Effects of Pediatric Palliative Care Programs for Children with Life-Threatening Conditions in Healthcare Resources Utilization and Costs: a Systematic Review of Comparative Studies

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Abstract

Background: Pediatric palliative care programs (PPCP) include holistic approaches to care for children with life-threatening conditions (LTC), with a focus on enhancing quality of life and supporting families. Program planning requires information on the impact of PPCPs on costs and resource utilization. Yet, this critically important field of healthcare is vastly understudied. We aimed to synthesize information on those outcomes to support informed decision-making around resource allocation.

Methods: A systematic review of the literature was undertaken. Outcomes of interest included hospital admissions, length of stay (LOS), and healthcare costs.

Results: The search produced 5,193 references, 109 were full-text reviewed and 11 articles were included. No randomized clinical trials were found. We observed mixed results of the effect of PPCPs on all outcomes. Four studies found decreases in the proportion of children admitted to hospital, rates of planned hospital admissions, and admission rates to critical care. Yet, five studies found either an increase or no difference in this outcome. When observing LOS, five studies reported an associated decrease, without investigating number of days spent in other facilities. A sole study with a broader measure of inpatient days found an increase in total LOS, demonstrating a shift in the setting of healthcare utilization. Four articles demonstrated an associated decrease in cost. However, the shift in healthcare setting was not accounted for. Two studies considered a broader perspective and found conflicting results.

Conclusions: Evidence suggests PPCPs decrease resource use. The considerable heterogeneity in outcome measurement was a key challenge of this review.

Background

Pediatric palliative care (PPC) can be summarized as "an active and total approach to care throughout the disease trajectory and beyond, embracing the multidimensionality of care for children and families providing physical, emotional, social and spiritual elements such as symptom management, respite for caregivers, and bereavement. It focuses on the enhancement of quality of life for the children with life-threatening conditions (LTC) and support for the family"[1]. LTCs can be defined as childhood conditions where there is no established cure, or where the available treatment has not succeeded, and survival into full adulthood is unlikely. Complex care plans and fluctuating patient needs necessitate a coordination of care within individualized support systems. Children requiring, but not enrolled in, a PPC program (PPCP) often access healthcare through uncoordinated acute care admissions, potentially compromising the continuity care and lacking critical components for family support.

PPC is a young and evolving field, and varies from adult palliative care in important respects, for instance, from a resource utilization perspective, PPC is usually delivered over a longer time frame[2]. It is unclear how the enrollment in a PPCP affects healthcare utilization and costs compared to those who rely exclusively on hospital care. There is interest in understanding these outcomes, as PPCPs may deliver services to this population more efficiently by coordinating various settings of health systems and home care, rather than relying solely on tertiary care. In order to support evidence-based PPCP planning and resource allocation, we undertook a systematic review of the published literature that compares inpatient healthcare resource utilization and costs between children with LTCs who have and have not accessed a PPCP.

Methods

Inclusion Criteria

This systematic review was performed according to PRISMA guidelines[3]. As ethical concerns surround the randomization of children to different approaches of care in Randomized Control Trials (RCTs), the inclusion criteria for studies included all types of comparative studies (experimental or observational studies, and secondary administrative databases analysis), regardless of length of follow up. Only studies that exclusively included children, up to 22 years old, with LTC were considered. Any study including a comprehensive PPCP or its components such as respite care, end-of-life (EOL) care or planning, hospice, community-based palliative care was eligible for inclusion.

Outcomes were chosen based on previous work in the adult literature that identified potential quality of end-of-life indicators that can be measured using administrative data.[4] Our primary outcomes of interest were: healthcare resource utilization including admissions and length of stay (LOS); and health care costs (direct, indirect and total expenditures). Secondary outcomes of interest include resource utilization in the last admission before death, measured by length

of the last hospitalization before death; number of invasive procedures to prolong life in the last admission; and number of resuscitative attempts.

Data sources and study selection

The search was applied to Medline, Embase, CINAHL and LILACS. For feasibility, and given the relatively recent development of PPCP, the search was limited to articles published from 2000 onwards. The search was completed on July 18th, 2013, with weekly-automated alerts for publications after this date. No language limitations were applied. Studies were identified by searching electronic databases, scanning reference lists, and consulting experts. In addition, a grey literature search was undertaken, targeting websites of specialized groups and societies in PC and hospice services. These search strategies are available in Appendix A. Two researchers conducted reviews independently. Discrepancies were discussed, or if required, consulted with an additional reviewer with clinical expertise in PC medicine.

Data extraction, analysis, and quality assessment

Bias was also assessed independently by the reviewers using the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions[5]. Discrepancies were handled in the same manner as study identification (details in Appendix B). Studies were displayed in tables, exploring each study's approach to program evaluation due to extensive heterogeneity to perform meta-analysis.

Results

Study selection

The search strategy retrieved 5,193 references, with 109 reviewed at the full-text level, with 9 meeting the inclusion criteria (Figure 1)[6–14]. Articles were excluded for the following reasons: 44 either did not exclusively constitute children, or did not evaluate any of the outcomes of interest; 42 only provided background information on PPCPs with no evaluation undertaken; and 10 contained only descriptive data from cohorts receiving PC with no comparison groups. Four studies were excluded during data extraction: 2 were descriptive analyses of a single cohort under a PPCP, 1 was a matched case-control study with adults as controls, and 1 compared groups with and without Do Not Resuscitate (DNR) orders (not a proxy for being in a PPCP). No RCTs were found. Two additional eligible studies were included after the initial search through the weekly-automated updates[15,16].

Study characteristics

Eleven retrospective observational studies were included. A meta-analysis was not feasible due to considerable heterogeneity in study populations, outcome measures, follow-up times and reporting of program components. Descriptive characteristics are presented in Tables 1.

Four cohort comparisons[7,8,11,12] used administrative data and survey techniques[11] to explore differences between cohorts of children with and without access to PPCP. Follow-up periods varied from the last day of admission before death to the period from referral to a PPC program to death. Two articles included only children who died of cancer[7,11] and two included children who died from any cause[8,12]. The interventions by which children were classified as being in the PPC group included: use of a hospice provider[7,12], billing for PC consultation[8] , or planned location of death (LOD)[11]. Three studies were based in the United States (US)[8,11,12], one in the United Kingdom (UK) [7].

Four pre-post studies[6,9,10,15] used administrative data[9,15] and chart reviews[6,10] to explore differences in outcomes before and after access to PPCP. Three studies compared outcomes within the same group of patients pre and post PPCP enrollment, and included children with all LTCs[9,10,15]. The other compared historical cohorts of children with brain tumors pre and post implementation of a standardized program for EOL care[6]. This article could be classified as a historical cohort comparison, with the intervention being the coordination of care, as children had access to hospice providers in both periods but without the standardization of a PC implemented care plan. Follow-up in all four studies varied from 12 months to 10 years. Determining the time point at which children entered the program was based on hospice use[10], explicit enrollment in the program[9,15], or date of program implementation[6]. Three were from the US[6,9,15] and one from Canada[10].

One published article classified as 'case-control' by the authors was actually a cohort comparison[14]. This US study relied on administrative data to compare children enrolled in a PPCP with those who were not, six-months prior to death.

One conference abstract [16] was a cohort comparison combined with a pre-post analysis in the group who received PPC. This study was based on an administrative database in the US, and identified those in the PPC group by the presence of a PPC consultation, with a 2-year follow-up.

The last article was a case-series[13] from the US that compared procedure costs carried out in a home based PPCP to those performed in hospital and included only three patients who were cared for one day.

Effects of pediatric palliative care programs on outcomes of interest

Table 2 presents a visual summary of the results from published articles and presented abstracts.

Seven articles investigated admissions[6–8,10,11,15,16], with results summarized in Table 3. An additional six studies investigated the influence of PPC on number of inpatient days or length of stay (LOS) [6,9–11,14,15] , the results are summarized in Table 4. Seven studies measured the

influence of PPC on healthcare costs[8–10,12–16] , we show the results in Table 5. It is important to mention that it is unclear whether costs of healthcare differ when studies refer to them as charges, expenditures or costs. Only one study compared LOS in the last admission before death[8]. The authors reported a shorter median LOS in the last admission before death among children who died from any cause of death and had access to PC services (PC group: 17 days [IQR 9–36] vs. No PC code: 21 days [10–47], p<0.001).

Invasive procedures to prolong life during last admission

Two cohort studies observed invasive procedures in the last admission before death. The first[8] demonstrated that among children who died from any cause, those with a PC consultation had a significantly lower relative risk of receiving certain procedures than those who did not. This included invasive mechanical ventilation (RR 0.14, 95% CI 0.12–0.16), adrenergics (RR 0.15, 95% CI 0.11–0.2), sedatives (RR 0.25, 95% CI 0.2–0.3) and analgesics (RR 0.53, 95% CI 0.47–0.6). These children also had a higher probability of accessing noninvasive mechanical ventilation (RR 1.6, 95% CI 1.3–1.9), and intracranial pressure monitoring or extra ventricular device (RR 2.8, 95% CI1.6–5.0). The second study[11] reported a lower proportion of intubations in the final 24 hours of life (21% vs. 48%, p= 0.029), and no difference in the proportion of withdrawal of other support measures (36% vs. 19%, p= 0.123) among cancer patients with planned LOD compared to those without one.

Resuscitation attempts

Two cohort studies examined resuscitation interventions. The first[8] showed that among all causes of death, those who had a PC consultation had a significantly lower relative risk of cardioversion (RR 0.49, 95% CI 0.38–0.62) than those who did not. The second[11] reported a lower proportion of cardiopulmonary resuscitation attempts (CPR) among cancer patients with a planned LOD (4% vs. 19%, p = 0.142) compared to those without.

Risk of bias

To assess risk of bias we adapted an instrument from the Cochrane Handbook Chapter on non-randomized studies[5] describing features of studies that may increase risk of bias. The visual summary is described in Table 6. Overall, studies were classified as having a moderate and high risk of bias due to their observational design and the nature of the intervention.

Observational studies rely on secondary analysis of administrative databases and medical reports not collected for research purposes. Consequently, they may be incomplete or representative of only one perspective (may not include all aspects of healthcare related costs, e.g. out of pocket expenses, drugs/procedures/uninsured admissions, alternative therapies, or full records of admissions across providers). Access to certain content may be limited (clinical outcomes and severity of disease may not be pre-defined in records) and may not apply to the general population (selection bias from insurance coverage/eligibility).

Furthermore, PPCP enrollment often requires referral by a healthcare professional. Following this, families must accept enrollment and consent to focusing treatment on enhancing quality of life, not often carried along with curative treatments. This may cause groups to be systematically different, and create a natural imbalance between children in a PPCP and those under usual care, invariably affecting cost and utilization. Given the often intensive and invasive curative treatments in this population, we would expect this bias to cause usual care to be more resource consuming and costly.

Information bias may have affected the allocation of patients to intervention groups for those who were defined as "recipients" of palliation through claims, bills or service codes. As PPC is a relatively new and evolving specialty, the mode of recording PPC services may have changed overtime. Consequently, utilization of PC services could have been underreported or reported differently from usual care, for while procedures and practitioners are comparable, the goals of care vary (curative vs. enhancement of quality of life). Further, practitioners in both PPCP and usual care may provide either type of care to children in both groups (e.g. increasing curative efforts for children in a PPCP or focusing on palliative care for those in usual care).

Only two articles addressed confounding in the outcome comparison between groups [7,15]. One cohort comparison [7] investigated the effect in number of hospital admissions in a PPC cohort in a pediatric hospice from time of referral to death. Age, disease, gender and deprivation category were controlled for, however, the authors did not address survival bias (whether the length of the study period was similar between groups). They further failed to include number of hospice admissions for the PPC group. Therefore, number of admissions for this group must be interpreted with caution due to shifts in admission setting rather than decreases in healthcare utilization. One pre-post study[15] addressed confounding by controlling for time exposed to the PPCP, but did not include a control group for comparison, making it unclear whether the observed decrease in LOS and costs observed in the PPC period is a consequence of PPCPs or a natural trend among patients approaching death. Additionally, place of death and costs associated with home care were not controlled for, both of which can bias results. The remaining studies did not address confounding. Appendix B describes additional features that could potentially bias results.

