costs for hospital treatment for patients with advanced cancer, and this effect is consistent across key sub-populations. |
| et al.| United        | Retrospective cohort  | Any              | –               | 712 specialized palliative care unit | 456 palliative care consultation services | Healthcare payer | Costing analysis                       | PCU patients had significantly lower mean daily costs than CS patients in the days following initiation of palliative care ($753, SE = $20; $1013, SE = $45, respectively, P <0.001). The average incremental effect of PCU in the adjusted GLM was -$240 (bootstrapped SE = $45, P < 0.001). |
| Study | Country | Study type | Diagnosis                  | Prognosis | Intervention                      | Control       | Perspective | Type of EE | Key results                                                                                                                                                                                                                                                                                                                                 |
|-------|---------|------------|----------------------------|-----------|-----------------------------------|---------------|-------------|------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Nguyen et al., 2017 | Australia | Modeling | Dementia | ≤ 1 year | Palliative care | Usual care | Healthcare payer | Incremental cost per quality-adjusted life years | Over a lifetime, compared to the current situation, a nationwide palliative care program was less costly while achieving the same QALY outcome. Sensitivity analysis shows the highest incremental cost to be $239/QALYs. The intervention resulted in a gain of 0.25 quality-adjusted life years, and cost analysis showed a significant cost reduction with the Palliative Advanced Home Care and Heart Failure Care intervention. The result of the intervention was a reduced cost of SEK600,000 ($61,000) over the 6-month intervention period. |
| Obermeyer et al, 2014 | United States | Retrospective cohort | Cancer | ≤ 6 months | 18,165 hospice care | 18,165 usual care | Healthcare payer | Costing analysis | Average daily care costs for hospice beneficiaries were $145 (95% CI, $143-$147) compared to $148 (95% CI, $146-$150) for non-hospice beneficiaries (difference, $3; 95% CI, $0-$5). Cumulative costs over the last year of life were $71,860 (95% CI, $71,094-$72,626) for non-hospice and $59,037 (95% CI, $58,353-$59,538) for hospice (difference, $12,823; 95% CI, $11,921-$13,726). |
| Ozcelik et al, 2014 | Turkey | Randomized controlled trial | Cancer | ≤ 1 year | 22 palliative case management | 22 usual care | Healthcare payer | Costing analysis | There was no significant difference in the direct health costs for both groups (P > .05). There was no statistical difference in the mean length of stay in hospital (P > 0.05). |
| Pace et al, 2012 | Rome | Retrospective cohort | Primary brain tumors | – | 77 Home care assistance | 71 No home care assistance | Healthcare payer | Costing analysis | Hospitalization rates of individuals assisted at home was lower than those of the group not assisted at home. Those assisted at home was 517 points whereas those not assisted at home was 2,407. Therefore, home care models can be an alternative to in hospital care for managing brain tum or patients. |
| Patel et al, 2017 | United States | Retrospective cohort | End stage liver disease | ≤ 6 months | 18,061 palliative care | 41,642 usual care | Healthcare payer | Costing analysis | Palliative care consultation was associated with lower overall costs (-$10,062; 95% CI, $7,276 to -$7,399). Doubly robust inverse probability of treatment weighted analysis also showed that the mean average treatment effect of palliative care consultation on cost was -$10,746. |
| Chippen et al, 2013 | United States | Modeling | Cervical cancer | – | Supportive care-based treatment strategies | Doublet chemotherapy | Healthcare payer | Incremental cost per quality-adjusted life years | Standard doublet chemotherapy is not cost effective compared to selective chemotherapy with ICER of $276 000/QALY. Selective chemotherapy is the most cost-effective strategy compared to single agent chemotherapy with home hospice with ICER of $78 000/QALY. Chemotherapy containing regimens come cost prohibitive with small decreases in quality of life. |
| Pinderhughes et al, 2018 | United States | Retrospective cohort | Any | – | 36 hospital-based palliative care | 31,36 usual care | Healthcare payer | Costing analysis | Cost differences were primarily driven by clear cost divergence in the last 3 months of life ($9,843 (PC) vs. $27,530. Patients with designated complex chronic diseases demonstrated a cost savings above non-palliative patients across all 21 months leading up to death. |
