**A systematic review and meta-analysis of home-based pain and other physical symptom management interventions for family caregivers of patients with life limiting conditions**

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**Abstract**

**Background**. Patients with life-limiting conditions are often cared for at home by family, typically without adequate training to carry out the challenging tasks performed. This systematic review assessed the efficacy of interventions designed to help family caregivers manage pain and other symptoms in adults and children with life-limiting conditions at home. **Methods**. A systematic search was performed on seven databases. A narrative synthesis was conducted, along with a meta-analysis comparing outcomes in those who received an intervention to those who did not, or to pre-intervention scores. **Results.** Eighty-four eligible studies were identified. Significant improvements in cancer patients’ pain and fatigue were found compared to patients in the control group and compared to baseline. Cancer patient caregivers receiving an intervention, compared control group caregivers, showed significant improvements in self-efficacy and active coping, and lower avoidant coping. This group also showed significant improvements in burden, self-efficacy, anxiety, and depression, and decreases in avoidant coping pre- to post-intervention. Dementia patients whose caregivers received an intervention showed significantly reduced pain intensity and improvements in quality of life pre- to post-intervention. Caregivers of patients with dementia showed significantly reduced distress pre- to post-intervention. No beneficial effects were found for caregivers of patients with Parkinson's disease or heart failure, although only limited analyses could be performed. **Conclusions.** Interventions targeting family caregivers can improve both patient symptoms and caregiver outcomes, as demonstrated in cancer and dementia care. Future mixed-methods research should collect data from caregiver and patient dyads, identifying key intervention components. There is also need for more studies on caregivers of paediatric patients.

**Keywords:** Familycaregivers, Symptom management, Home care, Life limiting condition, Systematic review, Meta-analysis

**Key Messages**

**What is already known on this topic.** Informal caregivers play a vital role in caring for patients with life-limiting conditions, though research mostly focuses on those caring for adults with cancer.

**What this study adds.** (i) Meta-analysis showed interventions targeting family caregivers of patients with cancer and dementia are efficacious at improving both patient symptoms (e.g., pain, fatigue) and caregiver outcomes (e.g., emotional distress); (ii) A comprehensive review of the outcome domains and outcomes measures used in studies evaluating the efficacy of interventions designed to help family caregivers manage pain and other symptoms in adults and children with life-limiting conditions at home. This will serve as a first-step in developing a core outcome set.

**How this study might affect research, practice or policy.** Key areas for future research include developing and evaluating interventions for young caregivers and parents of paediatric patients, as well as developing a core outcome set for patients and caregivers.

**Introduction**

Patients with life-limiting conditions (LLCs) are often cared for at home by family caregivers including spouses, parents, offspring or friends. Home-based care offers several advantages for both caregivers and patients, including increased flexibility, familiarity and comfort, and reduced transportation and financial burden. It also comes with its challenges however, as compared to the education and training formal caregivers such as nurses receive, family caregivers rarely receive adequate training or support to carry out the often complex and challenging tasks required of them [1, 2]. Tasks including assessing and managing symptoms and administering medication can be difficult for caregivers [3], who may be balancing this care alongside their own health needs and/or emotional or psychological difficulties that come with the prospect of a dying relative or friend [4]. Providing care for a family member is often a lonely endeavour [5] associated with considerable burden, including demand on time and resources, physical and mental exhaustion, and health deterioration [6]. When caregivers are adequately supported to perform their caregiving role, caregiving can be viewed as a positive experience however [7].

Numerous studies have developed and evaluated interventions to support the needs of family caregivers, although fewer have examined their efficacy in helping caregivers manage patient symptoms at home. This is important as complex care has increasingly moved from hospitals to homes, leading to a rise in patient self-management and family care [8]. Recent reviews show interventions aimed at caregivers have significant benefits, including improvements in quality of life, depression and anxiety in both caregivers [9] and patients [10]. Interventions have been developed specifically to support caregivers with management of pain medications, with one review suggesting they may have positive impacts on family caregiver knowledge and self-efficacy, even though no effect on patient pain outcomes was found [11]. A meta-analysis of caregiver interventions for individuals with cancer and non-cancer-related chronic pain reported moderate-quality evidence that such interventions were effective in reducing patient pain in the short-term, and very low-quality evidence they were beneficial for caregiver health-related quality of life [12].