Interpretation

With respect to the effect of PPCPs on hospital admissions**,** we observed mixed results**.** Three studies found a decreased association in the proportion of children admitted to hospital[6,11] and NICU[16], with lower rates of planned hospital admissions[7], and decreased admission rates to critical care[8]. Conversely, four studies found no difference in number of hospital admissions[7,15] either in the proportion of children or number of visits to the emergency department[7,38], with one finding a greater proportion of children admitted to PICU[16]. On balance, it is likely reasonable to conclude that PPCPs decrease both healthcare utilization and costs.

However, there are a number of challenges with this literature that mitigate the strength of this overall conclusion. For example, Keele et al [8] included only included children who died at least 5 days after admission, therefore excluding individuals who did not choose life-extending measures to prolong their stay beyond 5 days, or those who discharged to die at home. This definition would affect both hospital admissions and costs, leaving the true difference between programs to be greater. Further, the PPC children were allocated based on billing codes by the ICD code for palliative care (V66.7). If the service was billed under the ICD code for the primary condition or disease, it would misclassify children under PPC to the usual care group. The direction and magnitude of this bias is uncertain. As well, Fraser et al[7] did not measure and/or control whether children were still in disease-directed treatment in both groups - a factor for decreased planned admissions. Also, it is not clear whether symptom management admissions to the hospice were included in the overall number of admissions, making it unclear whether the results represent a shift in healthcare setting or a decrease in resource utilization. In addition, Smith et al's[16] conference abstract did not present sufficient information on methodology. Therefore, questions remain regarding risk of bias, selection and identification of participants, and intervention classification. Most studies focused on hospital admissions and did not account for different types of inpatients utilization (hospice, home care, other facilities).

Examining the effect of PPCP on LOS presented mixed results. Most articles found an associated decrease in LOS (per hospital admission[6], per patient[6], per patient month[9], mean LOS in 6 months[14], or conditional to non-cancer patients exposed to the program over 6 months [15]). However they did not investigate the number of days spent in hospice or other facilities, which again does not clarify whether a decrease in resource utilization or a shift in healthcare setting occurred. One study found no difference in median LOS in the last month of life[11]. The only study that measured both hospital and hospice admissions found an increase in the total combined LOS, demonstrating a shift in the setting of healthcare utilization[10].

We would expect changes in admissions and LOS to influence healthcare costs. However, the overall influence of a PPCP on cost was mixed. Most articles found an associated decrease (daily charge in the last admission[8]; healthcare expenditures per month [9,10]; cost of procedures out of hospital setting [13]; conditional to non-cancer patients exposed to the program over 6 months [15]). Yet only three studies considered a broader perspective to assess inpatient costs. The Canadian study[10] found that despite the increase of inpatient days per month, a shift in healthcare setting from hospital to hospice resulted in a significant decrease in monthly costs, owing to the difference in average daily costs between settings. Conversely, a study carried out in the US[12] showed that hospice users had higher expenditures in all types of admissions (hospice, inpatient, outpatient, emergency department) and pharmacy expenses. This study allocated patients to the PC group based on billing codes for hospice services. However, some patients in the non-hospice user group died at the hospice, demonstrating the limitation of using billings to identify patients. The third study[9] demonstrated a shift for those using PPC in resource utilization from inpatient to outpatient care and pharmaceutical costs, but with an 11% overall decrease after the implementation of the community based PPCP. However, this study did not test for statistical significance or adjust for survival time after program enrollment.

Two studies found mixed results in hospital cost differences between PPC users and non users[15,16], with no increase in daily cost after the initial PPC consultation.[16] Belasco et al[13] observed children referred to a home based PPCP and compared cost of equivalent care in home care to the hospital. The authors listed the procedures/services received at home and estimated the equivalent cost at the tertiary care centre. Costs were discrepant, however, for home care, uninsured procedures were not accounted for in cost estimates. It is unclear whether those costs were out-of-pocket for the families or waived by the healthcare providers. Therefore, charges do not appropriately reflect costs, introducing important measurement bias.

Limitations and Strengths of the study

We have performed a thorough search of the literature without any language restrictions. Despite this, we were not able to identify any RCTs or prospective studies in this field. We included only comparative studies of palliative care against usual care. No indirect comparison was contemplated with single-arm observational studies. The overall quality of evidence is very low. In particular, the risk of selection bias to PPCP given the nature of the referral process is a major concern. Furthermore, information bias and misclassification is a threat to internal validity in observational studies based on secondary databases. It is worth noting the considerable heterogeneity in outcome measures, follow-up times, reporting of program components, and whether reported interventions accurately represent the enrollment of children and families in a PPCP. Moreover, the specific context, policies and procedures for the different health systems might affect results. Therefore, both the evidence and its applicability should be interpreted with caution. This is the first systematic review on this topic and has highlighted numerous challenges with this literature that clearly need to be addressed in order to provide definitive conclusions. While the general interpretation of results tends to show PPCPs to be cost and resource saving, more rigorous study designs taking a broader perspective including expected costs incurred in other settings should be undertaken. Focusing solely on hospital admissions has limitations, and does not consider impact on the healthcare system in totality. Further, the financial burden borne by families is unknown.

Conclusion

There is currently low quality evidence to support the planning and reallocation of resources for PPC services and its impact on the overall healthcare system. PPC programs may positively affect hospital admissions, LOS and costs, however, a paucity of evidence with broad approaches to measurement are not only in conflict, but are very context dependent. We require prospective studies to evaluate the overall impact of PPCPs on the health system from perspectives beyond that of the tertiary care provider, and measure shifts in healthcare settings and family burden. Enhanced study designs can address the various aforementioned biases and classification issues. Standardization of outcome measures can enhance comparability and pooling of future research for increased power to better evaluate impact. Noting these limitations, this study provides an important first step towards a more comprehensive

understanding of the impact of PPC programs on healthcare resource utilization in different settings, and a proxy for quality of end-of-life care for children and families.

Funding and affiliations

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Figures and Tables

Figure 1: Flow diagram of study selection

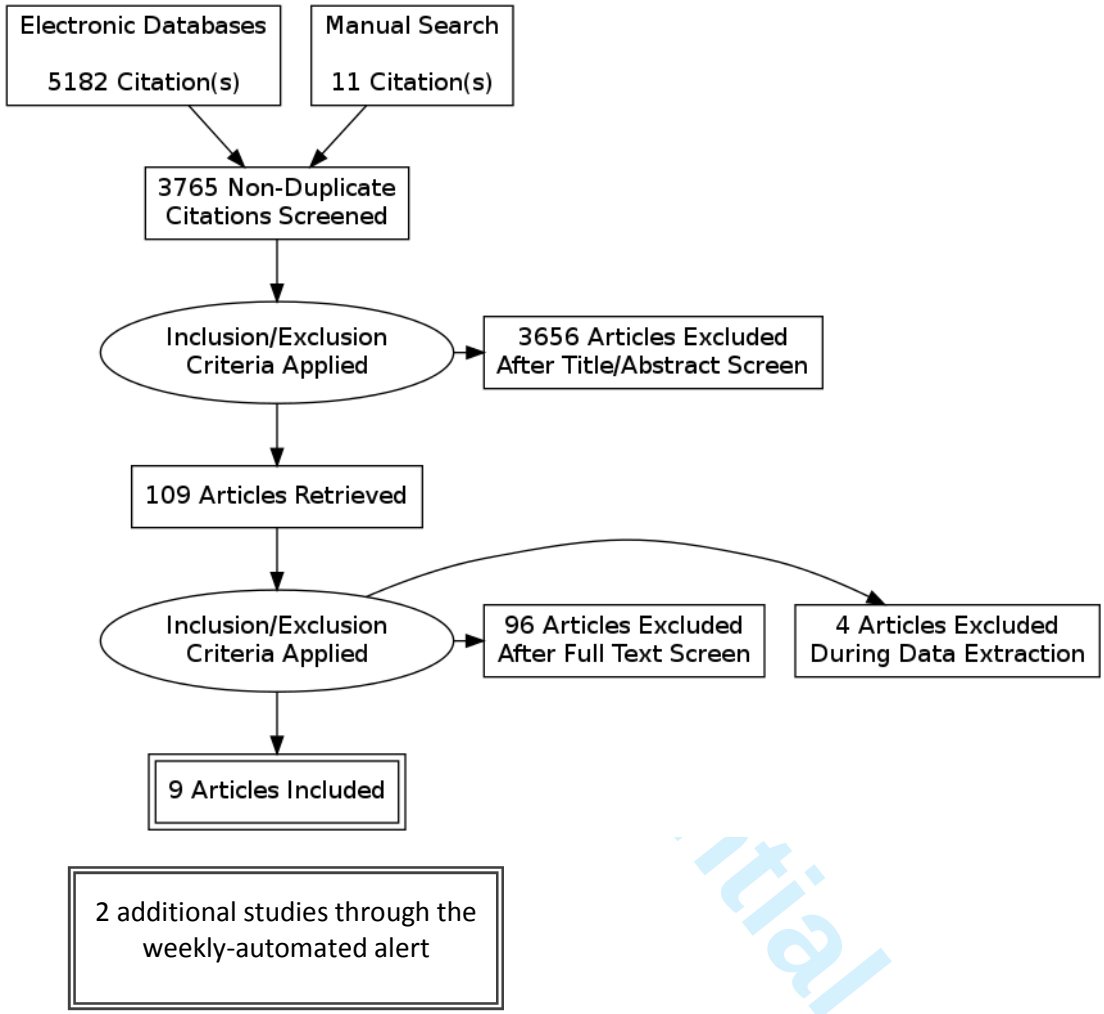


Table 1. Characteristics of the studies

Article	Fraser LK et al 2013[7]	Keele L et al 2013[8]	Dussel V et al 2009[11]
Objective	Assess the impact of specialist pediatric palliative care services (SPPCSs) carried by a pediatric hospice	Compare demographic and clinic characteristics of patients who received or not PC consultations	Determine association of modifiable clinical factors with parental planning of local of death (LOD), Explore planning of the child's LOD had any impact on patterns of care and the parent's experience with the child's EOL.
Participants	Children who died from cancer (0-19 years) Diagnosed between 1996 to 2009, died before Sep 2011	Children (<18 years of age) who died at the hospital >5 days after admission, from all causes of death who had complete administrative data on charges and hospital admissions on the database between 2001-2011 Patients discharged < 5 days under hospice care were not included	Children who died from cancer Cared for in 2 tertiary centres participant in the research whose physicians gave authorization to contact the family Children's deaths: between 1990 and 1999 Families' interviews: between 1997 and 2001
Study design	Cohort comparison	Retrospective administrative database analysis Pediatric Health Information System (PHIS) database developed by collaboration of >40 children's hospitals across the states	Retrospective cross-sectional survey of bereaved parents Retrospective Chart review
Follow-up	Referral to death	Last admission before death	Last month of life
n	497	24342	140
Data sources	Secondary data base analysis Linked data from SPPCSs, Register of Cancer, NHS Hospital episode statistics	Secondary analysis of the Pediatric Health Information System counting on > 40 hospitals across country	Parents survey: 390 questions, partially validated, carried over the phone or in person Patients charts
Intervention Group	**Hospice Group (n=132)** Patients referred to a specialist palliative care service carried by a pediatric hospice	**PC group (n=919)** Palliative Care Consultation in the last admission (measured by billing code for ICD9 - PC V66.7)	**Planned LOD (n=88)**
Comparator	**Control group (n = 311)** Patients not referred to the hospice services	**No PC (n=23423)** No palliative care consultation in the last admission (no billing code)	**Did not planned LOD (n=52)**
Setting	Residents in the Yorkshire Health Authority (UK)	Children who died across > 40 US Children's Hospitals part of the Children's Hospital Association (USA) database	Dana-Farber Cancer Institute/Children's Hospital Boston, and Children's Hospitals and Clinics of Minnesota (USA)
Outcomes	Primary: Total number of hospital admissions Secondary: Number of planned hospital admissions, Number of emergency hospital admissions	Age, Gender, LOS, Major group category diagnostic, medications, procedures in the last admission	EOL planning, EOL support from physicians Use of home care, Hospital resources utilization Place of death
Funding	Not disclosed	No external funding was received. The authors disclosed no conflict of interest	No conflict of interest was disclosed. Different sources of funding was supporting the authors (Agency for Health Research and Quality, National Cancer Institute, Child Health Research Grant from the Charles H. Hood Foundation, Pine Tree Apple Tennis Classic Oncology Research Fund)

Table 1. Characteristics of the studies (cont.)