| Sahlen et al., 2016 | Sweden | Randomized controlled trial | Heart Failure | ≤ 6 months | 36 palliative care | 36 usual care | Healthcare payer | Costing analysis and QALYs generated | The intervention resulted in a gain of 0.25 quality-adjusted life years, and cost analysis showed a significant cost reduction with the Palliative Advanced Home Care and Heart Failure Care intervention. The result of the intervention was a reduced cost of SEK600,000 ($61,000) over the 6-month intervention period. |
| Study                  | Country       | Study type                   | Diagnosis                  | Prognosis | Intervention                                      | Control                                      | Perspective | Type of EE | Key results                                                                                                                                                                                                 |
|-----------------------|---------------|------------------------------|----------------------------|-----------|--------------------------------------------------|----------------------------------------------|-------------|------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Simoens et al 2013    | Belgium       | Retrospective cohort         | Terminal patients          | 1 month   | 56 terminal patients with palliative care        | 108 terminal patients with usual care       | Healthcare payer | Costing analysis | Nursing home cost-3243 pounds / patient during final month of life. 3822 pounds for patients receiving usual care were higher than the costs of 2456 pounds for patients receiving palliative care. Research suggests that palliative care models in nursing homes need to be supported because they are less expensive than usual care and because they are able to better reflect the terminal patient's needs. |
| Starks et al 2013      | United States | Retrospective cohort         | Mixed comorbidities        | –         | 1815 palliative care patients                    | 1790 usual care                             | Healthcare payer | Costing analysis | Significant savings per admission were associated with shorter length of stay 1 to 7 days, costs were lower for all PC patients by 13% ($2141), and for survivors by 19.1%. 8 to 30 days, costs were lower for all PC patients by 49% ($2870), and for survivors by 6% ($2487). >30 days showed no differences in costs. |
| Tangeman et al 2014    | United States | Retrospective cohort         | Any                        | ≤6 months | 888 hospice care                                 | 1622 usual care                             | Healthcare payer | Costing analysis | Cost per admission was $1,401 lower, on average, among IPC patients than comparison patients (95% CI: $322 to $2,481 lower). IPC was also associated with lower cost per day: $228 lower overall, $164 lower among those who died, and $387 lower among live discharges, on average. |
| Unroe et al 2016       | United States | Retrospective cohort         | Any                        | ≤6 months | 1004 in-patient palliative care                  | 1003 usual care                             | Healthcare payer | Costing analysis | Patients on hospice had significantly lower total Medicare costs for all time periods up to and including 90 days prior to death. For example, in the 7 days prior to death, nursing home decedents who used hospice for that entire time period had total mean Medicare costs of $2,132 (± SD $6,337) and those who were not receiving hospice care had mean Medicare costs of $5,034 (± SD $9,367). |
| Yoo et al 2012         | United States | Before and after             | Critically ill older adults | –         | 618 Integration (Phase 2)                        | 673 Consultation (Phase 1)                  | Healthcare payer | Costing analysis | Integrative palliative care in phase 2 was associated with lower hospital costs ($57,162 versus $63,958), lower adjusted probability of in hospital deaths and higher adjusted probability of hospice care discharges. No difference in hospital outcomes by palliative care types in those with advance directives. |
| Yu et al 2015          | Canada        | Prospective cohort           | Cancer                     | ≤6 months | 105 home-based palliative care                   | 81 hospital palliative care                   | Societal     | Costing analysis | The estimated total societal cost of end-of-life care was $34,197.73 per patient over the entire palliative trajectory. Public health system costs comprised 46.72% of total costs; private costs comprised 53.28%. Average total cost was $37,699.37 for patients who died at home and $29,658.57 for patients who died in hospitals. Results showed no significant difference (P > 0.05) in total societal costs between home and hospital end of life care patients. Higher hospitalization costs for hospital death patients were replaced by higher unpaid caregiver time and outpatient service costs for home death patients. |

