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REVIEW

# Systematic Review of the Cost-Effectiveness of Home-Based Palliative Care Interventions in Patients with Cancer: A Critical Analysis

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**Background:** The increased prevalence of cancer and the negative impact of pain on the quality of life of patients underscore the need to implement efficient palliative care interventions and management of pain. The cost-effectiveness of palliative care interventions for cancer, mostly pharmacological and delivered through home-based palliative care services, is unclear. Most of the studies do not take into account indirect costs nor consider variations across different geographical regions.

**Objective:** To describe existing and cutting-edge knowledge on cost-effectiveness or item costs related to palliative home-based care for patients with cancer. We evaluated various costs, including direct medical, non-medical, and indirect costs in different geographical regions and analysed how different options for care affect the patients' quality of life and associated expenses.

**Methods:** This Prospero-registered systematic review (CRD42023404217) adhered to the PRISMA criteria. Following a multistep selection process, we selected 22 articles published between 2013 and 2023 focused on quality of life outcomes and cost-effectiveness of home-based palliative care for cancer patients.

**Results:** Home-based palliative care decreases the number of hospital visits, while its influence on patients quality of life is currently difficult to demonstrate across geographic regions based on available evidence. Overall, home care decreases the costs associated to the palliative care of patients with cancer. The cost structure analysis revealed that besides healthcare costs, informal care expenses and productivity losses represent a significant proportion of overall expenses). In Europe, the direct medical, non-medical, and indirect costs (in purchasing power parity) were on average $1,941, $842, and $1,241, per month per person, respectively. In the USA and Asia, direct medical and indirect costs are on average $1,095 (USA) vs $1,444 (Asia) and $2,192 (USA) vs $1,162 (Asia).

**Conclusion:** In conclusion, the studies reviewed highlight significant cost variations and potential savings associated with palliative home-based care for cancer patients. Home-based palliative care, particularly involving medications, has shown favorable cost-effectiveness compared to hospital care. Specialized palliative home care, psychological interventions, and outpatient services further contribute to overall cost savings. However, the economic impact varies across different geographical contexts and cost categories, emphasizing the need for tailored approaches in palliative care planning and implementation.

**Keywords:** cost-effectiveness, palliative care, treatment, interventions, review, pain management, cancer, quality of life

## Introduction

Recent epidemiological data demonstrate a significant rise in cancer cases worldwide. Cancers are among the leading causes of morbidity and mortality worldwide, responsible for 18.1 million new cases and 9.6 million deaths in 2018, significantly increasing the burden on patients, families, communities, and the health system. The quality of life of cancer patients in palliative care is significantly negatively affected by the pain associated with this disease, either as a consequence of the tumor or the treatment.[1] Pain is experienced by 55% of patients undergoing anti-cancer treatment and by 66% of patients who have advanced, metastatic, or terminal disease. In the terminal disease group, up to 80% of patients experience cancer pain.

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The increasing prevalence of cancer worldwide underscores the escalating demand for palliative care services, highlighting the necessity for effective home-based palliative care interventions and management of pain. The goal of palliative care is to improve patients' quality of life by relieving disease symptoms, reducing pain, or providing psychological help, among others.[2] According to the WHO, 34% of palliative care cases are cancer patients.[3] Palliative care can be provided either in inpatient facilities or as home care. According to a study by Tay et al, more than 58% of palliative care patients were in home care.[4]

Technological advancements such as telehealth and remote monitoring technologies can improve the delivery of high-quality palliative care to patients in their homes, their comfort, contentment, and quality of life. Although technological progress is still advancing and new options for cancer pain solutions are coming to the market, the standard care of cancer pain mainly relies on pharmacological treatment. Approximately 43% of cancer patients use opioids to treat cancer pain.[5]

To develop and implement new solutions for cancer pain patients and care interventions at home, it is necessary to have an overview of current approaches to palliative care, associated costs, and their impact on quality of life. The existing literature insufficiently addresses the cost-effectiveness of pharmacological and non-pharmacological solutions for cancer pain, often lacking a comprehensive analysis considering both formal and informal costs. Studies rarely consider indirect costs such as lost productivity due to illness, time off work for both patients and their caregivers, and other societal costs. These costs are essential as they affect the broader economic implications of care and the financial burden on families and society. Smith et al in 2013 published comprehensive literature review of available international evidence on the costs and cost-effectiveness of palliative care interventions in any setting (eg hospital-based, home-based and hospice care) over the period 2002–2011. With 46 included papers in the review, authors examined the cost and/or utilisation implications of a palliative care intervention with some form of comparator. The main focus of selected studies was on direct costs with very little attention being paid to informal care or out-of-pocket costs. 31 studies from the sample were from USA. Palliative care was most frequently found to be less costly relative to comparator groups with the difference in cost being statistically significant in most cases. Authors also concluded that there may be complex interactions between costs of care and diagnosis, age of the group and other factors (eg length of nursing home enrolment in US studies) that require further investigation and in particular the role played by informal care needs to be analyzed in more detail in future studies.[6]

Overall, no comprehensive review with focus on assessment of costs (both formal and informal) and cost-effectiveness of home-based palliative care currently exist, leaving a significant gap in understanding the most efficient and beneficial approach for patients also in the context of geographical variations. This lack of detailed analysis hampers the ability to implement best practices, allocate resources effectively, and ultimately improve patient outcomes in a cost-efficient manner.

Therefore, the aim of the paper is to review current treatment modalities, related costs and impact on quality of life for patients with cancer pain in home based palliative care. We will analyze separately all the types of costs and will also provide an overview of costs in 3 different geographical regions: Asia, USA, and Europe.

# Methods

## Study Design

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were adhered to in the conduct of this systematic review.[7] A systematic, comprehensive evaluation of palliative care was conducted in this review utilising the bibliometric mapping study method[8] and review technique[9] in accordance with the PRISMA guidelines.[7] The objective was to assess the direct and indirect costs as well as the cost-effectiveness outcomes different palliative care modalities with special focus on home care. By integrating these two approaches, one can attain a more profound comprehension of a subject matter and generate a framework for intellectual mapping.[8]

The protocol was prospectively registered with the International Prospective Register of Systematic Reviews (PROSPERO; www.crd.york.ac.uk/prospero) on 12 March 2023 (registration number: CRD42023404217)."

## Key Terms

To clarify following terms critical for our review and its focus, which need to be clearly defined before explanation of the focus of this review.

Three categories of costs will be considered: Direct medical costs- expenses directly associated with the medical care of a patient (hospital stays, physician fees, medications, medical procedures. Direct medical costs might cover home visits by healthcare professionals, medications delivered at home, and any medical equipment needed for home care). Direct non-medical costs refer to expenses that are not directly related to medical services but are necessary for facilitating care (eg, transportation to and from medical appointments, home adaptations to accommodate medical needs, costs for caregivers or home help). Indirect costs represent the economic impact of a disease or treatment on a patient's life beyond direct expenses (eg, productivity loss, time off work for both patients and their caregivers, and other societal costs).

For orientation in the large number of currently available care alternatives, cost-effectiveness analyses are used, which are capable of projecting not only the cost but also the effect on the patients health of these care alternatives. Cost-effectiveness analyses compare the costs and effectiveness of at least two care alternatives. Among the most commonly used cost effectiveness analyses are cost effectiveness analysis (CEA) and cost utility analysis (CUA). The CEA expresses the effect on the health status of natural units. In the case of cancer pain, the natural unit is, for example, the intensity of pain or the number of pain attacks. CUA expresses the effect on health status in Quality Adjusted Life Years (QALY), ie, in years of life adjusted to years of full quality life. To compare the effect and costs of two care alternatives, the Incremental Cost Effectiveness Ratio (ICER) calculation is used in cost analyses, the calculation of which consists of the ratio of the difference in costs to the difference in effectiveness.[10]

## Information Sources and Search Strategy

This review covered the period from 2013 to March 2023. The systematic search consisted of several steps: searching for and identifying relevant articles, screening them according to the set criteria. We first explored the number of articles in PubMed and Web of Science (WOS) database, using the keywords "palliative care", "cancer", "cost", "economic treatment", "cost-effectiveness", 'health economic evaluation,' 'home,' 'care' and their combinations (see Table 1).

After removing duplicates, the first screening of the papers was performed independently and blindly by four researchers who coded each study based on the title and abstract. The inclusion and exclusion criteria that guided the screening process can be found below. Then, to minimize bias and potential errors, two groups of reviewers (the first group, PM vs JH and the second group, KR vs LR) performed the data extraction. They collected study details such as methods and design, participants, settings, interventions, and results.

**Table 1** Distribution of the Identified Articles (from 2013 to June 2022) Using the Filter – 01 January 2013 to 1 July 2022

| Key Words Used "AND" Between All Words | WOS | PubMed |
|---|---|---|
| Palliative care AND Cost | 1845 | 956 |
| Palliative care AND Cost Effectiveness | 332 | 198 |
| Palliative care AND Health economic evaluation AND Home care | 52 | 1 |
| Palliative care AND Cost-effectiveness AND Home AND Care | 132 | 41 |
| Cancer AND Cost AND Home | 998 | 468 |
| Cancer AND Cost-effectiveness AND Home AND Care | 159 | 70 |
| Cancer AND Quality of life AND Home AND Pain | 546 | 199 |
| Cancer AND Quality of life AND Cost AND Pain | 435 | 351 |
| **Total** | **4499** | **2284** |

**Note**: Document type: articles or review articles.

## Search Strategies Eligibility Criteria

Specific inclusion and exclusion criteria were set to ensure that only the relevant studies were included. The exclusion and inclusion criteria are described in detail as follows:

### Inclusion Criteria

- Articles that were produced between 2013 and 2023, including both years.
- Full-text articles authored in English and approved by peers.
- Comparing home-based palliative care for adult cancer patients with treatment provided in a hospital setting.
- Studies including different therapies, drugs, or surgical procedures used to alleviate pain.
- Cost-effectiveness outcomes using quality-adjusted life years (QALY) and incremental cost-effectiveness ratio (ICER) indicators.
- Studies that described direct and indirect costs.