Article	Knapp CA et al 2009[12]	Arland LC et al 2013[6]	Postier et al 2014 [15]
Objective	Describe demographic characteristics, cause and location of death, and expenditure patterns of hospice users and nonusers. Investigate hospice expenditures variations and children's characteristics	Investigate relationship between changes in outcomes and a EOL program	Explore healthcare service utilization by children prior/after to enrollment in home-based PPC/hospice programs carried by a tertiary care provider
Participants	Children who died in Florida state (1-21 years) Between Jul 2003 - Jun 2006 Who were resident in Florida. Enrolled in the Medicaid program	Children who died from brain tumor (1 month - 19 years), with documented place of death, and documented reasons for hospital admission	Children enrolled in the home PPC/ hospice program (1 to 21 years old) For at least 1 day between 2000- 2010. Children < 1 year was excluded
Study design	Retrospective administrative data analysis.	Pre-post observational study. Both periods included hospice care as part of the EOL care.	Pre-post observational study.
Follow-up	Last year of life	Before standardization: 5 years After standardization: 10 years	Before enrollment: 12 months After enrollment: 12 months
n	1527	114	425
Data sources/ measurement	Medicaid claims, encounter and enrollment files. Death certificate	Retrospective chart review	Retrospective secondary data analysis Electronic medical records and accounting system for billed charges
Intervention Group	**Hospice use** (n= 85)	**After group (n= 92 / 1996-2005)** Standardized EOL care program carried by a hospital (comprehensive EOL discussions, medications for symptom control, primary family liaison, home visits)	**Pre-PPC**
Comparator	**Non-hospice use** (n= 848)	**Before Group (n= 22 /1990-1995)** Not standardized EOL care managed by individual hospices in the geographic area (not specialized in pediatric palliative care)	**Post-PPC**
Setting	Florida State (USA)	Hospital: Children's Hospital Colorado (USA) implemented the program in 1995.	Children's Hospitals and Clinics of Minnesota's (CHC) Homecare, Pain Medicine, Palliative Care & Integrative Medicine Programs (USA)
Outcomes measured	Hospice use Hospice expenditures	Symptoms Hospitalizations - number and LOS Location of death	Change in number of hospitalizations, LOS, and total billed charges for hospital/ER stays.
Funding	No conflict of interest was disclosed. Source of funding not disclosed	Do not state funding. Authors report no conflict of interest but some of them occupied positions in the Children's Hospital Colorado.	No funding was received for the research. Authors disclosed no conflict of interest. However, four authors are employees in the Department of Pain Medicine, Palliative Care & Integrative Medicine, Children's Hospitals and Clinics of Minnesota.

Table 1. Characteristics of the studies (cont.)

Article	Gans D et al 2012[9]	Pascuet E et al 2010[10]	Smith et al 2013 [16]
Objective	Demonstrate shift in healthcare resource use and cost with the implementation of a community palliative care program	Measure differences in hospital utilization and cost with the use of respite services at a pediatric hospice	Evaluated PPC utilization among the most costly hospitalized patients Examined factors associated with receipt of PPC and inpatient costs.
Participants	Children living with life-threatening conditions (0 to 20 years old) Enrolled in a community based pediatric palliative care program implemented in 2010	Children with life-limiting illness (age range not defined) Who had used Respite at the pediatric Hospice at least once May 2005 to Feb 2009	The most costly decile patients, in 2010, among all patients discharged from Primary Children's Medical Center (PCMC)
Study design	Pre-post assessment of healthcare utilization and expenditures Brief report	Pre-Post observational study	Cohort comparison between who received PPC and those who did not Pre-post assessment in the PPC cohort before/after the initial PPC consultation
Follow-up	Before: 12 months? (2009 not clear starting and final month) After: 18 months (January 2010 to September 2011)	Before 1st respite: 12 months After 1st respite: 12-months	Cohort comparison: up to 2 years Pre-post: undisclosed
n	123	66	1001
Data sources/ measurement	Secondary analysis of databases of claims (MIS/DSS claims, MEDS and CMS Net) Survey for family quality of life and satisfaction	Retrospective chart review Non-randomized	Undisclosed
Intervention Group	**After PPC program** Included coordination of care and community resources, massage, art, play and music therapy family education and training in devices operation family counseling and bereavement, pain and symptom management, respite out of home, hospice facilities (not necessarily specialized in pediatric population)	**Before respite**	**PPC Group** (n=81): patients who used the PPC program
Comparator	**Before PPC Program**	**After respite**	**Control Group** (n= 920): patients who did not use PPC program
Setting	11 counties in California (USA). The program counted in several healthcare providers (home care providers, hospices and contracted agencies who voluntarily decided to participate in the program	Roger's House Pediatric Hospice, Ontario, Canada (RH) Children's Hospital of Eastern Ontario (CHEO)	Primary Children's Medical Center (PCMC), Salt Lake City, UT
Outcomes measured	LOS Medical Expenditures Family's quality of life and satisfaction	LOS ER and Outpatient visits Overall Cost in hospital/hospice admission	Cost Demographics Use of technology
Funding	Policy brief supported by Children's Hospice & Palliative Care Coalition (CHPCC) All authors belonged to UCLA University.	Funded by the Hospice	Do not state funding. First author is employed by the hospital were the research was conducted

Table 1. Characteristics of the studies (cont.)

Article	Ward-Smith P et al 2008[14]	Belasco JB et al 2000[13]
Objective	Compare inpatients hospital cost associated with PPCP carried by a tertiary provider	Compare cost of care at home and at the hospital
Participants	Children enrolled in the PPCP within 6 months before death (age range not specified) Cases: identified within 18 months, 2 years after PPCP became fully implemented Control: criteria for matching was not stated (apparently by diagnostic), period not specified Exclusion criteria: children in the neonatal intensive care unit, those who died within 72 hours of their initial admission, those patients with an incomplete medical record, and those enrolled in the PPCP program less than 30 days prior to death.	Children referred to a home based pediatric palliative care program between 1988-1992 (age bracket not specified) carried by a tertiary care provider Applied costs from 1995 and 1996. Out of the 154 patients enrolled in the PPCP during the period, some were selected by the author to reflect medically complicated patients whose level of care at home approximately equal that in the hospital and differed only in palliative intent rather than intent to cure.
Study design	Retrospective matched case-control	Brief case report
Follow-up	Last 6 months before death	1 day
n	18	3
Data sources/ measurement	Hospital-based charges	Retrospective chart review
Intervention Group	**PPCP group (n=9)** Enrolled in the Pediatric Palliative Care Program	**Home care**
Comparator	**Non PPCP (n=9)** Not enrolled in the Palliative Care Program enrolment	**Hospital care**
Setting	Children's Mercy Hospital, Kansas, USA	Children's Hospital Philadelphia (USA)
Outcomes measured	Total hospital costs LOS Differences in types of procedures	Type of interventions delivered. Place of death Comparison of charges of care
Funding	No funding was disclosed. Authors are employees of the Hospital.	No funding was disclosed. Authors are employees of the Hospital.

Table 2. Visual summary of results

Design	Author	Hospital Admissions	LOS	Cost
Cohort	Keele L et at [8]	+		+
Cohort	Fraser LK et al [7]	?		
Cohort	Smith et al [16]	?		?
Cohort	Dussel V et al [11]	?	+	
Cohort	Knapp CA et al [12]			–
Pre/Post no control	Postier et al [15]	?	+	?
Pre/Post no control	Arland LC et al [6]	+	+	
Pre/Post no control	Gans D et al [9]		+	+
Pre/Post no control	Pascuet E et al [10]	?	–	+
Case-Control*	Ward-Smith P et al[14]		–	?
Case series	Belasco JB et al [13]			+

Low risk +

Moderate risk ?

High risk –

Table 3. Summary of comparison in admissions

Cohort Comparison
Keele L et al[8]
Admission to ICU – Relative Risk (95%CI) Lower among PC group: RR 0.29 (0.26–0.32) Follow-up: Last admission before death
Fraser LK et al[7]
Total hospital admissions **(controlled for age, disease, gender, deprivation category)** IRR 0.79 (CI 95% 0.59-1.05), p=0.10 **Planned hospital admissions** IRR 0.60 (CI 95% 0.43-0.85), p=0.004 **Emergency hospital admissions** IRR 1.15 (CI 95% 0.84-1.58), p=0.375 Follow-up: Referral to death
Dussel V et al[11]
Admission to hospital - last month of life Planned LOD: 54% (47/87) vs. Did not planned: 98% (51/52), p <0.001 **At least one emergency room - last week of life** Planned LOD: 6% (5/84) vs. Did not planned: 16% (8/50), p= 0.057 Died at the hospital: Planned LOD 28% vs. 75%, p<0.001 Follow-up: Last month of life
Smith et al [16]
Proportion of patients admitted to PICU PPC group: 90% (73/93) Control group: 56% (522/920), p<0.001 **Proportion of patients admitted to NICU** PPC group: 17% (14/93) Control group: 28% (262/920), p=0.04

Table 3. Summary of comparison in admissions (cont.)

Pre/Post - No Control
Arland LC et al [6]
Proportion of patients admitted to hospital After program (10 year): 29% vs. Before program (5 year): 54% (p< .05). Number of Hospital Admissions in the EOL period After group: 38 vs. Before group: 20 The authors stated a 46% fewer hospital admissions. No test applied
Postier et al [15]
Average number of hospital admissions Pre-PPC: 3.09±3.6 vs. Post-PPC 3.18±4.3, p = 0.538 Interaction - level of PPC exposure, Cancer or not, study period (p < 0.001), adjusting for other demographic and clinical characteristics. Cancer patients with the least amount of PPC/hospice exposure - decrease Cancer patients with the most exposure - increase 52% patients had 1 year or more of exposure to the program 16.9 died during the exposure
Pascuet E et al[10]
Median number of ER visits/monthly After - 0.03 (95% CI, -0.09 to 0.02, p=0.20) Median number of Outpatients visits/monthly After: - 0.5 (95% CI -1.0 to - 0.05, p=0.029)

ICU: intensive care unit; RR: relative risk; PC: palliative care; EOL: end-of-life; IRR: incidence rate ratio; PPC: pediatric palliative care; LOD: location of death; ER: emergency room; CI: confidence interval; PICU: pediatric intensive care unit; NICU: neonatal intensive care unit.

Table 4. Summary of comparison of LOS

Pre/Post - No Control	
Postier et al [15]	Gans D et al [9]
Mean total LOS Pre-PPC: 34.09±59.7 days vs. Post-PPC: 19.37±34.0 days ($p < 0.001$). Interaction - level of PPC exposure, Cancer/Non-cancer, and study period ($p < 0.001$). Non-cancer patients with at least six months of PPC exposure showed a significant decrease in total LOS by an average of 38 days.	**Average number of days spent in the hospital (per member, per month)** Before program: 4.0 vs. After program: 2.8 Reduction of 32%. No test applied.
Arland LC et al [6]	Pascuet E et al [10]
Total LOS in the EOL After group: 115 days vs. Before group: 81 days **Average LOS per hospital admission** After group: 3.03 days vs. Before group: 4.05 days Decrease 25%. No test applied **Average LOS per patient in the total group (not only among those admitted to the hospital)** After group: 1.25 days/patient vs. Before: 3.68 days/patient Decreased 66%. No test applied The research didn't show the number of days spent in hospice in both groups.	**Median number of Inpatient days/monthly** After: Variation: - 2.9 (95% CI -4.5 to -1.3, p=0.001). **Median number of Hospice days/monthly (min-max)** After: 2.4 (0.08-26.5) **Median number of Total Inpatient days /monthly** After: Variation: 0.9 (p=0.013).
Cohort Comparison	**Case Control***
Dussel V et al [11]	Ward-Smith P et al[14]
Median (IQR) LOS in days - last month of life Planned LOD: 17 (4-27) Did not planned LOD 21 (6-28), p=0.494	Mean LOS (min-max) PC: 4 days (5 to 17 days) Non-PC: 4 days (5 to 18 days)

* Technically is a cohort comparison; LOS: length of stay; EOL: end-of-life; IQR: interquartile range; LOD: location of death; PC: palliative care