While previous reviews of interventions for family caregivers of patients with LLCs have generally reported positive outcomes for both patient symptom management and caregiver wellbeing, most have specifically focused on caregiving of adult cancer patients. Little is known about the efficacy of interventions developed for caregivers of patients with different LLCs irrespective of age. The outcomes of interventions targeting caregivers should be insightful and, to some extent, applicable across various conditions and patient age. This is because LLCs often share significant characteristics and requirements for care [13]. This systematic review focused on interventions developed and tested to support family caregivers manage pain and other physical symptoms in adult and paediatric patients with any LLC when caring for them at home. It addressed the following questions:

1. Are interventions for family caregivers of patients with LLCs efficacious at improving patients’ pain and other physical symptoms?
2. Are interventions for family caregivers of patients with LLCs efficacious at improving caregiver outcomes such as coping or self-efficacy?

**Method**

This systematic review was conducted in accordance with guidelines from the Cochrane Collaboration [14], followed PRISMA reporting guidelines [15] and the protocol was registered on PROSPERO (ID: CRD42020169950 [16]. While there were no major protocol deviations, we used the Quality Assessment Tool for Before-After (Pre-Post) Studies With No Control Group [17] to assess methodological quality of single-group studies, which was not stated in the protocol. This review forms part of a large multi-centre study aiming to improve at-home paediatric palliative care pain management (PARAMOUNT) [18, 19].

**Literature Search**

Searches of the Cochrane Library (title, abstract, keyword), Embase (title), MEDLINE, CINHAL, PsycINFO (title), ProQuest Dissertations & Theses Database (main search field), and OpenGrey (main search field) were conducted from database inception to 27th November 2023. The search strategy is presented in Supplementary Material 1. Relevant keywords were combined from four blocks of search terms that related to: i) life-limiting conditions, ii) informal caregivers, iii) interventions, and iv) symptoms. Secondary searches included checking the reference list of all included studies and related reviews.

**Inclusion Criteria**

Studies were eligible for inclusion if they met the following criteria:

1. Included family caregivers of patients with any condition, illness or disease considered life-limiting or life threatening. All patient and carer age ranges were eligible.
2. Described an intervention in any format (delivered by a healthcare professional face to face, in person or online; paper-based or online) that includes support for carers to carry out tasks relating to physical symptom management in the home. (Interventions were operationalised as any task intended to manage physical symptoms, such as assessing levels of pain and other symptoms, administering medications, performing nursing duties, facilitating physical interventions such as physiotherapy and repositioning, or facilitating psychological interventions such as breathing exercises, relaxation strategies and others).
3. Available in English language.

In this review ‘life-limiting’ was considered any condition that has the potential to shorten a person’s life [20]. ‘Home-based’ was considered any situation in which the patient is cared for either in their own place of residence or the residence of an informal caregiver. Qualitative, quantitative and mixed-method studies were all eligible for inclusion. Studies only including healthcare professionals were not eligible, neither were interventions exclusively providing a health service, rather than an aim to bring about a change in carer behaviour. Studies featuring a controlled or uncontrolled (pre-post) design were eligible for inclusion. PhD theses were eligible, but Masters’ theses and conference presentations were not. All potentially relevant articles were reviewed by DES or SH and checked by CL.

**Data Extraction**

Data and information were extracted using standardised forms. Table S1 presents characteristics of studies included in the systematic review. Table S2 presents a description of the intervention used in each study and comments on the Template for Intervention Description and Replication (TIDieR) review and results [21]. Information in Tables S1 and S2 were extracted by SH and checked by DES, or extracted by DES and checked by CL. Raw numerical outcome data was extracted by DES and checked by SH or CL.

**Study Quality Assessment**

The quality of randomised controlled trials were assessed via the Cochrane Risk of Bias 2 (RoB2) tool [22], and single-group studies were assessed using the Quality Assessment Tool for Before-After (Pre-Post) Studies With No Control Group [17]. For both tools, studies were assessed by two authors and checked by a third author. Full details are provided in Supplementary Material 2

**Outcome Variables and their psychometric properties**

To explore outcome heterogeneity, a list of patient and caregiver outcome domains and measures used in the studies, along with any psychometric properties reported, was extracted by SH, DES or ELS, with details provided in Table S3.