### Exclusion Criteria

- Language other than English.
- Studies published before 2013.
- Review studies, meta-analyses, purely descriptive articles, or conference notes.
- Articles focused only on child treatments or the results of preclinical studies.
- Studies focusing on clinical efficacy without regard to cost.
- Comparison of two treatment approaches, without reference to costs.
- Diagnostic tools, their comparison, and their description of effectiveness have no relation to costs or QALY indicators.
- Studies on the definition of disease management in various contexts.
- Studies focused on non-cancer pain or cancer treatment (not palliative care).
- Studies have not focused on home-based care.

## Quality Assessment

We evaluated the quality of the research included in our analysis employing the CHEERS checklist,[11] which offers extensive criteria for studies that report health-economic evaluations. The findings are documented in the Supplementary Material Document 1. Furthermore, we have assessed selected articles through the lens of identified often appearing methodological challenges specific to the problem domain. Fischer et al in their review set to identify and summarise existing information on methodological challenges and potential solutions/recommendations for economic evaluations in the area of palliative care. In total, they identified challenges that were grouped into nine themes, but concluded that most of the studies were related to the three following: narrow costing perspective with non-standardised measurement and valuation of costs on top of it and ambiguity in the selection of outcome measures.[12]

# Results

We initially identified 4499 and 2284 articles from the Web of Science and PubMed databases, respectively. Because of the similarity in the search terms, we found many duplicates among the articles, depending on the different search terms. After removing 5531 duplicates, 1252 articles were screened. We then excluded 744 articles based on their titles and keywords, as well as 366 articles based on the review of their abstracts. After reading the full articles, we identified additional reasons for excluding articles that did not meet our criteria. For example, some articles did not sufficiently mention costs or QALY indicators, whereas others did not focus on home-based care or cancer pain analysis. Finally, we included 22 articles that fulfilled the set criteria (see Figure 1). Overall, these articles provide valuable insights into the effectiveness, costs, and impact of palliative care for patients with various types of cancer in different healthcare settings worldwide. Table 2 provides an overview of the 22 studies with data on the study design, type of cancer, country, and time of data collection. The publication years spanned from 2013 to 2023. Most of the articles (12 of 22) used observational study designs, such as prospective observational studies and longitudinal register- and questionnaire-

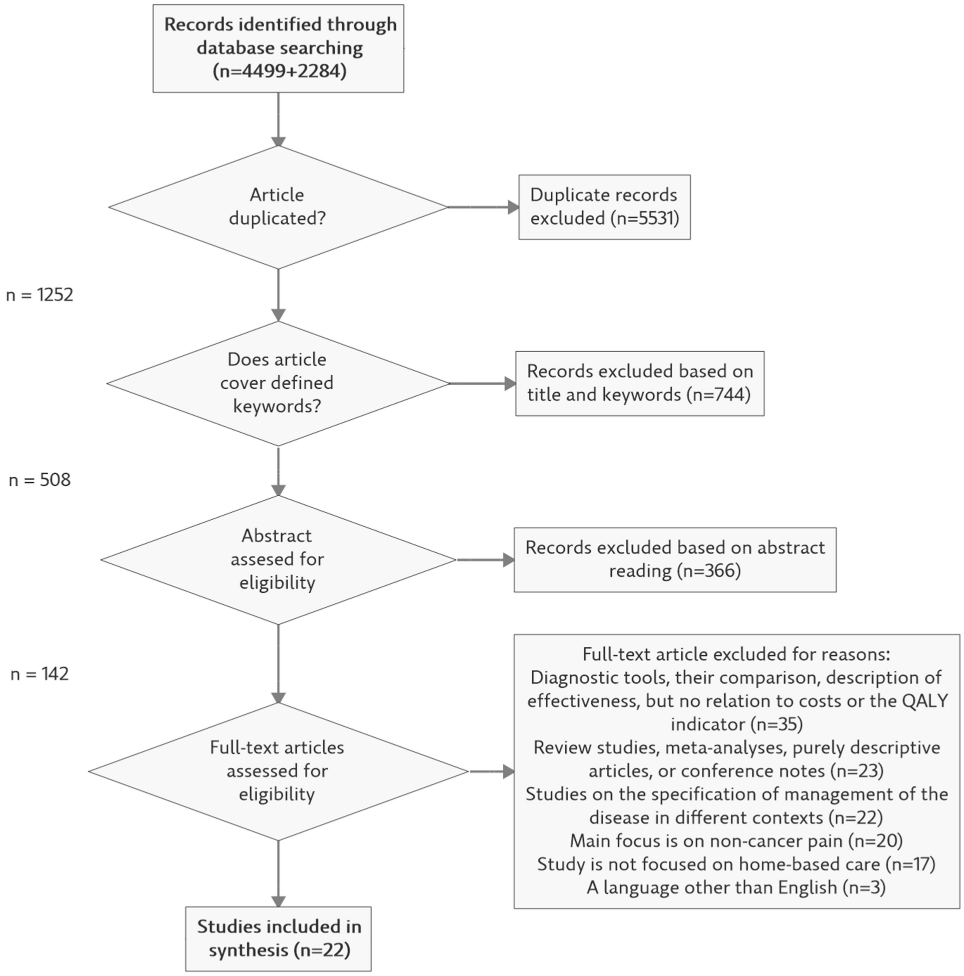

**Figure 1** PRISMA flow-chart of the systematic review process.

**Notes**: Adapted from Moher, D.; Liberati, A.; Tetzlaff, J.; Altman, D.G.; The PRISMA Group Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS Med*. **2009**, *6*, e1000097.[7]

based studies. Two retrospective cross-sectional studies and one retrospective analysis were included. Other study designs included randomized controlled trials, case-control studies, cohort studies, and cost-effectiveness analyses. Lung cancer was the most frequently reported type of cancer in five studies. The articles had 0–162 citations.

## QoL and Health Improvement Indicators

Table 3 includes information about the treatment modalities, sample analysed, palliative care modality, measures of QoL, other outcome variables, and the main results.

As shown in the table, the primary health outcomes were the indices of patients' QoL. The other outcome variables were pain relief, symptom management, and hospitalisation rates.

Table 3 includes data from various studies examining QoL measures and treatment modalities in patients with cancer, with a focus on palliative care. Analysis of sample sizes and characteristics revealed a diverse range of patient populations across studies. For instance, Zdun-Ryżewska et al compared 74 patients in an inpatient unit with 53 patients and 21 patients in home care, demonstrating a mix of inpatient and outpatient settings.[9] Piotrowska et al conducted a study on 44 adult patients,[13] whereas Nosek et al included 62 patients who received different opioid treatments.[14] The homogeneity of the data is variable, with some studies specifying patient characteristics such as age, sex, and treatment groups, while others provide less detailed information. For example, Götze et al compared the QoL of palliative patients and their family caregivers but did not elaborate on specific cancer types or treatment modalities.[19] Regarding the type of cancer, information on cancer subtypes or stages is

**Table 2** Overview of Included Studies - Health and Quality of Life Category in Home-Based Palliative Care

| Author | Study Design and Approach | Type of Cancer | Country | Time of Data Collection |
|---|---|---|---|---|
| Zdun-Ryżewska et al, 2019[9] | Prospective study | N/C | Poland | N/A |
| Piotrowska et al, 2019[13] | Prospective study | N/C | Poland | 06/2013 – 07/2016 |
| Nosek et al, 2017[14] | Prospective study | N/C | Poland | 12/2013 – 12/2015 |
| Cortesi et al, 2017[15] | Cost-effectiveness analysis | N/C | Poland | N/A |
| Delibegovic et al, 2016[16] | Prospective observational study | Lung | Bosnia and Herzegovina | N/A |
| Ruggeri et al, 2014[17] | Cost-effectiveness analysis | N/C | Italy | 2007 – 2009 |
| Leppert et al, 2014[18] | Prospective study | Lung, colon, kidney, prostate, breast, head and neck, ovary, pancreas | Poland | 7/2010 – 12/2010 |
| Götze et al, 2014[19] | Observational study | N/C | Germany | 3/2011 1/2013 |
| Leppert et al, 2012[20] | Observational study | Lung | Poland | N/A |
| Halling et al, 2020[21] | A randomised controlled trial | N/C | Denmark | 6/2013 – 8/2016 |
| Maetens et al, 2019[22] | Observational cohort study | N/C | Belgium | 2012 |
| Rowland et al, 2017[23] | Observational study | Lung, colorectal, prostate, breast, pancreas, oesophagus, all other malignant cancers | United Kingdom | 2015 |
| Haltia et al, 2018[24] | Observational study | Breast, colorectal, prostate cancer | Finland | 9/2009 – 4/2011 |
| Brick et al, 2017[25] | Observational study | N/C | Ireland | N/A |
| Tur-Sinai et al, 2022[26] | Observational study | N/C | Israel | 4/2008 – 12/2013 |
| Kato and Fukuda, 2017[27] | Observational comparative study | Lung, gastrointestinal liver/biliary tract/ pancreas, urinary organ, uterus/ovary, breast, other | Japan | 10/2014 – 03/2016 |
| Lustbader et al, 2017[28] | Observational study | N/C | USA | 1997 – 2011 |
| Chiang and Kao, 2016[29] | Observational study | Lung | Taiwan | 8/2010 – 10/2012 |
| Yu et al, 2015[30] | Observational study | N/C | Canada | 2018 – 2019 |
| Dumont et al, 2014[31] | Observational study | N/C | Canada | 3/2009 – 2/2012 |
| Chai et al, 2014[32] | Observational study | N/C | Canada | 7/2005 – 9/2007 |
| Bentur et al, 2014[33] | Comparative Study | N/C | Israel | 1/2009 – 9/2009 |

**Abbreviations**: N/C, Not Considered; N/A, Not Available.

inconsistent. While some studies, such as those by Ruggeri et al [17] and Cortesi et al, [15] focused on breakthrough cancer pain, others encompassed a broader range of patients with cancer without specifying the type.[15] In general, the studies show that home-based palliative care boosts patient satisfaction with care, decreases the number of hospital visits, and improves patient comfort and quality of life. Nevertheless, the heterogeneity of samples and data, and the lack of consideration of cancer type in some studies make it challenging to draw conclusions regarding specific cancer types.