Table 5. Summary of Cost comparison

<table>
<tr><td>Cohort</td></tr>
<tr><td>Keele L et al[8]</td></tr>
<tr><td>Average daily charges (adjusted for geography)
PC group: $9348 ($6070–$15,318),
No PC codes: $11 806 ($8017–$18352), p<0.001</td></tr>
<tr><td>Knapp CA et al[12]</td></tr>
<tr><td>
<table>
<tr><th></th><th>Deaths
n (%)</th><th colspan="5">Mean expenditures</th></tr>
<tr><th></th><th></th><th>Hospice</th><th>Inpatient</th><th>Outpatient</th><th>Emergency department</th><th>Pharmacy</th></tr>
<tr><td>Hospice users</td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>All causes of death</td><td>164 (100.0%)</td><td>$11,362</td><td>$49,621</td><td>$14,414</td><td>$873</td><td>$7,449</td></tr>
<tr><td>Perinatal</td><td>14 (8.5%)</td><td>$11,934</td><td>$65,814</td><td>$23,058</td><td>$971</td><td>$10,946</td></tr>
<tr><td>Chronic</td><td>138 (84.1%)</td><td>$10,887</td><td>$50,283</td><td>$14,366</td><td>$929</td><td>$7,582</td></tr>
<tr><td>External</td><td>9 (5.5%)</td><td>$19,140</td><td>$24,619</td><td>$2,028</td><td>$121</td><td>$2,027</td></tr>
<tr><td>Other</td><td>3 (1.8%)</td><td>$7,197</td><td>$18,581</td><td>$13,475</td><td>$67</td><td>$1,304</td></tr>
<tr><td>Nonhospice users</td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>All causes of death</td><td>1363 (100.0%)</td><td></td><td>$19,968</td><td>$12,954</td><td>$468</td><td>$3,207</td></tr>
<tr><td>Perinatal</td><td>122 (9.0%)</td><td></td><td>$35,770</td><td>$35,796</td><td>$832</td><td>$5,820</td></tr>
<tr><td>Chronic</td><td>511 (37.5%)</td><td></td><td>$38,232</td><td>$21,603</td><td>$632</td><td>$6,117</td></tr>
<tr><td>External</td><td>673 (49.4%)</td><td></td><td>$3,358</td><td>$2,257</td><td>$269</td><td>$484</td></tr>
<tr><td>Other</td><td>57 (4.2%)</td><td></td><td>$18,533</td><td>$12,829</td><td>$581</td><td>$3,683</td></tr>
</table>
*Extracted from the original article
</td></tr>
<tr><td>Case Control*</td></tr>
<tr><td>Ward-Smith P et al [14]</td></tr>
<tr><td>Mean total hospital costs (Min - Max)
PC: $231,900 ($33,283 to $783,953)
non-PC: $228,199 ($28,970 to $803,657)
No test applied

Excluding surgical charges Mean hospital costs (min-max)
PC: $78,780 ($33,283 to $130,970).

The highest costs were associated with respiratory treatments, and pharmacy charges.
Non-PC: $81,780 ($28,970 to $135,432).
The highest costs were associated with respiratory treatments and radiology charges.

Respiratory treatments did not vary among study groups and were provided an average of 1.6 times per hospitalized day.
Mean costs of respiratory treatments
PC: $7,009 vs. Non-PC: $7,011
Mean costs of radiology charges
PC: $4,903 vs. non-PC: $6,923

Differences type of radiologic procedures
PC: computerized tomography and MRI
Non-PC: portable chest x-rays and flat abdominal x-rays.</td></tr>
</table>

Table 5. Summary of Cost comparison (cont.)

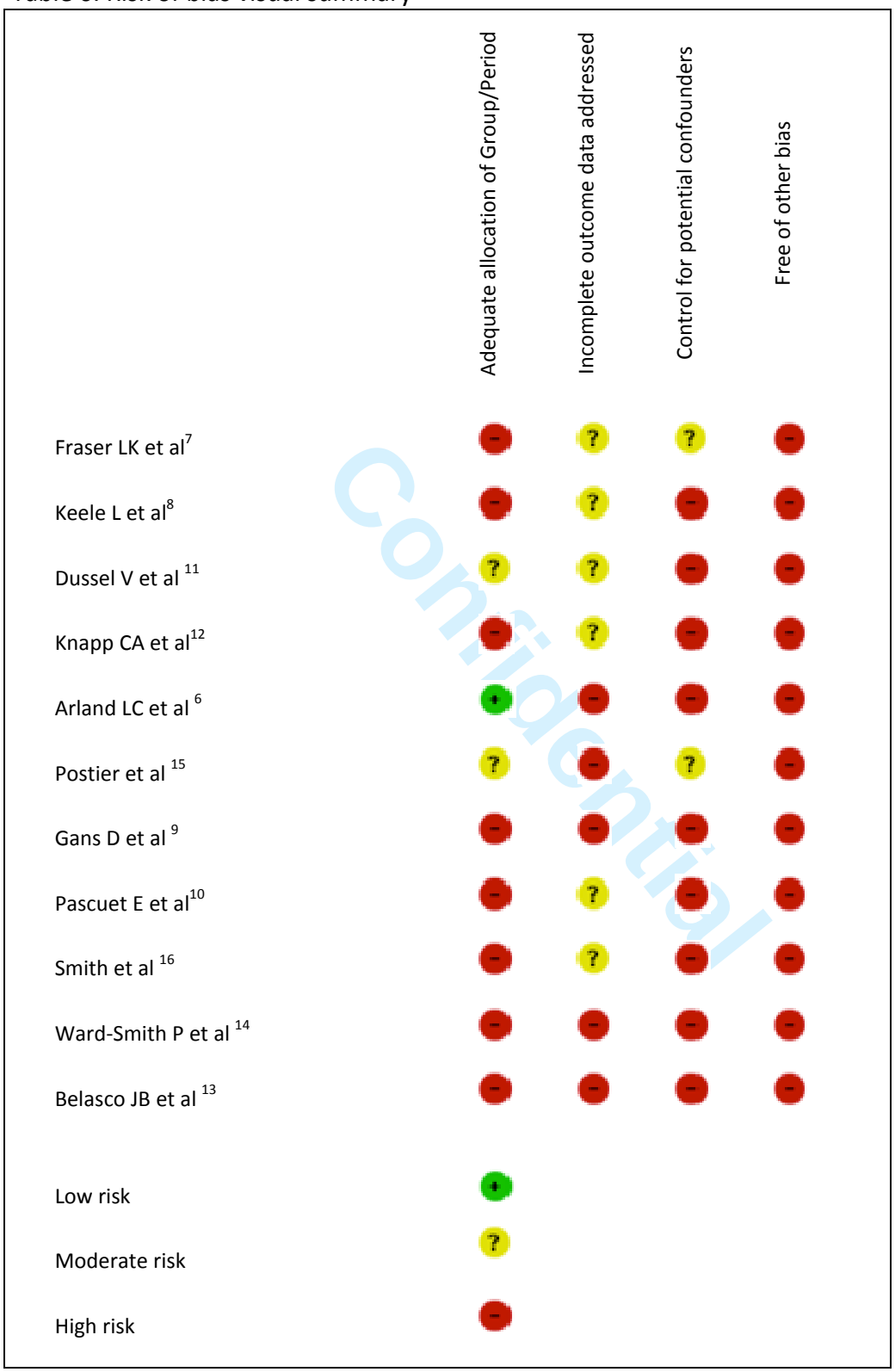
Pre/Post studies
Gans D et al[9]
Average Total Medical Expenditures (per member, per month) Before program: $15,653 After program: $13,976 Decrease 11% - nearly $1 million in 18 months Inpatient care: decrease 35% ($3,571) Outpatient Care: increase 34% ($1,398) Pharmaceutical costs: increase 35% ($495) Emergency visits: increase $2
Pascuet E et al[10]
Unit costs/day Hospital Inpatient day: $2,007 Hospice day: $500 **Change in total inpatient cost/month (inpatient + Hospice)** After: - $4,252/month (95% CI, - $953 to -$7,551, p=0.012).
Postier et al [15]
Average charges (divided by a factor of 10,000) Pre-PPC: 20.97± 43.3 Post-PPC 10.91± 21 (p < 0.001) Interaction - level of PPC exposure, Cancer/non-cancer, study period (p < 0.001). Non-cancer patients with at least six months of PPC exposure showed a significant decrease in total billed charges (nearly $275,000)
Smith et al 2013 [16]
Change in median daily cost (IQR) - Within PPC group 56 patients had inpatient hospitalizations in 2010 prior to receiving PPC Before PPC: $3827 ($2.9-3.9K) After PPC: $4013 ($3.1-5.1K), p=0.06. **Cost in 2010/2011** PPC group: $177K ($102K-$281K) Control: $103K ($64K-$187K), p<0.001 **Daily Cost 2010/2011** PPC group: $3.8K ($3.1K-$4.7K) Control: $3.4K ($2.7K-$4.5K), p=0.001 **Patients who died - median daily cost (IQR)** PPC group: $3976 ($3254-$4931) Control: $4693 ($3562-$6455), p=0.032

Table 5. Summary of Cost comparison (cont.)

Case series
Belasco JB et al[13]
Average charges per day AML patient (toddler) Hospital: $4,283 Home: $17 Neuroblastoma patient (pre-school child) Hospital: $2,300 Home: $325 Multiple chronic diseases patient (teenager) Hospital: $8,258 Home: $1,308 No test applied

* Technically is a cohort comparison; PC: palliative care; PPC: pediatric palliative care; IQR: interquartile range; AML: acute myeloid leukemia

Table 6. Risk of bias visual summary



References

1. Association for Children's Palliative Care. A Guide to the Development of Children's Palliative Care Services. 2009:34. Available at: http://www.rcpcf.ru/Files/pdf/ACT. A Guide to the Development of Children's Palliative Care Services.pdf.

2. Harrop E, Edwards C. How and when to refer a child for specialist paediatric palliative care. *Arch Dis Child Educ Pract Ed*. 2013;98(6):202–8. doi:10.1136/archdischild-2012-303325.

3. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions : explanation and elaboration. *BMJ*. 2009;339:b2700. doi:10.1136/bmj.b2700.

4. Liebert MA, Hays RM, Valentine J, et al. The Seattle Pediatric Palliative Care Project: Effects on Family Satisfaction and Health-Related Quality of Life. 2006;9(3):716–729.

5. Reeves B, Deeks J, Higgins J, Wells G. Including non-randomized studies. In: Higgins J, Green S, eds. *Cochrane Handbook for Systematic Reviews of Interventions.* Version 5. The Cochrane Collaboration; 2008. Available at: www.cochrane-handbook.org.

6. Arland LC, Hendricks-Ferguson VL, Pearson J, Foreman NK, Madden JR. Development of an in-home standardized end-of-life treatment program for pediatric patients dying of brain tumors. *J Spec Pediatr Nurs*. 2013;18(2):144–57. doi:10.1111/jspn.12024.

7. Fraser LK, van Laar M, Miller M, et al. Does referral to specialist paediatric palliative care services reduce hospital admissions in oncology patients at the end of life? *Br J Cancer*. 2013;108(6):1273–9. doi:10.1038/bjc.2013.89.

8. Keele L, Keenan HT, Sheetz J, Bratton SL. Differences in characteristics of dying children who receive and do not receive palliative care. *Pediatrics*. 2013;132(1):72–8. doi:10.1542/peds.2013-0470.

9. Gans D, Kominski GF, Roby DH, Diamant AL, Chen X. Health Policy Brief. 2012;(August).

10. Pascuet E, Cowin L, Vaillancourt R, et al. A comparative cost-minimization analysis of providing paediatric palliative respite care before and after the opening of services at a paediatric hospice. *Healthc Manag Forum*. 2010;23(2):63–66. doi:10.1016/j.hcmf.2010.04.009.

11. Dussel V, Kreicbergs U, Hilden JM, et al. Looking beyond where children die: determinants and effects of planning a child's location of death. *J Pain Symptom Manage*. 2009;37(1):33–43. doi:10.1016/j.jpainsymman.2007.12.017.

12. Knapp C, Shenkman E, Marcu M, Madden V, Terza J. Pediatric Palliative Care : Describing Hospice Users and Identifying Factors that Affect Hospice Expenditures. *J Palliat Med*. 2009;12(3):223–9.

13. Belasco JB. Supportive care : Palliative care in children , adolescents , and young ... 2000.

14. Ward-smith P, Korphage RM. Where Health Care Dollars Are Spent When Pediatric Palliative Care Is Provided. 2008;26(3):175–179.