*Any cells in the table with "-" indicate that the information was not available or reported in the respective article.*
different study types—6 before and after studies, 2 cross-sectional studies, 4 modeling studies, 6 prospective studies, 3 randomized controlled trials (RCTs), and 25 retrospective cohort studies. The studies were also assessed for primary progressive diagnoses. Palliative patients of all disease types were involved, but cancer, heart failure, dementia and end-stage renal and liver disease were the most common diagnoses among the patient population included in these economic evaluations.

The literature evaluates a variety of palliative care interventions including hospital-based, home-based, nursing home hospice care and community-based palliative care relative to usual care. While most studies analyzed palliative care interventions against disease focused or acute care (termed “usual care”), 6 studies made comparisons across 2 palliative care interventions, such as varied types of care (e.g. palliative care unit versus consultation), different locations (e.g. hospital versus home) or different methods of administration (e.g. early versus late) were evaluated, and 1 study compared end of life care between lung cancer and chronic obstructive pulmonary disease patients. Among the 46 included publications, all studies evaluated costs from a healthcare payer perspective with the exception of 1 study that evaluated the costs from a societal perspective.

Additionally, the studies were also characterized for the type of economic evaluation employed. While all the studies completed a costing analysis based on resource utilization, only 6 studies met the criteria of a formal cost-effectiveness study. Of these, QALYs generated by palliative care were measured in 5 studies and 1 study reported the economic impact of palliative care in incremental cost per life years saved. Of the 46 studies, all focused only on direct hospital costs, with the exception of 3. This includes, but is not limited to healthcare professional fees, procedure costs, imaging, diagnostic tests, laboratory tests and blood analysis, medication and length of stay in the hospital, emergency room or intensive care unit. In addition, 3 studies considered system-level costs such as overhead and 1 study included patient out-of-pocket and caregiver time. Finally, the country in which the economic evaluations were based on is important to note as the health care system and associated fees differ across nations. The studies included in this literature review were predominantly based on data from the United States (25). The remaining studies were based on data from Australia (4), Taiwan (6), Canada (1), Israel (1), South Africa (1), Sweden (1), Turkey (1), United Kingdom (1), Scotland (1), Singapore (1), Korea (1), Rome (1), and Belgium (1).

**Study Quality**

Appendix B provides a graphical summary of the evidence quality. For the most part, study description, measurement and conclusion scored high (>0.6) across study types. On the other hand, the quality of sample selection & size, reporting and analysis ranged from poor to high for all study types. Though randomized control trials are considered the gold standard for evaluating an intervention, poor quality in reporting and analysis questions the validity of the results. Of the 3 randomized control trials included in this literature review, one of them is strictly a costing analysis based on a small sample size while the other 2 are trial based economic evaluations with poor reporting and analysis.

Cohort studies are often scrutinized for the increased risk of variations in demographic and clinical characteristics across study groups. However, it’s important to note that more than 60% of the included cohort studies used propensity score matching to control for selection bias. The 6 before and after studies were of moderate quality in all indicators except for the analysis section where the details of statistical analysis were poorly reported.

**Costing Studies**

Consistent with the previous literature review, key findings of 43 out of 46 studies indicate palliative care to have lower costs compared to usual care. However, ~ 6% of reviewed studies suggest otherwise. A retrospective study from the United States that compared nursing home hospice care to usual care found hospice care to be associated with a reduction in aggressive end-of-life care, but it was also associated with a net increase of $6,761 in Medicare expenditures per patient in the last year of life. Similarly, a retrospective study from Taiwan that evaluated hospice care relative to usual care found costs for the last year of life to be higher for hospice users than for those using usual care ($68,273.38 SD $54,115.67 vs. $66,800.28 SD $55,416.09; p = 0.989). This increase in cost was attributed to lengthy stay in hospice care. Lastly, a study by Chou et al. (2013), found that the cost of hospice and non-hospice care for patients with COPD was $135, 483.50 and $117,530.00 respectively (p = 0.141) and for lung cancer patients the costs were $67,233.50 and $65,027.00 respectively (p = 0.764). With the exception of these 3 studies, all other costing studies found palliative care to be cost saving. Though not all studies report on statistical significance (p-value less than 0.05); 11 studies reported the observed cost savings to be statistically significant (p < 0.05) and 5 studies reported the observed cost savings to be statistically insignificant (p > 0.05). Across studies, the cost savings associated with palliative care interventions relative to usual care were largely driven by reduced resource utilization such as decreased hospital admissions and readmissions, reduced length of stay, and avoidance of aggressive treatments.