**Table 3** Summary of the Selected Studies – Health and QoL Indicators

| Study | QoL Measures | Treatment Modality | Sample Characteristics | Other Indices | Palliative-Care Modality | Result Pattern |
|---|---|---|---|---|---|---|
| Zdun-Ryżewska et al, 2019[9] | BPI, Karnofsky Scale, Illness Perception Questionnaire | The comparison of symptomatic treatment in terms of pain intensity: inpatient palliative care unit (PCU) and home care (HC) | N=74, from that at an inpatient unit (N = 53, age 60) and at home (N = 21, age 66) | Pain interference (PCU - 4.72; HC – 5.83). Pain intensity (PCU – 3.11; HC −3,2). Pain at its worst (PCU - 5.75; HC – 6.86). Pain at its least (PCU – 1.15; HC – 1.00). Pain on average (PCU – 3.37; HC – 3.24). Pain right now (PCU – 2.19; HC – 1.71). | Inpatient and outpatient | No statistically significant variations were observed among the groups with respect to pain interference or pain severity. |
| Piotrowska et al, 2019[13] | BPI, MMSE, QLQ-C15-PAL | ”Intravenous morphine, fentanyl nasal spray, and fentanyl buccal tablets” | 44 adult patients | Both intravenous morphine and rapid-onset fentanyl were highly effective in treating procedural pain caused by nursing procedures in cancer patients. They were well-tolerated and led to improved quality of life. | Inpatient and outpatient | Both drugs were highly effective with no significant differences in efficacy or tolerance. |
| Nosek et al, 2017[14] | BPI | Morphine, oxycodone, fentanyl and buprenorphine | 62 patients with average age of 69 participated | Patients were organized into four cohorts receiving substances stated in column 2. Immediate-release morphine was the rescue opioid utilised to address breakthrough pain episodes in all patient categories. Pain at its worst (Day 1–7.81; Day 28–2.62. Pain at its least (Day 1–5.34; Day 28–0.70). Pain on the average (Day 1–6.77; Day 28–1.57). Pain right now (Day 1–6.69; Day 28–1.57). | outpatient | Morphine improved daily activities impacted by pain as measured by BPI-SF. Scores decreased from day 1 to day 28, indicating improvement in pain measures and its impact on patients' lives. |
| Cortesi et al, 2017[15] | Episode of Breakthrough cancer pain | ”Sublingual fentanyl citrate (FCSL), fentanyl buccal soluble film (FBSF), fentanyl buccal tablet (FBT), oral transmucosal fentanyl citrate (OTFC) and fentanyl sublingual tablets (FST)” | Adult cancer patients with stable opioid medication for background pain, experiencing 1–4 episodes of BTcP daily. | QALYs (vs Placebo) results: FCSL (Costs €1,960.76; QALYs 0.0507), FST (Costs €2,069.18; QALYs 0.0489), FBSF (Costs €2,776.06; QALYs 0.0468), FBT (Costs €2,565.94; QALYs 0.0493), OTFC (Costs €2,540.36; QALYs 0.0489). | Inpatient and outpatient | FCSL outperformed other oral formulations in treating breakthrough cancer pain with lower patient cost of €1,960.8 and a higher efficacy of 18.7% of BTcP averted and 0.0507 QALYs gained. |

(*Continued*)

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**Table 3** (Continued).

| Study | QoL Measures | Treatment Modality | Sample Characteristics | Other Indices | Palliative-Care Modality | Result Pattern |
|---|---|---|---|---|---|---|
| Delibegovic et al, 2016[16] | SF-36 | The influence of palliative care on the quality of life:<br>intervention group: inpatient palliative care, control group: home care | "80 patients (40 patients in intervention group, 40 patients in control group)" | "General life quality: intervention (first testing 0.17; second testing 0.62); control (first testing 0.34; second testing 0.34)<br>Pain: intervention (first testing 0.29; second testing 0.67); control (first testing 0.45; second testing 0.44)" | Inpatient and outpatient | The intervention group had greater improvement in QoL, and pain scores compared to the control group after two weeks. |
| Ruggeri et al, 2014[17] | Episode of Breakthrough cancer pain | Morphine + transnasal fentanyl citrate, Morphine + placebo | Markov model, cohort of 100 patients | Base case results: Instanyl (Costs €9893; QALY 0.63), Placebo (Costs €6431; QALY 0.29). INCR COST: €3461, INCR QALY 0.34. ICER €10,140. | Inpatient and outpatient | Intranasal fentanyl citrate (Instanyl) had a greater cost and a higher QALYs compared to the placebo. |
| Leppert et al, 2014[18] | EORTC QLQ-C15-PAL, ESAS and KPS | Comparison of quality of life in cancer patients receiving treatment at home (HC), a day care centre (DCC), and an inpatient palliative care unit (PCU) | 129 patients, age 67 | GQL: PCU (Baseline – 35.62; Day 7–51.63); HC (Baseline 35.62; Day 7–53.27); DCC (Baseline – 44.44; Day 7–65.43)<br>Pain: PCU (Baseline – 79.74; Day 7–28.76); HC (Baseline – 75.49; Day 7–27.78); DCC ((Baseline – 72.22; Day 7–25.31) | Inpatient and outpatient | EORTC QLQ-C15-PAL scores showed significant improvements in pain and QoL (GQL) in all groups, with the greatest improvement in the DCC group. |
| Götze et al, 2014[19] | HADS, EORTC QLQ-C15, EORTC QLQ-C3O | Palliative patients (PP) and their family caregivers (FC) QoL comparison | 106 patients (age 69) and their family caregivers, age 64) | "Anxiety and depression (HADS): PP (anxiety 6.42; depression 11.11); FC (anxiety 8.24; depression 8.21)<br>QoL of palliative patients (EORTC): Fatigue 73; appetite loss 49; pain 47; dyspnoea 45; insomnia 39; nausea/vomiting 32; constipation 31." | outpatient | "There was a significant correlation between anxiety and depression scores of patients and caregivers."<br>The most severe symptoms reported by palliative patients were fatigue, appetite loss, and pain. |
| Leppert et al, 2012[20] | EORTC QLQ-C30 | QoL of Patients in Palliative care unit (PCU) and home care (HC) | 78 patients, age 68 | GQL: PCU (GQL1 20.33; GLQ2 13.33); HC (GQL1 16.00; GQL2 12.00)<br>Pain (PA): PCU (PA1 82.67; PA2 87.33); HC (PA1 71.33; PA2 77.33) | Inpatient and outpatient | Patients in the palliative care unit had higher scores on the GQL scale and pain than those receiving home care. |

**Abbreviations**: BPI: Brief Pain Inventory; PCU: Palliative Care Unit; HC: Home Care; MMSE: Mini-Mental State Examination; QLQ-C15-PAL: Quality of Life Questionnaire-Core 15-Palliative; BTcP: Breakthrough Cancer Pain; QALY: Quality-Adjusted Life Year; SF-36: Short Form (36) Health Survey; GQL: General Quality of Life; ICER: Incremental Cost-Effectiveness Ratio; ESAS: Edmonton Symptom Assessment System; KPS: Karnofsky Performance Status; EORTC QLQ-C15-PAL: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 15-Palliative; EORTC QLQ-C3O: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; HADS: Hospital Anxiety and Depression Scale.