15. Postier A, Chrastek J, Nugent S, Osenga K, Friedrichsdorf SJ. Exposure to home-based pediatric palliative and hospice care and its impact on hospital and emergency care charges at a single institution. *J Palliat Med*. 2014;17(2):183–8. doi:10.1089/jpm.2013.0287.

16. Smith A, Andrews S, Maloney C, Bratton SL. Pediatric Palliative Care in High Cost Patients. In: Poss WB, ed. *Pediatric Critical Care Medicine. Conference: American Academy of Pediatrics, Section on Critical Care National Conference and Exhibition*.Vol 26. Orlando: Lippincott Williams and Wilkins; 2013. Available at: https://aap.confex.com/aap/2013/webprogram/Paper21649.html.

Appendices

Appendix A Search strategy

A.1 Sub-Appendix: Medline strategy

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R)

1 adolescent/ or exp child/ or exp infant/
2 exp Pediatrics/
3 Minors/
4 or/1-3 [children]
5 *Palliative Care/ec, mt, st, sn, td, ut [Economics, Methods, Standards, Statistics & Numerical Data, Trends, Utilization]
6 *Hospice Care/
7 *Terminal Care/ec, mt, st, sn, td, ut [Economics, Methods, Standards, Statistics & Numerical Data, Trends, Utilization]
8 *Respite Care/
9 or/5-8 [Palliative Care narrow main topic]
10 4 and 9 [children and palliative care]
11 limit 10 to "review articles"
12 limit 10 to systematic reviews
13 limit 10 to meta analysis
14 systematic review?.mp.
15 Cochrane database of systematic reviews.jn.
16 or/14-15
17 10 and 16
18 or/11-13,17 [children and palliative care reviews] (
19 limit 18 to yr="1974 -Current" [reviews after 1974]
20 Adrenoleukodystrophy/
21 Alagille Syndrome/
22 Alexander Disease/
23 alpha-N-Acetylgalactosaminidase/df [Deficiency]
24 Argininosuccinic Aciduria/
25 Aspartylglucosaminuria/
26 Bartter Syndrome/
27 Canavan Disease/
28 Carbamoyl-Phosphate Synthase I Deficiency Disease/
29 "Congenital Disorders of Glycosylation"/
30 Carnitine O-Palmitoyltransferase/df [Deficiency]
31 Cholesterol Ester Storage Disease/
32 Citrullinemia/
33 Costello Syndrome/

34 Cri-du-Chat Syndrome/
35 De Lange Syndrome/
36 "Diffuse Cerebral Sclerosis of Schilder"/
37 DiGeorge Syndrome/
38 Farber Lipogranulomatosis/
39 Fucosidosis/
40 Gangliosidoses/
41 Gangliosidoses, GM2/
42 Glycogen Storage Disease Type II/
43 Glycogen Storage Disease Type IIb/
44 Glycogen Storage Disease Type IV/
45 Hereditary Central Nervous System Demyelinating Diseases/
46 Histiocytosis, Langerhans-Cell/
47 Huntington Disease/
48 Hyperglycinemia, Nonketotic/
49 Incontinentia Pigmenti/
50 Jacobsen Distal 11q Deletion Syndrome/
51 Kearns-Sayre Syndrome/
52 Klippel-Trenaunay-Weber Syndrome/
53 Lafora Disease/
54 Leigh Disease/
55 Lesch-Nyhan Syndrome/
56 Leukodystrophy, Globoid Cell/
57 Leukodystrophy, Metachromatic/
58 Lipidoses/
59 MELAS Syndrome/
60 Menkes Kinky Hair Syndrome/
61 MERRF Syndrome/
62 Methylmalonyl-CoA Mutase/df [Deficiency]
63 Mevalonate Kinase Deficiency/
64 Mitochondrial Encephalomyopathies/
65 Mitochondrial Myopathies/
66 Mucolipidoses/
67 Mucopolysaccharidosis I/
68 Mucopolysaccharidosis II/
69 Mucopolysaccharidosis III/
70 Mucopolysaccharidosis VII/
71 Multiple Acyl Coenzyme A Dehydrogenase Deficiency/
72 Multiple Sulfatase Deficiency Disease/
73 Myoclonic Epilepsies, Progressive/
74 Neuroaxonal Dystrophies/cn [Congenital]
75 Neuronal Ceroid-Lipofuscinoses/
76 niemann-pick disease, type a/ or niemann-pick disease, type b/ or niemann-pick disease, type c/

77 Oculocerebrorenal Syndrome/
78 Olivopontocerebellar Atrophies/
79 Ophthalmoplegia, Chronic Progressive External/
80 Ornithine Carbamoyltransferase Deficiency Disease/
81 Pelizaeus-Merzbacher Disease/
82 Peroxisomal Disorders/
83 Propionic Acidemia/
84 Pyruvate Carboxylase Deficiency Disease/
85 Pyruvate Dehydrogenase Complex Deficiency Disease/
86 Pyruvate Metabolism, Inborn Errors/
87 Refsum Disease/
88 Refsum Disease, Infantile/
89 Rett Syndrome/
90 Rubinstein-Taybi Syndrome/
91 Sandhoff Disease/
92 Sea-Blue Histiocyte Syndrome/
93 Sialic Acid Storage Disease/
94 Smith-Lemli-Opitz Syndrome/
95 Spasms, Infantile/
96 Sphingolipidoses/
97 sulfatidosis/
98 Unverricht-Lundborg Syndrome/
99 von Hippel-Lindau Disease/
100 Wolf-Hirschhorn Syndrome/
101 Wolman Disease/
102 Zellweger Syndrome/
103 Aicardi Syndrome/
104 Aicardi? Syndrome.mp.
105 alpha-N-Acetylgalactosaminidase/df [Deficiency]
106 alpha-NAGA deficiency.mp.
107 alpha-Mannosidosis/
108 Argininosuccinic Aciduria/
109 Argininosuccinicaciduria.mp.
110 Argininosuccinate lyase deficiency.mp.
111 ASAuria.mp.
112 ASL deficiency.mp.
113 ARSACS.mp.
114 Autosomal Recessive Spastic Ataxia of Charlevoix-Saguenay.mp.
115 beta-Mannosidosis/
116 Charlevoix-saguenay spastic ataxia.mp.
117 Dubowitz.mp.
118 Escobar Syndrome.mp.
119 Galactosidases/
120 Glutaric Acidemia Type I.mp.

121 Glutaric Aciduria Type I.mp.
122 Glutathione/df [Deficiency]
123 Infantile Neuroaxonal Dystrophy.mp. or Neuroaxonal Dystrophies/
124 Seitelberger's Disease.mp.
125 Jeune Thoracic Dystrophy.mp.
126 Asphyxiating Thoracic Dystrophy.mp.
127 Kanzaki Disease.mp.
128 Lennox-Gastaut Syndrome.mp.
129 3-methylcrotonyl-CoA carboxylase deficiency.mp.
130 Methylcrotonyl-CoA carboxylase deficiency.mp.
131 3-MCC deficiency.mp.
132 3MCC.mp.
133 MCC deficiency.mp.
134 Muscular Dystrophy, Duchenne/
135 exp Leukemia, Lymphoid/
136 Cerebral Palsy/
137 Neuroblastoma/
138 Muscular Atrophy, Spinal/
139 Neuroectodermal Tumors, Primitive/
140 Leukemia, Myeloid, Acute/
141 Mitochondrial Diseases/
142 Mitochondrial Diseases/
143 Friedreich Ataxia/
144 Osteosarcoma/
145 Trisomy 18.mp.
146 Medulloblastoma/
147 "Spinal Muscular Atrophies of Childhood"/ or SMA Type II.mp.
148 Pontine Glioma.mp.
149 Rett Syndrome/
150 Rhabdomyosarcoma/
151 Sarcoma, Ewing/
152 Brain Neoplasms/
153 Cystic Fibrosis/
154 Hypoxia-Ischemia, Brain/
155 Trisomy 13.mp.
156 Batten's Disease.mp.
157 Brain stem glioma.mp.
158 San Filippo Syndrome.mp.
159 Brain Stem Neoplasms/
160 CHARGE Syndrome/
161 Ependymoma/
162 Carcinoma, Hepatocellular/
163 exp HIV Infections/
164 Microcephaly/

165 Mitochondrial Diseases/
166 Adrenoleukodystrophy/
167 Biliary Atresia/
168 Glioblastoma/
169 Hodgkin Disease/
170 Hurler's syndrome.mp.
171 Leigh Disease/
172 Epilepsy/
173 Arthrogryposis/
174 Astrocytoma/
175 Atypical Teratoid Rhabdoid Tumour.mp.
176 Burkitt Lymphoma/
177 Chromosome Aberrations/
178 Down Syndrome/
179 Dravet Syndrome.mp.
180 Glioblastoma/
181 Glutaric aciduria.mp.
182 Hydranencephaly/
183 Hypoplastic Left Heart Syndrome/
184 Krabbe Disease.mp.
185 Muscular Dystrophies, Limb-Girdle/
186 Metabolism, Inborn Errors/ or Metabolic Diseases/
187 Leukodystrophy, Metachromatic/
188 Mitochondrial enzyme complex IV.mp.
189 Mitochondrial Myopathies/
190 Enterocolitis, Necrotizing/
191 NYD.mp.
192 Pallister-Killian Syndrome.mp.
193 Pelizaeus-Merbacher Syndrome.mp.
194 Polymicrogyria.mp.
195 Propionic Acidemia/
196 Hypertension, Pulmonary/
197 Severe brain injury.mp.
198 Tay-Sachs Disease/
199 Wilms Tumor/
200 Chromosome Inversion/
201 Adams-Oliver Syndrome.mp.
202 Aicardi-Goutieres Syndrome.mp.
203 Alpers Syndrome.mp. or "Diffuse Cerebral Sclerosis of Schilder"/
204 Aminoacid decarboxylase deficiency.mp.
205 Anaplastic Astrocytoma.mp.
206 Brain/ab [Abnormalities]
207 Adrenoleukodystrophy/
208 Anomalous left coronary artery from pulmonary artery.mp.

209 Anterior Horn Cell Disease.mp.
210 Askin's Tumour.mp.
211 ATRT.mp.
212 Atypical Di George Syndrome.mp.
213 Menkes Kinky Hair Syndrome/ or Atypical Menkes.mp.
214 Lymphoma, B-Cell/
215 Rassmussen's Encephalitis.mp.
216 Ependymoma/
217 Burkitt Lymphoma/ or Burkett Lymphoma.mp.
218 Heart Neoplasms/
219 Cardiomyopathies/
220 Cerebral AV Malformation.mp.
221 Renal Insufficiency, Chronic/
222 Renal Insufficiency/
223 Chronic lung disease.mp.
224 Central Nervous System/ab [Abnormalities]
225 Heart Defects, Congenital/
226 "Tetralogy of Fallot"/ or Complex Tetralogy.mp.
227 De Lange Syndrome/
228 Dandy-Walker Syndrome/
229 severe neurological impairment.mp.
230 Failure to Thrive/
231 Neoplasms/
232 or/20-231
233 adolescent/ or exp child/ or exp infant/
234 exp Pediatrics/
235 Minors/
236 or/233-235
237 232 and 236
238 terminal care/ or hospice care/ or resuscitation orders/
239 *Palliative Care/
240 *Terminally Ill/
241 *Respite Care/
242 *Progressive Patient Care/
243 *Long-Term Care/
244 or/238-243
245 237 and 244
246 limit 245 to "review articles"
247 limit 245 to systematic reviews
248 systematic review?.mp.
249 Cochrane database of systematic reviews.jn.
250 or/248-249
251 245 and 250
252 limit 245 to meta analysis

253 or/246-247,251-252 [reviews in LTC and palliative care]
254 limit 253 to yr="1974 -Current" [reviews after 1974]
255 19 or 254 [LTC and/or Children and Palliative care reviews after 1974]
256 comment/ or editorial/ or letter/ or news/
257 10 or 245
258 257 not (255 or 256) [LTC and/or Children and Palliative care - primary articles total]
259 limit 258 to yr="2000 -Current" [LTC and/or Children and Palliative care - primary articles after 2000]