**Cost Effectiveness Studies**

Since the focus of this literature review is more on the use of QALYs in palliative care economic evaluations and the use of formal cost-effectiveness studies, key results from publications that met this criterion were assessed more closely. Amongst the
46 studies, there were 6 formal cost effectiveness studies of varying quality (Table 2).

**Perspective of Economic Evaluation**

In addition to the type of economic evaluations completed, the perspective under which the intervention was evaluated was also of interest to this literature review. All the studies comparing palliative care to usual care were conducted from a healthcare payer perspective with the exception of 1 cohort study evaluating home-based palliative care against hospital-based palliative care which was completed with a societal perspective.\(^3\)

This costing analysis estimated the total societal cost per patient over 6 months of palliative care to be $34,197.73 CAD. 46.72\% of the cost was attributed to public health system costs and 53.28\% was out-of-pocket costs. The average total cost of home-based and hospital-based palliative care showed no statistically significant difference (p > 0.05). Higher hospitalization costs for hospital-based palliative care patients were neutralized by the high unpaid caregiver time and outpatient service costs among home-based palliative care patients.\(^3\)

A similar study that evaluated inpatient hospice care and home hospice care reported significantly less costs in the home-hospice group ($1,385-$1,370 USD versus $2,155-$1,739, p < 0.001).\(^4\) However, this was expected as the costing analysis was conducted from a healthcare payer perspective.

### Discussion

#### Main Findings

In the previously published literature review by Smith et al. (2014), there were 5 RCTs, 2 prospective cohort studies, 34 retrospective cohort studies, and 3 before and after studies.\(^5\) The distribution of study types has not evolved much since 2011. For example, the majority of included studies (54\%) were still retrospective cohort studies. However, up until 2011, there was only 1 formal cost-effectiveness study conducted to evaluate palliative care interventions.\(^6\) Though patient and caregiver outcomes were measured on Palliative Care Outcome Scale and Zarit Carer Burden Inventory, respectively; the results from that 1 cost-effectiveness study were not presented in QALYs. Between 2011 and 2019, there have been 6 cost-effectiveness studies evaluating the value for money of palliative care interventions. Among them, only 5 studies measure the effect of the intervention in QALYs and only 4 of the 5 performed a sensitivity analysis (Table 2). Amongst the studies that investigated cost-effectiveness only 1 study evaluated the uncertainty in evidence using probabilistic analyses as recommended by some guidelines (UK and Canada). In addition, it is important to note that all 5 studies that evaluated cost-effectiveness in QALYs found palliative care interventions to be less expensive than standard care. In contrast, the study by Greer et al. found palliative care to be more cost effective unless it was in the patient’s final 30 days of life.\(^3\)
The quality of costing studies is also varied. Even though most cohort studies do undertake propensity score matching to decrease the risk of selection bias, this is not a significant evolution in methods since 2011. As Smith et al (2014) also reports that majority of the cohort studies in their review also controls for selection bias this way. Finally, a key finding of the previous literature review was the lack of focus on informal care or out-of-pocket costs. Since palliative care impacts patients as well as caregivers, societal perspective is of high value in the economic evaluation of this intervention. However, since 2011, there has only been 1 study that evaluated palliative care from a societal perspective which contrary to the majority of economic evaluations from a healthcare payer perspective did not find that palliative care significantly reduced costs compared to usual care.23 Regardless, when discounting study type and methods, most economic evaluations consistently found palliative care to be associated with lower costs relative to a comparator group. However, further investigation from a societal perspective is required to capture all relevant costs and consequences.