## Treatments Identified for Pain Relief in Oncological Patients

Therapies included medication (eg, morphine, fentanyl, buprenorphine, and oxycodone), radiation, different therapies, and interventions. Pharmacology is the most common therapeutic modality. Medications included various pharmacological agents, analgesics, and medications targeted at managing specific symptoms or conditions. The listed medication options include opioids such as morphine, oxycodone, fentanyl, and buprenorphine, administered via various routes such as intravenous, sublingual, and buccal routes. Specific formulations of fentanyl, such as FCSL, FBSF, FBT, OTFC, and FST, are used for rapid pain relief.[13–15,17] Studies evaluating specific medications, such as intravenous morphine and rapid-onset fentanyl, have demonstrated high analgesic efficacy and good tolerance, leading to improvements in patients' QoL. Morphine was particularly effective in improving daily activities affected by pain, as indicated by Brief Pain Inventory - Short Form (BPI-SF) scores.[14] Sublingual fentanyl citrate (FCSL) is more cost-effective and efficacious than other oral formulations for treating breakthrough cancer pain. Overall, patients in palliative care showed significant physical and mental health improvements after receiving treatment.[18–20] Specifically, Piotrowska et al [13] showed the analgesic efficacy and tolerance of intravenous morphine and rapid-onset fentanyl for managing procedural pain induced by nursing procedures in patients with cancer. Both drugs were highly effective, with no significant differences in efficacy or tolerance. Although the data indicate the effectiveness and tolerability of these drugs, they do not directly compare their effects on QALYs. Nosek et al [14] focused on the effects of morphine on the daily activities of patients with pain. Descriptive statistics from the Brief Pain Inventory-Short Form (BPI-SF) are provided, showing improvements in various pain measures from days 1 to 28. This demonstrated the positive effects of morphine on pain reduction and daily activities. In Cortesi et al, the comparison of various formulations for managing breakthrough cancer pain showed that sublingual fentanyl citrate (FCSL) was more cost-effective and efficacious compared to the other oral formulations.[15] In the base-case analysis, FCSL had a patient cost of €1,960.76, resulting in a gain of 0.0507 QALYs. Other oral formulations, such as FST, FBSF, FBT, and OTFC, have higher patient costs and lower QALY gains than FCSL. This suggests that FCSL provides better value-for-money in terms of both cost and QALYs gained in managing breakthrough cancer pain. Additionally, there was a significant correlation between the anxiety and depression scores of patients and their caregivers, highlighting the importance of addressing emotional well-being in palliative care. The data underscore the importance of choosing appropriate medication tools and interventions to effectively manage pain and enhance the overall health and QoL of patients receiving palliative care.

## Palliative Care Modalities

Concerning palliative care modality, Zdun-Ryżewska et al [9] compared patients at palliative care unit (PCU) and home care (HC) using BPI, HADS, Karnofsky Scale, and Illness Perception Questionnaire. Notably, this study did not involve specific medications, but compared patients from different care settings. The findings revealed no significant differences in pain intensity or pain interference between the two groups. Leppert et al [20] analysed the differences between HC programmes and PCU. Physicians and nurses followed up with patients in the PCU every day. Two nurses and one doctor checked in with patients in the home palliative care programme every week. Both the PCU and home therapies were comparable; however, whereas patients in the PCU had rapid access to oxygen, those receiving treatment at home had to wait a few hours after a visiting doctor's order for it. Low scores on functional measures were seen among palliative care patients, according to Leppert's observation, and that these scores generally deteriorated. The most severe symptoms reported by these patients' included dyspnoea, fatigue, loss of appetite, pain, and constipation. Descriptive statistics revealed that in the comparison between two groups, Group 1, receiving palliative care in a unit, had a mean score of 20.33 ± 3.39 on the General Quality of Life (GQL) scale, while those in home care (Group 2) had a lower mean score of 16.00 ± 3.39. This indicates that patients in palliative care units reported a higher GQL. These findings underscore the challenges faced by patients in palliative care and emphasise the need for comprehensive symptom management and support to improve their overall QoL. In the second study, Leppert et al [20] added a group of patients treated in day care center (DCC). Results were in accordance with their previous study, QoL improved in all patient groups, with better results in DCC patients and similar scores in those staying at home and at the PCU. Regarding Zdun-Ryżewska et al, [9] patients at an inpatient unit and those receiving home care were assessed using BPI, HADS, Karnofsky Scale, and Illness Perception Questionnaire. Descriptive statistics revealed that patients in PCU had a higher mean score in the GQL scale than those in HC (20.33 ± 3.39 vs 16.00 ± 3.39). Zdun-Ryżewska et al [9] compared patients at PCU and HC using BPI, HADS, Karnofsky Scale, and Illness Perception Questionnaire. Notably, this study did not involve specific medications, but compared patients from different care settings. The findings revealed no significant differences in pain intensity or pain interference between the two groups. Götze et al conducted a study[19] involving 106 patients and their family caregivers, assessing anxiety, depression, and symptoms in palliative patients. This study found significant correlations between the patients' and caregivers' anxiety levels and depression scores. According to the EORTC symptom scales, the most severe symptoms reported by palliative care patients were fatigue, appetite loss, and pain.

In total, only three studies from the sample addressed difference in inpatient vs outpatient palliative care in relation to QoL measures. Two studies were performed in Denmark and had similar co-author group with results unfavorable for outpatient palliative care. Third study by Zdun-Ryżewska et al [9] revealed no significant QoL differences between the inpatient and outpatient PC groups. Therefore, there is no evidence in our sample of studies for superior QoL outcomes of outpatient palliative care.

## Costs Associated with Palliative Care

Table 4 provides a comprehensive overview of the various studies that have examined the cost structures, outcomes, and characteristics of palliative care interventions. The cost structures vary, with some studies detailing specific cost components such as inpatient and outpatient costs, caregiver expenses, and informal care costs. Healthcare expenditures make up a significant amount of palliative care costs, as shown in the costs for various cancer types reported by Haltia et al.[24] Kato and Fukuda (2017) and Lustbader et al, among others, have shown that home-based palliative care reduces treatment costs.[27,28] The financial viability of palliative therapy cannot be universally determined due to the diversity of study methods and interventions. There has to be nuanced interpretations when looking at cost results and the generalizability of findings across varied patient demographics and locations since data variability represents the complicated nature of such care strategies and their monetary implications.

The cost structure includes various components grouped into the following categories: direct medical costs, direct non-medical costs, and indirect costs. Direct medical costs included those for drugs, inpatient care, outpatient visits, and medical devices. Direct non-medical costs include travel costs, private caregivers, alternative therapies, and special food. Indirect costs included productivity loss (opportunity costs) and informal care (Table 4, Table 5).

In general, the analysis of the cost outcomes revealed that home-based palliative care offered cost-saving advantages, according to three studies.[27–29] Yu et al presented contradictory evidence, their analysis revealed that end-of-life care expenses for patients who passed away at home incurred significantly higher average total cost than those who perished in hospitals.[30]

Overall, the data demonstrate the importance of tailored pain relief interventions in palliative care, focusing on improving patient well-being and providing cost-effective and compassionate end-of-life care.

### Costs and Cost Effectiveness of Medication

In the context of cost-effectiveness and medication, Ruggeri et al [17] presented the lowest ICER at €10,140, indicating that transnasal fentanyl citrate (Instanyl) is a more cost-effective strategy for treating breakthrough cancer pain than placebo. In Cortesi et al's study,[15] although FCSL was considered more cost-effective and efficacious than the other oral formulations, specific ICER values for these comparisons were not provided. In another study,[21] the intervention group had a higher ICER of €118,292/QALY, suggesting that the intervention may not be cost-effective, particularly at a willingness-to-pay threshold of €80,000/QALY. Overall, Ruggeri et al [17] demonstrated the most favourable cost-effectiveness profile among the presented data, with a relatively lower ICER for transnasal fentanyl citrate (Instanyl) than for placebo. Halling et al found that specialised palliative care at home, along with psychological intervention, was cost-effective, with an ICER of Shekel(₪) 118,292/QALY.[21] Kato and Fukuda[27] showed that home care was associated with lower treatment costs, saving $7,523 per patient. Lustbader et al [28] demonstrated that HC led to significant cost savings of $12,000 per patient. Chiang et al found that HC is cost-effective, resulting in lower healthcare costs than inpatient hospice care.[29]

**Table 4** Summary of the Selected Studies – Types of Intervention and Associated Costs

| Study | Intervention Description | Relevant Characteristics of the Study Population | Patient Sample Diagnosis/ Identification | Time Horizon | Payers' Perspective | Description of Cost Structure (Text Separated by ;) | Primary Cost Outcome |
|---|---|---|---|---|---|---|---|
| Bækø Halling et al, 2020[21] | A dyadic psychological intervention and a streamlined process for patients to go from a full-service cancer centre to home specialised palliative care (SPC) comprise the intervention group. | A total of 321 patients participated in the study, including 162 in the intervention group and 159 in the control group. | Cancer | The last 6 months of life | Formal and informal, both groups of patients were at home | Intervention – Patients: Hospital (€1,366); Public Health insurance (€225); Home care nursing (€403); Home care (€697); Caregivers: Hospitals (€100); Public Health Insurance (€164)<br>Control - Patients: Hospital (€2,727); Public Health insurance (€214); Home care nursing (€578); Home care (€357); Caregivers: Hospitals (€282); Public Health Insurance (€229) | The intervention group experienced increased costs and a higher quality of life. The Incremental Cost-Effectiveness Ratio (ICER) was calculated to be €118,292 every Quality-Adjusted Life Year (QALY). At a willingness to pay threshold of €80,000 per Quality-Adjusted Life Year (QALY), the base case scenario indicates a 15% probability that the intervention is cost-effective. |
| Maetens et al, 2019[22] | Palliative home care support – yes/ no | 8,837 patients who received palliative home care support | All causes | The last 14 days of life | Formal and informal. Palliative home care support vs Home care without the use of palliative support | Yes – Inpatient Costs (€1,766); Outpatient Costs (€1,314)<br>No – Inpatient Costs (€4,222); Outpatient Costs (€476) | Total costs were higher in the last 2 weeks of life in the unexposed group of patients, by €1,617. |
| Rowland et al, 2017[23] | Total time spent on caregiving and money spent as a result of caregiving in a typical week in last 3 months of life | 1,504 patients | Cancer patients | The last 3 months of life | Informal | Time – mean 94:59 hours, median 69:30 hours<br>Money - Nursing home/private care home (£3,138,58); Privately employing nurse/carer (£1,785,9); Child care (£545.9); Odd jobs not normally paid for (£372.74); Respite/ holidays/day trips (£780.08); Medical equipment/care supplies (£289.1); Prescription/non-prescription drugs (£107.47); Household bills (£235.62); Travel expenses (£208.2); Meals/snacks while out (£113.1); Extra food/supplements/vitamins (£123.03); Other (£602.27); One-off expense any time since diagnosis £8,759.84) | In the last three months of the decedent's life, more than 90% of respondents said they spent time caring for them, with a median of 69 hours and Thirty minutes of caregiving every week. In the last three months of the decedent's life, those who supplied spending details (72.5%) spent a median of £370. |
| Haltia et al, 2018[24] | Costs of palliative care in three groups of patients: breast cancer, colorectal cancer and prostate cancer | 70 cancer patients in palliative care | Cancer patients | Not available | Formal and informal | Breast cancer (mean 59 days): Total cost (€12,825); Outpatient cost (€3,698); Inpatient cost (€3,505); Productivity cost (€2,492); Informal care (€3,130)<br>Colorectal cancer (mean 181 days): Total cost (€22,57); Outpatient cost (€4,334); Inpatient cost (€ 6,137); Productivity cost (€4,502); Informal care (€7,604)<br>Prostate cancer (mean 239 days): Total cost (€26,080); Outpatient cost (€7,453); Inpatient cost (€9,191); Productivity cost (€4,231); Informal care €5,205) | Palliative treatment lasted an average of 179 days. Expenses related to healthcare constituted 55%, informal care 27%, and productivity 18% of the total. |