A.2 Sub-Appendix: EMBASE strategy

Ovid EMBASE

1 adrenoleukodystrophy/
2 Alagille syndrome/
3 Alexander disease/
4 Fabry disease/
5 argininosuccinic aciduria/
6 aspartylglycosaminuria/
7 Bartter syndrome/
8 Canavan disease/
9 carbamoyl phosphate synthetase I deficiency/
10 "congenital disorder of glycosylation"/
11 Carnitine O-Palmitoyltransferase Deficiency.mp.
12 cholesterol ester storage disease/
13 citrullinemia/
14 Costello syndrome/
15 cat cry syndrome/
16 de Lange syndrome/
17 Schilder disease/
18 DiGeorge syndrome/
19 Farber disease/
20 fucosidosis/
21 gangliosidosis/
22 GM2 gangliosidosis/
23 glycogen storage disease type 2/
24 Danon disease/
25 glycogen storage disease type 4/
26 demyelinating disease/
27 Langerhans cell histiocytosis/
28 Huntington chorea/
29 hyperglycinemia/
30 incontinentia pigmenti/

31 Jacobsen syndrome/
32 Kearns Sayre syndrome/
33 angioosteohypertrophy syndrome/
34 myoclonus epilepsy/
35 Leigh disease/
36 Lesch Nyhan syndrome/
37 globoid cell leukodystrophy/
38 metachromatic leukodystrophy/
39 lipidosis/
40 MELAS syndrome/
41 Menkes syndrome/
42 MERRF syndrome/
43 Methylmalonyl-CoA Mutase Deficiency.mp.
44 mevalonate kinase deficiency/
45 mitochondrial encephalomyopathy/
46 mitochondrial myopathy/
47 mucolipidosis/
48 Hurler syndrome/
49 Sanfilippo syndrome/
50 mucopolysaccharidosis type 7/
51 multiple acyl CoA dehydrogenase deficiency/
52 multiple sulfatase deficiency/
53 myoclonus epilepsy/
54 neuroaxonal dystrophy/cn [Congenital Disorder]
55 neuronal ceroid lipofuscinosis/
56 Niemann Pick disease/
57 Lowe syndrome/
58 olivopontocerebellar atrophy/
59 chronic progressive external ophthalmoplegia/
60 ornithine transcarbamylase deficiency/
61 Pelizaeus Merzbacher disease/
62 "disorders of peroxisomal functions"/
63 propionic acidemia/
64 pyruvate carboxylase deficiency/
65 pyruvate dehydrogenase complex deficiency/
66 "disorders of carboxylic acid metabolism"/
67 Refsum disease/
68 infantile Refsum disease/
69 Rett syndrome/
70 Rubinstein syndrome/
71 Sandhoff disease/
72 histiocytosis/
73 sialic acid storage disease/
74 Smith Lemli Opitz syndrome/

75 infantile spasm/
76 lipidosis/
77 metachromatic leukodystrophy/
78 myoclonus epilepsy/
79 von Hippel Lindau disease/
80 Wolf Hirschhorn syndrome/
81 Wolman disease/
82 Zellweger syndrome/
83 Aicardi syndrome/
84 Aicardi? Syndrome.mp.
85 alpha-N-Acetylgalactosaminidase Deficiency.mp.
86 alpha-NAGA deficiency.mp.
87 mannosidosis/
88 argininosuccinic aciduria/
89 Autosomal Recessive Spastic Ataxia of Charlevoix-Saguenay.mp.
90 beta mannosidosis/
91 Dubowitz syndrome/
92 webbed neck/ or Escobar Syndrome.mp.
93 galactosidase/
94 Glutaric Acidemia Type I.mp.
95 Glutaric Aciduria Type I.mp.
96 Glutathione Deficiency.mp.
97 neuroaxonal dystrophy/
98 Jeune Thoracic Dystrophy.mp.
99 Asphyxiating Thoracic Dystrophy.mp.
100 Kanzaki Disease.mp.
101 Lennox Gastaut syndrome/
102 3-methylcrotonyl-CoA carboxylase deficiency.mp.
103 Methylcrotonyl-CoA carboxylase deficiency.mp.
104 3-MCC deficiency.mp.
105 3MCC.mp.
106 MCC deficiency.mp.
107 Duchenne muscular dystrophy/
108 exp lymphatic leukemia/
109 cerebral palsy/
110 neuroblastoma/
111 spinal muscular atrophy/
112 neuroectoderm tumor/
113 acute granulocytic leukemia/
114 "disorders of mitochondrial functions"/
115 Friedreich ataxia/
116 osteosarcoma/
117 trisomy 18/
118 medulloblastoma/

119 hereditary spinal muscular atrophy/
120 pontine glioma/
121 rhabdomyosarcoma/
122 Ewing sarcoma/
123 brain tumor/
124 cystic fibrosis/
125 hypoxic ischemic encephalopathy/
126 trisomy 13/
127 neuronal ceroid lipofuscinosis/
128 Brain stem glioma.mp.
129 brain stem tumor/
130 syndrome CHARGE/
131 ependymoma/
132 liver cell carcinoma/
133 Human immunodeficiency virus infection/
134 microcephaly/
135 "disorders of mitochondrial functions"/
136 adrenoleukodystrophy/
137 bile duct atresia/
138 glioblastoma/
139 Hodgkin disease/
140 Leigh disease/
141 epilepsy/
142 arthrogryposis/
143 astrocytoma/
144 rhabdoid tumor/
145 Burkitt lymphoma/
146 chromosome aberration/
147 Down syndrome/
148 severe myoclonic epilepsy in infancy/
149 glioblastoma/
150 Glutaric aciduria.mp.
151 hydranencephaly/
152 hypoplastic left heart syndrome/
153 globoid cell leukodystrophy/
154 limb girdle muscular dystrophy/
155 "inborn error of metabolism"/
156 metabolic disorder/
157 metachromatic leukodystrophy/
158 Mitochondrial enzyme complex IV.mp.
159 mitochondrial myopathy/
160 necrotizing enterocolitis/
161 NYD.mp.
162 Pallister Killian syndrome/

163 Pelizaeus Merzbacher disease/
164 microgyria/
165 propionic acidemia/
166 pulmonary hypertension/
167 brain injury/
168 Tay Sachs disease/
169 nephroblastoma/
170 chromosome inversion/
171 Adams Oliver syndrome/
172 Aicardi Goutieres syndrome/
173 Alpers disease/
174 Schilder disease/
175 Aminoacid decarboxylase deficiency.mp.
176 glioblastoma/
177 brain malformation/
178 adrenoleukodystrophy/
179 coronary artery anomaly/
180 anterior horn cell disease/
181 Askin's Tumour.mp.
182 ATRT.mp.
183 DiGeorge syndrome/
184 Menkes syndrome/
185 B cell lymphoma/
186 Rassmussen's Encephalitis.mp. (4)
187 ependymoma/
188 Burkitt lymphoma/
189 heart tumor/
190 cardiomyopathy/
191 brain arteriovenous malformation/
192 chronic kidney failure/
193 kidney failure/
194 chronic lung disease/
195 central nervous system malformation/
196 congenital heart malformation/
197 Fallot tetralogy/
198 de Lange syndrome/
199 Dandy Walker syndrome/
200 severe neurological impairment.mp.
201 failure to thrive/
202 exp *neoplasm/
203 or/1-202 [LTC]
204 adolescent/
205 exp child/
206 exp infant/

207 child*.ti,ot,sh,hw,kw.
208 infant?.ti,ot,sh,hw,kw.
209 adolescent?.ti,ot,sh,hw,kw.
210 exp pediatrics/
211 P?ediatric*.ti,ot,sh,hw,kw.
212 exp juvenile/
213 minor?.ti,ot,sh,hw,kw.
214 youth?.ti,ot,sh,hw,kw.
215 teen?.ti,ot,sh,hw,kw.
216 or/204-215 [children broad strategy]
217 203 and 216 [LTC and Children]
218 hospice care/
219 terminal care/
220 *palliative therapy/
221 *terminally ill patient/
222 *hospice patient/
223 *respite care/
224 *progressive patient care/
225 *long term care/
226 (care adj3 (terminal or Palliative or hospice or respite or bereavement or end-of-life or terminally ill or dying)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
227 (palliative adj3 (treatment* or medicine or therap* or care)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
228 or/218-227 [palliative care broad search]
229 217 and 228 [Palliative care in children with LTC]
230 limit 229 to "systematic review"
231 limit 229 to meta analysis
232 Cochrane database of systematic reviews.mp.
233 systematic review?.mp.
234 232 or 233
235 229 and 234
236 limit 229 to evidence based medicine
237 or/230-231,235-236 [reviews EMBASE for palliative care in child with LTC]
238 limit 237 to yr="1974 -Current"
239 or/204-206,210-212 [Children specific search strategy]
240 or/218-223 [palliative care more specific strategy]
241 239 and 240 [children and palliative care]
242 limit 241 to "systematic review"
243 limit 241 to meta analysis
244 241 and 234
245 limit 241 to evidence based medicine
246 or/242-245 [reviews EMBASE for palliative care in child - more specific no key words]

247 limit 246 to yr="1974 -Current"
248 238 or 247
249 241 or 229 [Palliativa care in children and/or LTC total]
250 comment/ or editorial/ or letter/ or news/
251 249 not (248 or 250) [Palliativa care in children and/or LTC primary studies no reviews or comments]
252 limit 251 to yr="2000 -Current" [LTC and/or Children and Palliative care - primary articles after 2000]

A.3 Sub-Appendix: CINAHL strategy

Search Terms	Search Options	Actions
S11	(((MH "Child") OR (MH "Infant") OR (MH "Minors (Legal)") OR (MH "Adolescence") OR (MH "Pediatric Units+") OR (MH "Pediatric Care")) AND ((MH "Terminal Care") OR (MH "Hospice Care") OR (MH "Palliative Care") OR (MH "Resuscitation Orders"))) NOT (S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7)	**Limiters** - Published Date: 20000101-20131231 **Search modes** - Boolean/Phrase
S10	(((MH "Child") OR (MH "Infant") OR (MH "Minors (Legal)") OR (MH "Adolescence") OR (MH "Pediatric Units+") OR (MH "Pediatric Care")) AND ((MH "Terminal Care") OR (MH "Hospice Care") OR (MH "Palliative Care") OR (MH "Resuscitation Orders"))) NOT (S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7)	**Limiters** - Published Date: 19900101-20131231 **Search modes** - Boolean/Phrase
S9	(((MH "Child") OR (MH "Infant") OR (MH "Minors (Legal)") OR (MH "Adolescence") OR (MH "Pediatric Units+") OR (MH "Pediatric Care")) AND ((MH "Terminal Care") OR (MH "Hospice Care") OR (MH "Palliative Care") OR (MH "Resuscitation Orders"))) NOT (S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7)	**Search modes** - Boolean/Phrase
S8	(((MH "Child") OR (MH "Infant") OR (MH "Minors (Legal)") OR (MH "Adolescence") OR (MH "Pediatric Units+") OR (MH "Pediatric Care")) AND ((MH "Terminal Care") OR (MH "Hospice Care") OR (MH "Palliative Care") OR (MH "Resuscitation Orders"))) AND (S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7)	**Search modes** - Boolean/Phrase
S7	((MH "Child") OR (MH "Infant") OR (MH "Minors (Legal)") OR (MH "Adolescence") OR (MH "Pediatric Units+") OR (MH "Pediatric Care")) AND ((MH "Terminal Care") OR (MH "Hospice Care") OR (MH "Palliative Care") OR (MH "Resuscitation Orders"))	**Limiters** - Publication Type: Statistics **Search modes** - Boolean/Phrase