Limitations

This was a comprehensive review of the literature that investigated the financial implications of palliative care relative to a comparator. While the review does summarize the key findings of economic evaluations since 2011, it was rather designed to address the change in characteristics and methods of economic evaluations. Therefore, this review was limited to the defined scope of work as an assessment that focuses on the evolution of economic evaluation methods since 2011. Consequently, a meta-analysis of cost and outcomes from the literature was not completed.

In addition, a limitation of a literature review of this nature is the availability of these studies using the methods outlined in the methodology. Specifically, 9 articles were excluded because they did not have a full-text available. It is possible that these studies could have influenced the overall results.

Lastly, the quality of evidence was assessed using a tool adapted from various evaluations guidelines. Although they are drawn from credible guidelines, the 6 core categories and the 31 indicators within them is one of many approaches that could've been taken to assess the quality of evidence. Since this review aimed to update the literature review by Smith et al. (2014), the included studies were evaluated using the same quality assessment tool developed by Smith and colleagues. However, taking a different approach to appraising the quality of evidence may have resulted in a more precise assessment as the used tool only allowed 3 possible scores (0, 2 and 4). Moreover, the quality of the papers was judged by a single individual. Although measures were taken to minimize interpretation bias by having randomized checks completed by a second reviewer, a revision of quality assessment with a panel of reviewers will strengthen the study results and ensure consistency.

What This Study Adds

As for future directions, more formal cost-effectiveness studies are warranted in evaluating the economic impact of palliative care interventions. Though there have been 6 studies completed since 2011, the generalizability of results is limited due to the variability in healthcare reimbursement models in different countries. Additionally, 5 of the 6 cost-utility studies did not employ probabilistic analyses. Utilization of probabilistic distribution in modeling studies and bootstrap regression models in trial-based economic evaluations can significantly enhance the quality of economic analysis and meet the current guidelines of pharmacoeconomic evaluations.

Lastly, 2 studies that compared home hospice care to hospital-based hospice care provided a perfect example of how different the results of an economic evaluation can be depending on the perspective in which the analysis is completed.23,50 While the evaluation from the payer perspective found cost of care to be significantly less for home-based palliative care group, the evaluation from societal perspective found no significant difference in cost of care between hospital and home-based hospice care. Given the vital role informal caregivers play in the end-of-life care of terminally ill patients, future economic evaluation must consider both direct and indirect cost and QALYs.

Conclusion

Economic evaluation of palliative care is challenging but also a necessity given the disproportional share of healthcare expenditure for patients at the end-of-life. While the use of QALYs in measuring outcomes in palliative care has been debated in the past, recent guidelines for pharmacoeconomic evaluations calls for the use of cost-utility analysis. For that reason, a literature review was completed to examine whether methods of palliative care economic evaluations have evolved since the deficiency in cost-utility analysis was last reported in 2011. Despite the small increase in cost-utility studies since 2011, the methods of palliative care economic evaluations have not evolved significantly. Aligned with the guidelines for the economic evaluation of healthcare programs in several countries (e.g. Canada, UK and the US), researchers are encouraged to compare palliative care interventions in terms of costs and QALYs from a payer (e.g. Ministry of Health) or a societal (e.g. also taking into account productivity losses or out of pocket expenditures) perspective.67,68 To truly evaluate value for money and improve decision making, it is also very important that researchers take into account in their analyses the different types of uncertainty inherent to the economic evaluation according to best practices (e.g. sampling uncertainty for trial-based economic evaluations, parameter uncertainty when conducting model-based economic evaluations).53-55,67,69-71 Finally, researchers should follow reporting guidelines for economic evaluations of healthcare programs.72
Supplemental Material

Supplemental material for this article is available online.

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