(*Continued*)

**Table 4** (Continued).

| Study | Intervention Description | Relevant Characteristics of the Study Population | Patient Sample Diagnosis/ Identification | Time Horizon | Payers' Perspective | Description of Cost Structure (Text Separated by ;) | Primary Cost Outcome |
|---|---|---|---|---|---|---|---|
| Aoife Brick et al, 2017[25] | Costs of palliative care in the Midlands, Mid-West and Southeast regions. | 214 patients (ca 70 cancer:30 non-cancer) | All causes | The last 12 months of life | Formal and informal | Community services (€6,007.96); SPC costs (€2,652.99); Allied health professional (€850.72); Hospital (€30,667.86); Nursing Home (€7,190.99); Medication (€1,926.10); Equipment (€774.52); Formal Care (€50,071.15); Basic activities of daily living (€8,404.00); Instrumental activities of daily living (€5,447.27); Informal care (€13,650.53)<br>Mid-West: Community services (€5,625.17); SPC costs (€14,577.40); Allied health professional (€512.65); Hospital (€22,408.26); Nursing Home (€4,234.36); Medication (€2,009.62); Equipment (€668.28); Formal Care (€50,035.74); Basic activities of daily living (€12,472.78); Instrumental activities of daily living (€5,493.08); Informal care (€17,965.86)<br>Southeast: Community services (€5,440.51); SPC costs (€2,964.69); Allied health professional (€591.08); Hospital (€25,420.31); Nursing Home (€2,211.38); Medication (€1,956.73); Equipment (€1,542.11); Formal Care (€40,136.82); Basic activities of daily living (€8,723.60); Instrumental activities of daily living (€7,313.14); Informal care (€16,036.75) | During the period of nine months, the costs of informal care for activities of daily living (IADLs) constitute the biggest share of the total mean costs of informal care. In the final three months of life, the expenses of informal care for BADLs are higher than the costs of informal care for IADLs in each area, according to a range of 55% to 60%. When looking at the total mean informal care expenditures in the final year of life, the most significant quantities are accounted for by the mean costs of personal care (basic activity) and assistance with home duties (instrumental). |
| Tur-Sinai et al, 2022[26] | "Out-of-pocket spending by persons who died from cancer and by their families in the last half-year of patients' life (percent)" | 491 relatives of patients with cancer | cancer | The last 6 months of life | Informal (out of pocket spending only) | Travel (70%); Food (60%); Other (56%); Medications (42%, average $5,800); Private caregiver (32%, average $8,000); Accommodations (12%); Private nurse (9%, average $2,800) | Around 84% of cancer patients and their family members spent money out of their own pockets in the final six months of their lives. The typical amounts spent were $5,800 on medications, $8,000 on personal caretakers, and $2,800 on private nurses. |
| Kato and Fukuda, 2017[27] | The case group - home care and the control group – hospital care | The case group (home care) Forty-Eight patients and control (hospital-care) group 99 patients | Cancer patients | Not available | Formal and Informal | Home: the mean total treatment costs ($9,958)<br>Hospital: the mean total treatment costs ($17,481) | Home care was strongly correlated with a decrease of $7,523 in treatment expenses. |
| Lustbader et al, 2017[28] | Home based palliative care and control group | Patients in home based palliative care (82, 57% cancer) and control group (569) | All causes | The last 12 months of life | Formal (described patient cases without involvement of informal care) | "HBPC - Part A: inpatient hospital, emergency-room, hospice, home health services ($36,941); Part B - outpatient, medical ($11,599) and Part D – pharmaceutical ($1,134)<br>Control group - Part A: inpatient hospital, emergency-room, hospice, home health services ($45,170); Part B - outpatient, medical ($12,548) and Part D – pharmaceutical ($889)" | The average cost for each patient throughout the last three months of life was $12,000 less with Home-Based Palliative Care (HBPC) compared to standard care ($20,420 vs $32,420; p=0.0002). |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Chiang et al, 2016[29] | Home hospice care group (HH group) and inpatient hospice group (IH group) | 238 patients in home hospice, 330 patients in inpatient hospice | Lung Cancer | The last 1 month of life | Formal | IH group $2,155 – $1,739; HH group $1,385 – $1,370 | Patients in the HH group had much lower mean health care expenses in the final month of their lives compared to those in the IH group (US $1,385.00 – $1,370.00 versus US $2,155.00 – $1,739.00, $p < 0.001$), indicating that the two groups had dramatically different health care costs. |
| Yu et al, 2015[30] | Home death, hospital death | 186 patients | Cancer | The last 6 months of life | Formal and informal | Home death: Total cost ($31,910); Outpatient services cost ($12,103); Hospitalisation cost ($2,111); emergency-room visits cost ($59); Out-of-pocket cost ($1998); Unpaid caregiver time cost ($15,324); Third party cost ($312)<br>Hospital death: Total cost (29,116 $); Outpatient services cost ($7,837); Hospitalisation cost ($7,733); ER visits cost ($156); Out-of-pocket cost ($1,800); Unpaid caregiver time cost ($11,416); Third party cost ($171) | An analysis of end-of-life care expenses by site of passing revealed that patients who passed away at home incurred an average total cost of $37,699.37, while those who perished in hospitals incurred a cost of $29,658.57 (a difference of $8040.80). |
| Dumont et al, 2014[31] | Payments from Public Healthcare system (PHCS), Family (FA), Non-for-profit organizations (NFPO), Others | Eighty-Two palliative care patients and their main informal caregivers | All causes | The last 6 months of life | Formal and informal, at home patients only | PHCS: Total 24,445 CA$ ± 1,073; Daily - 134.3 CA$ ± 5.9<br>FA: Total - 6,754 CA$ ± 267; Daily - 37.1 CA$ ± 1.5<br>NFPO: Total - 454 CA$ ± 12; Daily - 2.5 CA $ ± 0.1<br>Others: Total - 24 CA$ ± 4; Daily - 0.1 CA$ ± 0.0 | When a patient participated in a palliative care programme for a period of six months, the average total cost per patient was $31,678 ± 1,160 Canadian dollars. Inpatient hospital stays were responsible for a significant portion of this expense, which was borne by the Public Health Care System (PHCS). There was a contribution from the patient's family that was less than a fifth of the average total cost for each patient. |
| Chai et al, 2014[32] | Sources of financing the costs of palliative care | 129 caregivers of patients with cancer in palliative care | Cancer | The last 12 months of life | Formal and informal, at home patients only | Monthly costs: The average cost $14,924; the unpaid caregiving costs $11,334; publicly financed healthcare costs $3211; privately financed costs $379. | In the final Twelve months of the patient's life, the mean monthly expenditure amounted to $14,924. The largest component of total palliative care expenses was unpaid caregiving costs, amounting to $11,334, which constituted 77% of the total. Public costs followed at $3,211 (21%) and out-of-pocket expenditures at $379 (2%). |
| Bentur et al, 2014[33] | Home hospice care, without home hospice care | 193 patients | Cancer | The last 6 months of life | Formal | Home hospice care (US$13,648); without home hospice care (US$18,503) | The study's findings showed that patients with metastatic cancer who got home hospice care in addition to regular community care had lower expenditures associated with the final six months of their lives compared to those who only received regular community care. This was the case for patients who received both types of treatment. |

**Abbreviations**: SPC: Specialised Palliative Care; ICER: Incremental Cost-Effectiveness Ratio; QALY: Quality-Adjusted Life Year; HH: Home Hospice; IH: Inpatient Hospice; ER: Emergency-Room; PHCS: Public Healthcare System; FA: Family; NFPO: Non-for-Profit Organizations; BADL: Basic Activities of Daily Living; IADL: Instrumental Activities of Daily Living; HBPC: Home-Based Palliative Care.

**Table 5** Cost Overview for Europe, USA and Asia

| Region | Cost Type | Average Monthly Cost (per Person) | Average Annual Cost (per Person) |
|---|---|---|---|
| Europe | Direct Medical[21–25] | $1,941 | $23,293 |
| | Direct Non-Medical[21,23–25] | $842 | $10,109 |
| | Indirect[24] | $1,241 | $14,898 |
| USA | Direct Medical[28,30,32] | $1,095 | $13,140 |
| | Direct Non-Medical | N/A | N/A |
| | Indirect[30,32] | $1,444 | $17,331 |
| Asia* | Direct Medical[26,29,33] | $2,192 | $26,302 |
| | Direct Non-Medical[26] | $1,162 | $13,947 |
| | Indirect | N/A | N/A |

**Notes**: N/A. Not Available, Currency units were converted to purchasing power parity (Geary-Khamis international dollars). * Data for Asia contains only Taiwan and Israel.