S6	((MH "Child") OR (MH "Infant") OR (MH "Minors (Legal)") OR (MH "Adolescence") OR (MH "Pediatric Units+") OR (MH "Pediatric Care")) AND ((MH "Terminal Care") OR (MH "Hospice Care") OR (MH "Palliative Care") OR (MH "Resuscitation Orders"))	**Limiters** - Publication Type: Review **Search modes** - Boolean/Phrase
S5	((MH "Child") OR (MH "Infant") OR (MH "Minors (Legal)") OR (MH "Adolescence") OR (MH "Pediatric Units+") OR (MH "Pediatric Care")) AND ((MH "Terminal Care") OR (MH "Hospice Care") OR (MH "Palliative Care") OR (MH "Resuscitation Orders"))	**Limiters** - Publication Type: Meta Synthesis **Search modes** - SmartText Searching
S4	((MH "Child") OR (MH "Infant") OR (MH "Minors (Legal)") OR (MH "Adolescence") OR (MH "Pediatric Units+") OR (MH "Pediatric Care")) AND ((MH "Terminal Care") OR (MH "Hospice Care") OR (MH "Palliative Care") OR (MH "Resuscitation Orders"))	**Limiters** - Publication Type: Meta Synthesis **Search modes** - Boolean/Phrase
S3	((MH "Child") OR (MH "Infant") OR (MH "Minors (Legal)") OR (MH "Adolescence") OR (MH "Pediatric Units+") OR (MH "Pediatric Care")) AND ((MH "Terminal Care") OR (MH "Hospice Care") OR (MH "Palliative Care") OR (MH "Resuscitation Orders"))	**Limiters** - Publication Type: Meta Analysis **Search modes** - SmartText Searching
S2	((MH "Child") OR (MH "Infant") OR (MH "Minors (Legal)") OR (MH "Adolescence") OR (MH "Pediatric Units+") OR (MH "Pediatric Care")) AND ((MH "Terminal Care") OR (MH "Hospice Care") OR (MH "Palliative Care") OR (MH "Resuscitation Orders"))	**Limiters** - Publication Type: Masters Thesis **Search modes** - SmartText Searching
S1	((MH "Child") OR (MH "Infant") OR (MH "Minors (Legal)") OR (MH "Adolescence") OR (MH "Pediatric Units+") OR (MH "Pediatric Care")) AND ((MH "Terminal Care") OR (MH "Hospice Care") OR (MH "Palliative Care") OR (MH "Resuscitation Orders"))	**Limiters** - Publication Type: Systematic Review **Search modes** - Boolean/Phrase

A.4 Sub-Appendix: LILACS strategy

"cuidado PALIATIVO" or "tratamento PALIATIVO" or "cuidado PALIATIVO a doentes terminais" or "cuidados PALIATIVOs" or "programas de cuidados PALIATIVOs" or "cuidados PALIATIVOs na terminalidade da vida" or "cuidados INTERMITENTES" or "programas de cuidados INTERMITENTES" [Descritor de assunto] and "hospitais pediatricos" or "PEDIATRIA" or "crianca" or "cuidado da crianca" or "saude da crianca" or "servicos de saude da crianca" or "crianca pos-termo" or "crianca pre-escolar" or "criancas" or "criancas pre-escolares" or "ADOLESCENTE" or "ADOLESCENTEs" [Descritor de assunto]

A.5 Sub-Appendix: Grey literature

Organization/Conference	Website
American Academy of Hospice and Palliative Medicine (AAHPM)	http://www.aahpm.org/resources/
American Academy of Pediatrics (AAP)	http://www.aap.org/
American Cancer Society	www.cancer.org
Association for Children with LifeThreatening or Terminal Conditions and their Families (ACT)	http://www.act.org.uk
Center to Advance Palliative Care	www.capc.org
Children's Hospice and Palliative Care Organization	http://www.childrenshospice.org
Children's Hospice International (CHI)	http://www.chionline.org
Children's Oncology Group	www.childrensoncologygroup.org
ChiPPS of the National Hospice and Palliative Care Organization Children's Project on Palliative/Hospice Services (ChiPPS)	http://www.nhpco.org/resources/pediatric-hospice-and-palliative-care

City of Hope Pain & Palliative Care Resource Center (COHPPRC)	http://www.cityofhope.org/PRC/
Education in Palliative and End-of-Life Care (EPEC)	http://www.epec.net/
End of Life Nursing Education Curriculum	www.aacn.nche.edu/ELNEC
End-of-Life/Palliative Education Resource Center (EPERC)	http://www.eperc.mcw.edu/
Hospice and Palliative Nurses Association	www.hpna.org
National Alliance for Children with Life-Threatening Conditions	http://www.nacwltc.org
National Consensus Project on Quality Palliative Care	http://www.nationalconsensusproject.org
The Children's Room	www.childrensroom.org
The Initiative for Pediatric Palliative Care (IPPC)	http://www.ippcweb.org/
CAPC National Seminar 2012 - posters	http://www.capc.org/capc-resources/capc-poster-sessions/
Canadian Hospice Palliative Care Association	http://www.chpca.net/
International Congress in Palliative Care	http://www.palliativecare.ca/en/index.html
Canadian Network of Palliative Care for Children	http://cnpcc.ca/

Appendix B : Study design features for non-observational studies

Article		Fraser LK et al 2013
Allocation		Individual level
Study design		RCS
Study design features		**Support for judgment**
Was there a comparison:		
Between two or more groups of clusters receiving different interventions?	Y	Children referred to a hospice service compared to those not referred within a health authority involving all the hospitals in the area. Regression model also allowed for comparison within group overtime
Within the same group of clusters over time?	Y	
Were participant/clusters allocated to groups by:		
Concealed randomization?	N	Record of acceptance onto the program from the Pediatric Hospice. It's unknow wheter in the same period only 1/3 of the cohort was referred to the hospice program (family preferences, stigma, distance to the hospice, etc)
Quasi-randomization?	N	
By other action of researchers?	N	
Time differences?	N	
Location differences?	U	
Policy/public health decisions?	Y	
Cluster preferences?	U	
Some other process? (specify)	U	
Which parts of the study were prospective:		
Identification of participating clusters?	N	Administrative database analysis - entirely retrospective
Assessment of baseline and allocation to intervention?	N	
Assessment of outcomes?	N	
Generation of hypotheses?	U	
On what variables was comparability between groups assessed:		
Potential confounders?	Y	"- The regression model controlled for confounders including the covariates: age at diagnosis, disease category, gender and deprivation category.
Baseline assessment of outcome variables?	N	
Other potential sources of bias/confouding/limitations/comments		
-There was no comparison of the outcome variable before the "referral" point between the groups to check for baseline differences. - Whether the patients where still in disease-directed treatment in both groups was not measured and/or controlled, and could be an explanatory factor for decrease in planned admissions. - The authors didn't include days spent in hospice for the referred group to complement the total number of admissions for that group. It might conceal some shifting in resource utilization important to be measured in terms of healthcare resources consumption. - In the hospice group, median time from the diagnosis date to referral was calculated by cancer category and then applied to the same category in the control group, to create a point for comparison before/after referral. Interquartile range for time to referral varied widely between categories from 85 to over 1100 days. - Negative binomial regression modeling was used including each person's post referral follow-up time in the model as an exposure term. - The patients who did not linked to the NHS hospital admission system (10.1%) differed from the patients included in this analysis and tended to be male, diagnosed under age of 5, and diagnosed towards the beggining of the stydy period. - Among the patients included in the analysis, the groups did differ in some demographics such as smaller % of patients between 15-19 referred to the hospice services, and disease category of Central Nervous System being the largest group disease among those referred to the hospice.		

Article		**Keele L et al 2013**[8]
Allocation		Individual level
Stydy design		RCS
Study design features		**Support for judgment**
Was there a comparison:		
Between two or more groups of clusters receiving different interventions?	Y	Database from >40 hospital acrros USA. Didn't compare caractheristics over time other than proportion of patients accessing PC services
Within the same group of clusters over time?	N	
Were participant/clusters allocated to groups by:		
Concealed randomization?	N	Based on billing code, which changed overtime according to guidelines for PC
Quasi-randomization?	N	
By other action of researchers?	N	
Time differences?	N	
Location differences?	N	
Policy/public health decisions?	Y	
Cluster preferences?	U	
Some other process? (specify)	U	
Which parts of the study were prospective:		
Identification of participating clusters?	N	Administrative database analysis - entirely retrospective
Assessment of baseline and allocation to intervention?	N	
Assessment of outcomes?	N	
Generation of hypotheses?	N	
On what variables was comparability between groups assessed:		
Potential confounders?	Y	LOS and Cost were not adjusted for other possible confounders, other than geography. Differences in the distributions of some caractheristics were presented (age, health insurance, race, diagnosis)
Baseline assessment of outcome variables?	N	
Other potential sources of bias/confouding/limitations/comments		
- Children who received PC consultations in the last admission before death were different in some characteristics such as older age, race distributions with less access by blacks, having more private insurance, and increase access along the years. - Diseases categories varied significantly. In a subgroup analysis of complex chronic conditions(CCCs) patients (85% of the entire cohort) compared to those not having CCCs, patients with CCCs were more likely to have had a PC consultation (RR 2.2; 95% CI 1.7–2.8). - Comparison included all causes of death, no subgroup analysis for CCC group were presented on the differences in demographics and clinical characteristics. - The authors discussed limitations of the study regards to exclusion of patients discharged under hospice program and admissions < 5 days which may have underestimated the total numbers. - Changes in coding practices and maturation of PC services also represent a potential bias because it cannot be measured.		

Article	**Dussel V et al 2009**[11]	
Allocation	Individual level	
Stydy design	RCS	
Study design features		**Support for judgment**
Was there a comparison:		
Between two or more groups of clusters receiving different interventions?	Y	Cross-sectional survey with retrospective chart review, that originate a retrospective cohort comparison.
Within the same group of clusters over time?	Y	
Were participant/clusters allocated to groups by:		
Concealed randomization?	N	Children from 2 clusters were separate in 2 groups (had or had not planned the LOD by their parents) based in the survey response
Quasi-randomization?	N	
By other action of researchers?	Y	
Time differences?	N	
Location differences?	N	
Policy/public health decisions?	Y	
Cluster preferences?	U	
Some other process? (specify)	U	
Which parts of the study were prospective:		
Identification of participating clusters?	N	Retrospective chart review Cross-sectional survey
Assessment of baseline and allocation to intervention?	N	
Assessment of outcomes?	N	
Generation of hypotheses?	U	
On what variables was comparability between groups assessed:		
Potential confounders?	Y	For the determinants of having or not planned LOD there was some control for confounders. For the health resource utilization no confounding was addressed. The impact of LOD planning on healthcare resources was a secondary outcome and was not controlled for any confounder or further explored.
Baseline assessment of outcome variables?	N	
Other potential sources of bias/confouding/limitations/comments		
- Eligibility of the families depended upon physician's consent, which was declined for 19 families. It might introduce some selection bias. - Only one parent was interview which might have introduced some non-response bias. - Some Interviews were done long time after the fact which might represent somo recall bias (median 3 years). - Response rate 64%. The non-respondents were similar at child's age at death and diagnosis. - The study used regression with stepwise approach to study the determinants of planning LOD and control for confounders. The authors run sensitivity analysis for missing data and by physicians cluster. No differences in the results were shown. - Children with hematological cancer, those who died from treatment related complications, those families who were very religious were less likely to have planned LOD. - Children who had private insurance, families who had experience previous losses, those who reported that oncologist clearly explained treatment options and those who access home care were more likely to have planned LOD.		

Article	**Knapp CA et al 2009**[12]	
Allocation	Individual level	
Stydy design	RCS	
Study design features		**Support for judgment**
Was there a comparison:		
Between two or more groups of clusters receiving different interventions?	Y	Included children from several hospitals and hospice catchment areas within province
Within the same group of clusters over time?	Y	
Were participant/clusters allocated to groups by:		
Concealed randomization?	N	The authors allocated the 2 groups based on claims for hospice services. It has its limitations regarded to unbilled and unpaid services, which was observed since 5 patients in the non hospice users group had died in hospice.
Quasi-randomization?	N	
By other action of researchers?	Y	
Time differences?	N	
Location differences?	N	
Policy/public health decisions?	Y	
Cluster preferences?	U	
Some other process? (specify)	U	
Which parts of the study were prospective:		
Identification of participating clusters?	N	Administrative database entirely retrospective
Assessment of baseline and allocation to intervention?	N	
Assessment of outcomes?	N	
Generation of hypotheses?	U	
On what variables was comparability between groups assessed:		
Potential confounders?	N	There was soubgroup analysis per diagnosis group but no regression was carried, controling for other covariates sucs as gender, race, time enrolled in the insurance to determine the differences between groups in healthcare expenditures. No statistical test was applied to differences between group in healthcare expenditures.
Baseline assessment of outcome variables?	N	
Other potential sources of bias/confouding/limitations/comments		
Although the authours found some patients caractheristics to be associated to more or less hospice use, when analysing the expenditures, only subgroup analysis by diagnostic category were presented. No other factor was control as confounder (gender, race and time enrolled in the Medicaid program, place of death). The authors discussed the limitations of the study such as the limited generalizability for children with private insurance or uninsured, which represents 2/3 of the pediatric population dying in the province.		