## Costs and Cost Effectiveness of Other Therapies

In terms of the average total treatment cost, home care seems to be a more economically viable alternative to hospital care when comparing various care settings. In comparison to the control group, HC is associated with decreased costs for inpatient hospital, emergency room, hospice, and home health services, indicating the potential cost-saving benefits of home-based care. Regarding end-of-life care, home death incurred a marginally higher expense than hospital death, owing to discrepancies in outpatient services, hospitalisation, emergency room visits, personal funds, unpaid carer time, and third-party charges.

In particular, Halling et al [21] reached the conclusion that a dyadic psychological intervention in conjunction with a rapid transition to specialised palliative care at home resulted in increased expenditures and quality of life, but an ICER of €118,292/QALY. The cost-effectiveness of palliative home-care support was examined by Maetens et al.[22] In the fourteen days preceding death, 8,837 patients who received palliative home care were evaluated. During the final two weeks of life, patients in the unexposed group incurred greater total expenses than those receiving palliative home care assistance, according to the study. Rowland et al [23] investigated the financial and time investments made by 1,504 cancer patients during their final three months of life to provide care. The median quantity of time spent providing care by carers per week was 69 hours and 30 minutes. The median expenditure incurred by those who disclosed it during the final three months of their deceased loved ones was £370. Tur-Sinai et al [26] investigated the out-of-pocket expenses incurred by family members of cancer patients during the final six months of life. This research, which included 491 relatives of cancer patients, discovered that the most frequently incurred costs were food and travel, while medications, private carers, and private nurses incurred extraordinary expenditures. In their study, Kato and Fukuda[27] contrasted hospital and home care for a total of 99 patients and 48 patients in the former. Treatment expenses are substantially reduced by the provision of home care, amounting to a savings of $7,523. In their study, Lustbader et al [28] compared HC to a control group and enrolled in the research for the final Twelve months of life. HC was associated with substantial cost savings per patient, amounting to $12,000. According to the findings of Haltia et al,[24] the average palliative care duration was 179 days. Of the total costs incurred, healthcare expenses comprised 55%, informal care costs 27%, and productivity costs 18%. According to a study by Chiang and Kao,[29] patients who received home hospice care incurred substantially fewer mean healthcare costs in their final month of life compared to those who received inpatient hospice care. A disparity of $8,040.80 was observed between the average total costs incurred by patients who passed away at home and those who perished in hospitals, according to Yu et al.[30] Chai et al[32] reported that unpaid caregiving expenses comprised 77% of total palliative care costs, making them the largest component of such costs. According to the findings of Bentur et al,[33] patients with metastatic cancer who received home hospice care in addition to regular community care incurred fewer expenses during the final six months of life compared to those who received regular community care alone.

In cost studies, it is necessary to carefully compare different contexts. Only two studies compared costs of home vs hospital cost of care whilst simultaneously recording both formal and informal cost of care. In the study of Kato and Fukuda, home care was strongly correlated with a decrease of $7,523 in treatment expenses.[27] That is in contrast to analysis of end-of-life care expenses by site of passing by Yu et al which revealed that patients who passed away at home incurred an higher average total cost of $8040.80 compared to those who perished in hospitals.[30]

Another two studies assessed the same comparison (costs of home vs hospital cost of palliative care), but authors recorded formal costs only. Study by Lustbader et al found that the average cost for each patient throughout the last three months of life was $12,000 less with HC.[28] That's in accordance with study performed by Chiang et al, where patients in the home hospice care group had much lower mean health care expenses in the final month of their lives compared to those in the inpatient hospice group with difference, on average being $569.[29]

The aforementioned findings emphasise the criticality of cost structure and cost efficacy in the development and implementation of palliative care interventions, specifically, those involving pain relief. The implementation of home-based care and resource optimisation has the capacity to generate cost reductions in palliative care settings without compromising the quality of care provided to patients.

## Costs Comparison in the Geographical Context and Different Cost Categories

The cost of palliative care can vary widely, depending on an individual's needs, available health services, and healthcare systems in different countries. A summary of the results is shown in Table 5. All publication data were converted into USD through purchasing power parity conversion rates chosen based on the source publication currency and its publication year (ratio of a purchasing power parity conversion rates were obtained from OECD: https://data.oecd.org/conversion/purchasing-power-parities-ppp.htm. The average direct medical costs are $1,679 per month per person and $20,145 per year. Direct non-medical costs are, on average, $854 per month per person and $10,246 per year. The average indirect cost is $1,343 per month per person and $16,114 per year. Direct medical expenses include the cost of medical services, such as doctor visits, hospital stays, and medication. Direct non-medical costs include the cost of non-medical services, such as transportation, home care, and respite care. Indirect costs include lost productivity and other expenses incurred by patients and their families as a result of palliative care.

Now focusing in detail on the informal cost of care, from the viewpoint of data comparability and overall proportion of informal care cost in the total cost of care, the following group of three studies is of utmost importance, as they analyze both home care and hospital care. Haltia et al reported that informal cost of care in palliative treatment, which lasted an average of 179 days, comprised 27% (5,951 Eur) of the total cost of care for all patient groups.[24] In the study of Aoife Brick et al, performed in three communities, authors found out that informal care in the last three months of life, on average, comprised 15,884 Eur or 34% of the total costs incurred.[25] In the study of Yu et al, focused on the final 6 months of life, informal costs comprised 54% of total costs or $17,322 for the group of patients who died at home vs 45% or $13,216 for patients who died in hospital.[30,31]

The following two studies also focused on both formal and informal costs, but with clear preference to outpatient setting. Dumont et al in their study find out that from the mean total cost per patient in six months of palliative care, 77.2% was assumed by the PHCS (Canada healthcare system) and 21.3% by the family ($6,754 CAD ($5,447 PPP), from which 72.5% was caused by caregiver's time)[31] According to Chai et al, in the final Twelve months of the patient's life, the mean monthly caregiver's expenditure amounted to $14,924 CAD ($12,035 PPP). The largest component of total palliative care expenses was unpaid caregiving costs, amounting to $11,334 CAD ($9,140 PPP), which constituted 77% of the total.[32]

Finally, the last two studies presented only data for the informal care in heterogeneous format. In the study of Bækø Halling et al, informal care cost was estimated to be € 11,338 - € 12,052 ($17,310 – $18,400 PPP), corresponding to 253 h - 269 h of time spent on care per caregiver, in the intervention and control group, respectively, in the 6 months long period.[21] Rowland et al showed that during the last 3 months of life, carers spent a median total of 69 h 30 min each in a typical week on caregiving. On top of that, participants had a median total of £370 ($540 PPP) of out-of-pocket expenditure during those last 3 months of caregiving.[23] When we consider costs in the context of different continents, we observe the following differences:

In our opinion, the most comparable and consistent information is found in the chosen cost groups. When we focus on inpatient care across all studies, the direct medical costs of inpatient care are, on average, $4,397 per month per person and $52,759 per year, ranging from $18,103 to $153,527.[22,23,28] Outpatient direct medical costs are, on average, $1,696 per month per person and $20,355 per year, ranging from $11,599 to $47,782.[18,22,24,30] The average cost of medication was $254 per month per person and $3,048 per year.[23,25,26,28]

The data heterogeneity can also confound final comparison of costs. To evidence heterogeneity, we differentiated first according to (1) costing perspective (formal vs informal), (2) patient disease identification (cancer vs undifferentiated), (3) care mode (inpatient vs outpatient) and (4) by length of data collection period. Some studies can take part in multiple categories, eg if they contain both formal and informal costing perspectives. Observed heterogeneity is considerable as it is visible that finally, we get triplets or doubles of studies where costs should be comparable after accounting for previously mentioned confounding variables. The overview of studies by cost and type of care can be seen in Table 6.

**Table 6** Cost Perspective and Study Distribution

| Cost Perspective | Study | Patient Illness Identification | Study | Care Mode | Study | Length of Monitored Time Period Before Death | Study |
|---|---|---|---|---|---|---|---|
| Formal | [21,22,24,25,27–33] | Cancer | [21,24,27,29,30,33] | Inpatient | [24,27,29,30,33] | 1 month | [29] |
| | | | | | | 6 months | [21,30,33] |
| | | | | | | Not available | [24,27] |
| | | | | Outpatient | [21,24,29,30] | 1 month | [29] |
| | | | | | | 6 months | [21,30] |
| | | | | | | Not available | [24,27] |
| | | Undifferentiated | [22,25,28,31,32] | Inpatient | [25,28,31] | 6 months | [31] |
| | | | | | | 12 months | [25,28] |
| | | | | Outpatient | [22,25,28,31,32] | 14 days | [22] |
| | | | | | | 6 months | [31] |
| | | | | | | 12 months | [25,28,32] |
| Informal | [21–27,30–32] | Cancer | [21,23,24,26,27,30] | Inpatient | [21,24,26,27,30] | 6 months | [21,26,30] |
| | | | | | | Not Available | [24,27] |
| | | | | Outpatient | [21,23,24,26,27,30] | 3 months | [23] |
| | | | | | | 6 months | [21,26,30] |
| | | | | | | Not available | [24,27] |
| | | Undifferentiated | [22,25,31,32] | Inpatient | [25,31] | 6 months | [31] |
| | | | | | | 12 months | [25] |
| | | | | Outpatient | [22,25,31,32] | 14 days | [22] |
| | | | | | | 6 months | [31] |
| | | | | | | 12 months | [25,32] |

**Notes**: N/A. Not Available, Currency units were converted to purchasing power parity (Geary-Khamis international dollars). * Data for Asia contains only Taiwan and Israel.

## Discussion

Treatment for cancer pain is mostly pharmacological and delivered through home-based palliative care services. However, the cost-effectiveness of these and other interventions remains unclear. Limited healthcare resources make it essential to evaluate resource utilisation. This study compares treatment modalities, their impact on QoL, and the related costs of treatment and care. The cost aspect of palliative care is an essential factor to consider when planning and delivering interventions, not only from a public health perspective but also from patients' and caregivers' perspectives. The analysis of the cost structure revealed variations in healthcare costs, informal care expenses, and productivity costs, with unpaid caregiving costs representing a sizable proportion of the overall expenses. In Europe, direct medical costs are on average $1,941 per month per person (PPP); direct non-medical costs are on average $842 PPP; and indirect costs are on average $1,241 PPP per month per person. In the USA, direct medical costs are, on average, $1,095 and indirect costs are, on average, $1,444. Finally, in Asia, direct medical costs are on average $2,192 PPP, and direct non-medical costs are $1,162 PPP per month per person. Home-based palliative care has been found to boost patient satisfaction with care, decrease hospital visits, and improve patient comfort and QoL, particularly for those with terminal illnesses.[34–37] Also, it has been shown to be more cost-effective than hospital care, suggesting the potential cost-saving advantages of home-based interventions. From the data collected on QoL and costs, comparable findings to those from other reviews or cohort studies were confirmed. A study by Gardiner et al [38] presented a review of evidence on the cost of palliative care in the UK. The total cost of palliative care for three months ranged from £4140 - £12,444 in the UK. The range was influenced by the type of illness and the need for informal care. Informal care services arose in 2017, costing between £3,396 and £8926. Yadav et al [39] corroborated our results, indicating that palliative care decreased healthcare expenditures by the following amounts: $1285–$20,719 for inpatient palliative care, $1000-$5198 for outpatient and inpatient palliative care combined, $4258 for home-based palliative care, and $117–$400 per day for home/hospice and combined outpatient/inpatient palliative care. Furthermore, Gordon et al [40] demonstrated that home-based palliative care for adults, provided by a population of multiple vendors (encompassing various insurance product lines), effectively reduces annual total medical costs by 16.7% when compared to a control group. Gross savings for participants with a duration of 6–12 months (17.9%) exceeded those with a duration of 1–5 months (15.8%). Isenberg et al [41] concluded that individuals who underwent home-based palliative care during their final three months of life exhibited a reduced likelihood of dying in acute care and incurred a lower estimated total healthcare cost in comparison to those who did not receive home care services. Nurse practitioner palliative care visits had the most significant impact on reducing the incidence of fatalities in acute care. The ICER determined that fewer hospital mortality occurs for every $0.25 invested in home-based palliative care, when costs and benefits are considered in tandem. Notwithstanding the inconsistent findings pertaining to expenses, it is possible to assert that the projected costs of palliative care have exhibited a degree of stability in recent times.

Many aspects influence the results of the studies reviewed. Regional differences in healthcare systems significantly impact the applicability and generalizability of the findings. Developed countries often possess well-established healthcare infrastructures, enabling comprehensive services such as home-based and inpatient palliative care, while developing countries may lack such infrastructure, limiting accessibility. Cost structures for palliative care also vary significantly across regions, influenced by the costs of medical services, availability of informal care, and economic policies. Direct medical costs include expenses for doctor visits, hospital stays, and medication, which can differ greatly due to varying healthcare pricing and insurance coverage. Direct non-medical costs, such as transportation and home care, can be substantial in some regions due to logistical challenges and the need for specialized services. Indirect costs, covering lost productivity and other expenses incurred by patients and families, can be significant, especially where social support systems are weak.

Despite this considerable variation, which can be attributed to the nature of the care rendered, palliative care seems to generate overall cost savings for the healthcare system. Among recommendations for policy implications may be included reallocating resources from expensive inpatient care to HBPC programs, maximizing limited healthcare budgets, especially in resource-constrained regions. Developing funding models that support HBPC, such as adjusting insurance reimbursement policies and directing government grants towards HBPC programs, can incentivize the adoption of home-based care practices. Improvements in quality of life (QoL) for patients receiving HBPC highlight the need for policies that prioritize patient-centered care models, integrating patient and family feedback to ensure responsiveness to their needs and preferences. Funding models, patient-centered care, and training for caregivers are also crucial, Technological advancements like telehealth and remote monitoring tools can be integrated into HBPC, and standardizing data collection can improve care coordination. Public policy should promote the integration of these technologies by providing funding for adoption and training for healthcare professionals. Addressing barriers like socioeconomic disparities and integrating HBPC into universal health coverage schemes can ensure equitable access to high-quality palliative care. Continuous research and quality metrics can drive continuous improvement in HBPC services, benefiting patients and their families.

## Study Limitations

Several limitations affect the generalizability of findings, including data heterogeneity, incomplete geographical coverage, and issues with currency conversion and inflation.

Notwithstanding the diligent pursuit of attaining the most pertinent and comparable outcomes feasible, this research does possess certain constraints. In the domain of health-related QoL measures, there is considerable heterogeneity in the outcome measures of selected studies. Three studies use BPI, three studies use QLQ-C15-PAL or QLQ-C30-PAL (2 instances) with only one study using SF-36. This makes study results directly uncomparable in many cases.

As stated previously, the second limitation of the studies is data heterogeneity. While some studies present aggregate measures (eg, direct and indirect costs), others present disaggregated items (eg, pharmaceutical costs and informal care cost estimates). Only the study by Kato et al explicitly states use of opioids and their costs related to treatment.[27] As a result, we were unable to combine costs for some studies into a single aggregate estimation of the total expense that results from palliative care. Another limitation of this study is cost data comparability. The first problem connected to this is the lack of a clear and well-defined standard of care in the countries included in our study. Additionally, Bentur et al did not report how the local currency was converted to dollars, and consequently, we could not apply currency conversion based on purchasing power parity to USD.[33] Many studies collected data long before publication[21,29] which is problematic because of the ongoing inflation process that makes it difficult to account for it in the aforementioned studies. Fortunately, the decade before 2020 was marked by steady inflation in the targets of most of the central banks; therefore, it should not be a major confounding factor. These factors limit the usefulness of our findings from the perspective of policymakers. Furthermore, the studies included in this review failed to cover some of the most populous and developed countries in the EU, such as France, Germany, and Spain.

## Conclusion

Home-based palliative care is successful in lowering hospital admissions, while evidence of its influence on patients quality of life is currently sparse with conflicts regarding the superiority of its outcomes.

The analysis of cost structures highlighted variations in healthcare, informal care, and productivity costs, with unpaid caregiving expenses comprising a sizable portion of the overall financial burden. Home-based palliative care has demonstrated cost-saving advantages in specific cases, indicating the potential benefits of optimising resources and prioritising cost-effectiveness in palliative care delivery.

Future research should focus on a deeper comparison of different models of home-based palliative care according to the type of cancer, stage of disease, social and cultural contexts, and availability of resources. Special attention should be paid to the development and testing of new tools and technologies to support home-based palliative cares, such as mobile applications, telemedicine, virtual reality, and robotics. Furthermore, conduct long-term studies to evaluate the sustainability and long-term economic benefits of home-based palliative care compared to traditional hospital-based care. Finally, attention to barriers and challenges for providing home-based palliative care, such as ethical issues, is important, as these findings may bring more savings for society and improve the QoL of patients and caregivers.

These results support evidence-based decision-making regarding patient care, appropriate tools, and interventions to provide effective pain relief, enhance patients' QoL, and ensure cost-efficient palliative care.

## Data Sharing Statement

All data are provided within this manuscript.

## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

The authors have no competing interests to declare that are relevant to the content of this article.