Article	**Arland LC et al 2013**[6]		
Allocation	Group Level		
Stydy design	ChBA		
Study design features	**Support for judgment**		
Was there a comparison:			
Between two or more groups of clusters receiving different interventions?	N	Children with brain tumour from a pediatric-oncology in a single hospital that implemented a EOL program	
Within the same group of clusters over time?	Y		
Were participant/clusters allocated to groups by:			
Concealed randomization?	N	Study Before/after the implementation of a standardized EOL program carried by a hospital	
Quasi-randomization?	N		
By other action of researchers?	N		
Time differences?	Y		
Location differences?	N		
Policy/public health decisions?	Y		
Cluster preferences?	na		
Some other process? (specify)	na		
Which parts of the study were prospective:			
Identification of participating clusters?	N	Chart review entirely prospective	
Assessment of baseline and allocation to intervention?	N		
Assessment of outcomes?	N		
Generation of hypotheses?	U		
On what variables was comparability between groups assessed:			
Potential confounders?	N	Authors disclosed not having addressed any potential confounders and dificulties such as missing data (demographics), unclear EOL period before the program was implemented and changes in treatment course/disease management	
Baseline assessment of outcome variables?	na		
Other potential sources of bias/confouding/limitations/comments			
The groups had different criteria to determine EOL period with several individuals in the historical control having that determine by based on radiology reports of the disease progression. It doesn't mean they had been treated as EOL patients. The intervention group had a date for EOL discussion, referral to hospice or complete DNR order. The historical control cohort period was reduced because there was no formal onco-pediatric program previous to this date compromising the quality of data quality. Authors explain exclusion of only 22/52 patients excluded from the initial cohort of 166 patients. The authors aimed to measure symptoms but didn't present any data on that other than hospitalizations. In the discussion session authors stated fewer complication after the implementation of the program but didn't show data. No demographic data comparison was presented. No ethics approval was mentioned. Although the authors extensively stated the limitations for the study such as temporality, demographics information missing, no symptom measurement scale available, maturation of the disease management and EOL care, changes in health insurance policies, no statistical analysis were applied to some outcomes presented.			

Article	**Postier et al 2014** [15]		
Allocation	Individual level		
Stydy design	ChBA		
Study design features		**Support for judgment**	
Was there a comparison:			
Between two or more groups of clusters receiving different interventions?	N	Children enrolled in the PPC program carried by a tertiary provider Pre/Post cost and hospital admissions comparison	
Within the same group of clusters over time?	Y		
Were participant/clusters allocated to groups by:			
Concealed randomization?	N	Authors classified the pre/post period based on the first day to the PPC/hospice program utilization	
Quasi-randomization?	N		
By other action of researchers?	Y		
Time differences?	N		
Location differences?	N		
Policy/public health decisions?	N		
Cluster preferences?	U		
Some other process? (specify)	U		
Which parts of the study were prospective:			
Identification of participating clusters?	N	Administrative database entirely retrospective	
Assessment of baseline and allocation to intervention?	N		
Assessment of outcomes?	N		
Generation of hypotheses?	N		
On what variables was comparability between groups assessed:			
Potential confounders?	Y	Multivariate regression accounting for exposure to the program, disease group and study period	
Baseline assessment of outcome variables?	Y		
Other potential sources of bias/confouding/limitations/comments			
As any other pre/post design without a control group for comparison, if the decrease in LOS and charges observed are due to the PPC program or a natural trend among those type of patients. Its not clear the proportion of patients who died at the hospital/home, which would deeply affect charges closer to death. Selection bias regardless to the referral to the program is always present in this type of program. Charges with home care were not accounted for. Non-parametric test applied to compare the outcomes pre/post doesn't take into account the different time exposed to the program or time/per person/in the post period of the study which may overestimated the diferences pre/post. Authors do not report the estimates from the regressions.			

Article	Gans D et al 2012[9]	
Allocation	Individual level	
Stydy design	ChBA	
Study design features	**Support for judgment**	
Was there a comparison:		
Between two or more groups of clusters receiving different interventions?	Y	Children enrolled in the community palliative care program in California, using several healthcare providers in the different counties
Within the same group of clusters over time?	Y	
Were participant/clusters allocated to groups by:		
Concealed randomization?	N	Before-after enrollment in the program criteria not clearly stated. It seems to be a registry for the enrollees.
Quasi-randomization?	N	
By other action of researchers?	N	
Time differences?	Y	
Location differences?	N	
Policy/public health decisions?	Y	
Cluster preferences?	U	
Some other process? (specify)	U	
Which parts of the study were prospective:		
Identification of participating clusters?	N	Administrative database entirely retrospective
Assessment of baseline and allocation to intervention?	N	
Assessment of outcomes?	N	
Generation of hypotheses?	N	
On what variables was comparability between groups assessed:		
Potential confounders?	N	Authors did not address confounders that could influence the outcomes such as diagnosis type, cities, age, availability of services, proximity to death, etc
Baseline assessment of outcome variables?	N	
Other potential sources of bias/confouding/limitations/comments		
The enrollment in the program depended on financial criteira to be covered by MediCal. Which included life-threatning conditions and were expanded to all conditions expected to consume more than 30days/year of hospital admissions. Not clear if all the patients enrolled in the same point in time, and if the before and after expenditures were flagged as such, independent of how long they were under the program. Unbilled or unpaied claims were excluded from the data, possibily overestimating cost savings. Survey used a likert scale of 4 points the author's called quality of life. No validation mentioned. No control group was used to compare natural trends in shift of healthcare resources utilization. The authors briefly mention certain limitations of the study and the need to use full administrative data with control, to better estimate the differences suggested by this report on the shift of healthcare resource allocation.		

Article	**Pascuet E et al 2010**[10]	
Allocation	Individual level	
Stydy design	ChBA	
Study design features		**Support for judgment**
Was there a comparison:		
Between two or more groups of clusters receiving different interventions?	N	Children who used the respite admission at least once, had their total hospital/hospice admissions measured before and after the access of the first respite
Within the same group of clusters over time?	Y	
Were participant/clusters allocated to groups by:		
Concealed randomization?	N	It is not clear whether the groups were determine by the date of hospice opening, or the date of first utilization of respite services from a pediatric hospice
Quasi-randomization?	N	
By other action of researchers?	N	
Time differences?	N	
Location differences?	N	
Policy/public health decisions?	Y	
Cluster preferences?	U	
Some other process? (specify)	U	
Which parts of the study were prospective:		
Identification of participating clusters?	N	Administrative database entirely retrospective
Assessment of baseline and allocation to intervention?	N	
Assessment of outcomes?	N	
Generation of hypotheses?	N	
On what variables was comparability between groups assessed:		
Potential confounders?	N	Authors did not address confounders that could influence the outcomes such different types of inpatient utilization, diseases categories age or proximity to services.
Baseline assessment of outcome variables?	N	
Other potential sources of bias/confouding/limitations/comments		
The authors stated that the cost for inpatient admissions at the hospital had a fixed cost per day (based on 2007 cost), based on the interprovincial billing rate (including direct healthcare cost and overhead costs). Costs were not differentiated per type of admission - general, critical care. Not clear if costs included emergency and outpatients visits, and how their cost were addressed. Cost for hospice care was calculated by average cost per day , being the anual hospice budget /number of beds per year. It seems that hospice only provided respite care. Not clear if all patients included had 24 months of follow up. Not clear, in case of shorter follow up time, if the outcomes were weighted by time in the study. The authors recognize the limitations of the different cost analysis in each institution.		

Article	**Smith et al 2013** [16]	
Allocation	Individual level	
Stydy design	ChBA/RCS	
Study design features		**Support for judgment**
Was there a comparison:		
Between two or more groups of clusters receiving different interventions?	N	Children discharged from a single tertiary care provider
Within the same group of clusters over time?	Y	
Were participant/clusters allocated to groups by:		
Concealed randomization?	N	Authors classified the groups based on utilization of PPC program consultation
Quasi-randomization?	N	
By other action of researchers?	N	
Time differences?	Y	
Location differences?	N	
Policy/public health decisions?	Y	
Cluster preferences?	na	
Some other process? (specify)	na	
Which parts of the study were prospective:		
Identification of participating clusters?	na	Abstract doesn't bring enough information on the methods
Assessment of baseline and allocation to intervention?	na	
Assessment of outcomes?	na	
Generation of hypotheses?	na	
On what variables was comparability between groups assessed:		
Potential confounders?	N	Authors did not controll for any confounders
Baseline assessment of outcome variables?	N	
Other potential sources of bias/confouding/limitations/comments		
Abstract presented at a conference. It doesn't bring enough information about the methods applied in this research. We are unabled to evaluate risk of bias, selection and identification of participants, intervention definition. The authors didn't control for differences in the population found in the research such as gender, comorbidities, technology dependence.		

Article	Ward-Smith P et al[14]	
Allocation	Group Level	
Stydy design	CC	
Study design features		**Support for judgment**
Was there a comparison:		
Between two or more groups of clusters receiving different interventions?	Y	Cases and controls at 1 hospital who carried the PPC program
Within the same group of clusters over time?	Y	
Were participant/clusters allocated to groups by:		
Concealed randomization?	N	The authors chose the cases and controls, not randomly but made to provide a range of diagnostics and enrollment in the PPCP within 6 months before death.
Quasi-randomization?	N	
By other action of researchers?	Y	
Time differences?	U	
Location differences?	N	
Policy/public health decisions?	N	
Cluster preferences?	U	
Some other process? (specify)	U	
Which parts of the study were prospective:		
Identification of participating clusters?	N	Administrative database entirely retrospective
Assessment of baseline and allocation to intervention?	N	
Assessment of outcomes?	N	
Generation of hypotheses?	N	
On what variables was comparability between groups assessed:		
Potential confounders?	N	None
Baseline assessment of outcome variables?	N	
Other potential sources of bias/confouding/limitations/comments		
Although the authors named the study as case-control, it is technically a cohort comparison, where the cohorts were distinct by the intervention – received services from the pediatric palliative care program. Among the 133 possibles cases identified under the inclusion criteria, 9 were chosen by the authors. This choice was not random but made by the authors to provide a range of diagnostics and because they had being enrolled in the PPCP within 6 months before death. Do not state the matching criteria and if it was randomly selected or, as the cases, chosen by nurses. Not clear if the controls were contemporary to the cases or if they were selected from the period before the implementation of the program. Controls were slightly different in gender, and race. It doesn't specify if the cost was adjusted to reflect the inflation, or if they incurred in the same period for cases and controls.		

Article	Belasco JB et al[13]	
Allocation		
Stydy design	CR/CS	
Study design features		**Support for judgment**
Was there a comparison:		
Between two or more groups of clusters receiving different interventions?	na	
Within the same group of clusters over time?	na	Case series with 3 patients
Were participant/clusters allocated to groups by:		
Concealed randomization?	N	Out of the 154 patients enrolled in the PPCP during the period, some were selected by the author to reflect medically complicated patients whose level of care at home approximatelly equal that in the hospital and differed only in palliative intent rather than intent to cure.
Quasi-randomization?	N	
By other action of researchers?	Y	
Time differences?	N	
Location differences?	N	
Policy/public health decisions?	N	
Cluster preferences?	U	
Some other process? (specify)	U	
Which parts of the study were prospective:		
Identification of participating clusters?	N	Administrative database entirely retrospective
Assessment of baseline and allocation to intervention?	N	
Assessment of outcomes?	N	
Generation of hypotheses?	N	
On what variables was comparability between groups assessed:		
Potential confounders?	na	None
Baseline assessment of outcome variables?	na	
Other potential sources of bias/confouding/limitations/comments		
Do not state how the patients were selected. Do no describe how the number and types of procedures for charges comparison were measured and the comparison was created. It's not clear if the type of prcoedures were compared to a control or if it was estimated to adapt to the home care model for the same patient, or if it was measured from the same patient in both settings. The authors stated that for home care, because the way the insurances operate locally, charges per day did not included physicians home visit, social worker, coordinator of care, skilled nurse visits longer than 2 hours. ALso, visits and procedures not authorized by insurance were not included, which may represent part of the out-of-pocket expenses for families, and not reflected in this comparison. Charges do not appropriately reflect costs introducing important measurement bias.		