## References

1. The University of Texas MD Anderson Cancer Center Cancer Pain Management. Available from: https://www.mdanderson.org/patients-family/diagnosis-treatment/emotional-physical-effects/cancer-pain-management.html. Accessed 27, June 2024.
2. Nickolich MS, El-Jawahri A, Temel JS, LeBlanc TW. Discussing the Evidence for Upstream Palliative Care in Improving Outcomes in Advanced Cancer. *Am Soc Clin Oncol Educ Book*. 2016:e534–e538. doi:10.1200/EDBK_159224
3. Global Atlas of Palliative Care at the End of Life; Connor, S.R, Bermedo, M.C.S, Eds.; Worldwide Palliative Care Alliance: London, 2014; ISBN 978-0-9928277-0-0.
4. Tay RY, Choo RWK, Ong WY, Hum AYM. Predictors of the Final Place of Care of Patients with Advanced Cancer Receiving Integrated Home-Based Palliative Care: a Retrospective Cohort Study. *BMC Palliat Care*. 2021;20:164. doi:10.1186/s12904-021-00865-5
5. Page R, Blanchard E. Opioids and Cancer Pain: patients' Needs and Access Challenges. *J Oncol Pract*. 2019;15(5):229–231. doi:10.1200/JOP.19.00081
6. Smith S, Brick A, O'Hara S, Normand C. Evidence on the Cost and Cost-Effectiveness of Palliative Care: a Literature Review. *Palliat Med*. 2014;28(2):130–150. doi:10.1177/0269216313493466
7. Moher D, Liberati A, Tetzlaff J, Altman DG. The PRISMA Group Preferred Reporting Items for Systematic Reviews and Meta-Analyses: the PRISMA Statement. *PLoS Med*. 2009;6(7):e1000097. doi:10.1371/journal.pmed.1000097
8. Leung XY, Sun J, Bai B. Bibliometrics of Social Media Research: a Co-Citation and Co-Word Analysis. *Int J Hosp Manag*. 2017;66:35–45. doi:10.1016/j.ijhm.2017.06.012
9. Zdun-Ryżewska A, Chojnacka-Szawłowska G, Basiński K, Leppert W, Majkowicz M. Cognitive and Emotional Representations of Pain in Cancer Patients at an Inpatient Unit and Home Palliative Care. *Curr Probl Cancer*. 2019;43(6):100464. doi:10.1016/j.currproblcancer.2019.01.005
10. Swarm RA, Paice JA, Anghelescu DL, et al. Adult Cancer Pain, Version 3.2019, NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Canc Netw*. 2019;17(8):977–1007. doi:10.6004/jnccn.2019.0038
11. Husereau D, Drummond M, Augustovski F, et al. Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022) Statement: updated Reporting Guidance for Health Economic Evaluations. *BMC Med*. 2022;20(1):23. doi:10.1186/s12916-021-02204-0
12. Fischer C, Bednarz D, Simon J. Methodological Challenges and Potential Solutions for Economic Evaluations of Palliative and End-of-Life Care: a Systematic Review. *Palliat Med*. 2024;38(1):85–99. doi:10.1177/02692163231214124
13. Piotrowska W, Leppert W, Majkowicz M. Comparison of Analgesia, Adverse Effects, and Quality of Life in Cancer Patients during Treatment of Procedural Pain with Intravenous Morphine, Fentanyl Nasal Spray, and Fentanyl Buccal Tablets. *Cancer Manag Res*. 2019;11:1587–1600. doi:10.2147/CMAR.S179012
14. Nosek K, Leppert W, Nosek H, Wordliczek J, Onichimowski D. A Comparison of Oral Controlled-Release Morphine and Oxycodone with Transdermal Formulations of Buprenorphine and Fentanyl in the Treatment of Severe Pain in Cancer Patients. *Drug Des Devel Ther*. 2017;11:2409–2419. doi:10.2147/DDDT.S141007
15. Cortesi PA, D'Angiolella LS, Vellucci R, et al. Cost-Effectiveness Analysis of Oral Fentanyl Formulations for Breakthrough Cancer Pain Treatment. *PLoS One*. 2017;12(6):e0179523. doi:10.1371/journal.pone.0179523
16. Delibegovic A, Sinanovic O, Galic G, Sabic A, Sabic D. The Influence of Palliative Care on Quality of Life in Patients with Lung Cancer. *Mater Socio Medica*. 2016;28(6):420. doi:10.5455/msm.2016.28.420-423
17. Ruggeri M, Turriziani A, Oradei M. Cost-Effectiveness Analysis of Transnasal Fentanyl Citrate for the Treatment of Breakthrough Cancer Pain. *Expert Rev Pharmacoecon Outcomes Res*. 2014;14(3):459–464. doi:10.1586/14737167.2014.904750
18. Leppert W, Zdun-Ryzewska A, Forycka M, Mess E, Majkowicz M. Quality of Life Assessment in Advanced Cancer Patients Treated at Home, an Inpatient Unit, and a Day Care Center. *Oncol Targets Ther*. 2014;687. doi:10.2147/OTT.S57338
19. Götze H, Brähler E, Gansera L, Polze N, Köhler N. Psychological Distress and Quality of Life of Palliative Cancer Patients and Their Caring Relatives during Home Care. *Support Care Cancer*. 2014;22(10):2775–2782. doi:10.1007/s00520-014-2257-5
20. Leppert W, Turska A, Majkowicz M, Dziegielewska S, Pankiewicz P, Mess E. Quality of Life in Patients With Advanced Lung Cancer Treated at Home and at a Palliative Care Unit. *Am J Hosp Palliat Med*. 2012;29(5):379–387. doi:10.1177/1049909111426135

21. Halling CMB, Wolf RT, Sjøgren P, et al. Cost-Effectiveness Analysis of Systematic Fast-Track Transition from Oncological Treatment to Specialised Palliative Care at Home for Patients and Their Caregivers: the DOMUS Trial. *BMC Palliat Care*. 2020;19(1):142. doi:10.1186/s12904-020-00645-7
22. Maetens A, Beernaert K, De Schreye R, et al. Impact of Palliative Home Care Support on the Quality and Costs of Care at the End of Life: a Population-Level Matched Cohort Study. *BMJ Open*. 2019;9(1):e025180. doi:10.1136/bmjopen-2018-025180
23. Rowland C, Hanratty B, Pilling M, van den Berg B, Grande G. The Contributions of Family Care-Givers at End of Life: a National Post-Bereavement Census Survey of Cancer Carers' Hours of Care and Expenditures. *Palliat Med*. 2017;31(4):346–355. doi:10.1177/0269216317690479
24. Haltia O, Färkkilä N, Roine RP, et al. The Indirect Costs of Palliative Care in End-Stage Cancer: a Real-Life Longitudinal Register- and Questionnaire-Based Study. *Palliat Med*. 2018;32(2):493–499. doi:10.1177/0269216317729789
25. Brick A, Smith S, Normand C, et al. Costs of Formal and Informal Care in the Last Year of Life for Patients in Receipt of Specialist Palliative Care. *Palliat Med*. 2017;31(4):356–368. doi:10.1177/0269216316686277
26. Tur-Sinai A, Urban D, Azoulay D, Bar-Sela G, Bentur N. Understanding Out-of-Pocket Spending and Financial Hardship among Patients Who Succumb to Cancer and Their Caregivers. *Isr J Health Policy Res*. 2022;11(1):1. doi:10.1186/s13584-021-00511-8
27. Kato K, Fukuda H. Comparative Economic Evaluation of Home-based and Hospital-based Palliative Care for Terminal Cancer Patients. *Geriatr Gerontol Int*. 2017;17(11):2247–2254. doi:10.1111/ggi.12977
28. Lustbader D, Mudra M, Romano C, et al. The Impact of a Home-Based Palliative Care Program in an Accountable Care Organization. *J Palliat Med*. 2017;20(1):23–28. doi:10.1089/jpm.2016.0265
29. Chiang J-K, Kao Y-H. Impact of Home Hospice Care on Patients with Advanced Lung Cancer: a Longitudinal Population-Based Study in Taiwan. *J Palliat Med*. 2016;19(4):380–386. doi:10.1089/jpm.2015.0278
30. Yu M, Guerriere DN, Coyte PC. Societal Costs of Home and Hospital End-of-Life Care for Palliative Care Patients in Ontario, Canada. *Health Soc Care Community*. 2015;23(6):605–618. doi:10.1111/hsc.12170
31. Dumont S, Jacobs P, Turcotte V, Turcotte S, Johnston G. Distribution and Sharing of Palliative Care Costs in Rural Areas of Canada. *J Palliat Care*. 2014;30(2):90–98. doi:10.1177/082585971403000204
32. Chai H, Guerriere DN, Zagorski B, Coyte PC. The Magnitude, Share and Determinants of Unpaid Care Costs for Home-Based Palliative Care Service Provision in Toronto, Canada. *Health Soc Care Community*. 2014;22:30–39. doi:10.1111/hsc.12058
33. Bentur N, Resnizky S, Balicer R, Eilat-Tsanani T. Utilization and Cost of Services in the Last 6 Months of Life of Patients With Cancer - With and Without Home Hospice Care. *Am J Hosp Palliat Med*. 2014;31:723–725. doi:10.1177/1049909113499604
34. Curiale V, Cella A, Luzzani M, Prete C. Home-Based Palliative Care for Adults with Cancer. In: *Cochrane Database of Systematic Reviews; the Cochrane Collaboration*. Chichester, UK: John Wiley & Sons, Ltd; 2007:CD006510.
35. Kahveci K, Koç O, Aksakal H. Home-Based Palliative Care. *Bezmialem Sci*. 2020;8(1):73–80. doi:10.14235/bas.galenos.2019.3208
36. Kerr CW, Donohue KA, Tangeman JC, et al. Cost Savings and Enhanced Hospice Enrollment with a Home-Based Palliative Care Program Implemented as a Hospice–Private Payer Partnership. *J Palliat Med*. 2014;17(12):1328–1335. doi:10.1089/jpm.2014.0184
37. Klinger CA, Howell D, Marshall D, Zakus D, Brazil K, Deber RB. Resource Utilization and Cost Analyses of Home-Based Palliative Care Service Provision: the Niagara West End-of-Life Shared-Care Project. *Palliat Med*. 2013;27(2):115–122. doi:10.1177/0269216311433475
38. Gardiner C, Ryan T, Gott M. What Is the Cost of Palliative Care in the UK? A Systematic Review. *BMJ Sup Palliat Care*. 2018;8(3):250–257. doi:10.1136/bmjspcare-2018-001519
39. Yadav S, Heller IW, Schaefer N, et al. The Health Care Cost of Palliative Care for Cancer Patients: a Systematic Review. *Support Care Cancer*. 2020;28(10):4561–4573. doi:10.1007/s00520-020-05512-y
40. Gordon MJ, Le T, Lee EW, Gao A. Home Palliative Care Savings. *J Palliat Med*. 2021;2021:0142. doi:10.1089/jpm.2021.0142
41. Isenberg S, Hsu A, Spruin S, et al. Evaluating the Impact and Costs of Home-Based Palliative Care at the System Level (FR420C). *J Pain Symptom Manage*. 2019;57(2):410. doi:10.1016/j.jpainsymman.2018.12.122