**Data-analysis and Synthesis**

The Cochrane Handbook for Systematic Reviews and Interventions was followed [14]. For between-group comparisons, Hedges’ *g* effect sizes (standardized mean difference) were computed using group means and standard deviations in Comprehensive Meta-Analysis 3.0 [23]. Random-effects models were used which assumes the average effect size varies between studies and therefore heterogeneity is to be expected [24, 25]. Cochrane’s Q and the I² statistic were used to assess study heterogeneity. Cochrane’s Q is the traditional test for statistical heterogeneity, with a significant result indicative of heterogeneity. The I² statistic describes the percentage of variability in effect estimates due to heterogeneity as opposed to sampling error [26]. The Cochrane Collaboration suggest as a rough guide 0% to 40%: might not be important; 30% to 60%: may represent moderate heterogeneity; 50% to 90%: may represent substantial heterogeneity; and 75% to 100% may represent considerable heterogeneity [14]. However, uncertainty in I² is considerable when the number of studies is small. Several studies included more than one intervention group. As it is not appropriate to include data from the same control group more than once in an analysis, in such instances the meta-analysis was conducted separately with data from each intervention group along with the control group.

 For pre- versus post-intervention comparisons, Cohen’s *d* effect sizes (standardized mean difference) were computed based on study means and the average standard deviations [27, 28]. Random-effects models were used to compute average effect sizes using ESCI [27]. An unbiased estimate of the population effect size, referred to as *d*unb, was calculated [27]. As *d* overestimates the population effect size, especially for smaller sample sizes, the adjustment is advocated [27, 29, 30]. Cochrane’s Q and the I² statistic were used to assess study heterogeneity.

Analyses were stratified by disease to capture the similarities of specific diseases in their symptoms, progression, and prognosis, along with similarities in care requirements and associated physical and emotional caregiver burden. We were unable to further stratify analyses by caregiver type because many studies recruited informal caregivers who had a range of different relationships with the patients, with data only provided as an overall group.

**Results**

**Search Results**

A PRISMA 2020 [15] flow diagram depicting the literature search and study selection process is shown in Figure 1. From an initial identification of 24,346 records, 84 studies were eligible for inclusion. Additional articles reporting secondary data or further analyses were also identified and used for study extraction where relevant (five interventions published data across multiple articles).

**Summary of Identified Studies**

Characteristics of the 84 eligible studies are shown in Table S1. Full extracted study details are available on the Open Science Framework (OSF)[31] (<http://tinyurl.com/nc3cjz79>). Fifty-eight studies were conducted in the USA (one of which was also include a site in Canada), three in Hong Kong, Colombia and India, two in Iran, and one study each was conducted in Australia, Colombia, Demark, France, Indonesia, Ireland, Italy, Malawi, the Republic of Korea, Singapore, Sweden, Switzerland, Taiwan, Turkey, Uganda, and the United Kingdom. Seventy-eight studies recruited caregivers of adult patients, of which 58 studies included a patient population with a type of cancer, four studies patients with dementia, four studies patients with heart failure, two studies patients with idiopathic pulmonary fibrosis, two studies with patients with Parkinson’s disease, and one study each including patients with end stage renal disease, HIV/AIDS, stroke, patients who underwent lung resection surgery, and five studies recruiting patients with mixed life limiting diseases (one of which recruited frail older adults with serious illness, but did not provide further details). Six studies recruited caregivers of paediatric patients, including four studies with children with sickle cell disease, one study with children scheduled for cardiac surgery, and one study with children with coagulation factor deficiencies. Thirty-eight studies recruited a mixed sample of informal caregivers, 22 studies specifically stated family caregivers were recruited, 10 studies recruited partners, two studies recruited spouses, two studies stated the majority of caregivers were spouses or partners, two studies specifically stated recruiting parents, and for eight studies the caregivers were not clearly stated.

**Methodological Quality and Intervention Reporting**

Fifty-seven RCTs were assessed via the RoB2 tool [22]. Traffic light plots of the domain-level judgements for each individual study are provided in Figure 2. Twenty-seven non-RCTs studies were assessed using the Quality Assessment Tool for Before-After (Pre-Post) Studies With No Control Group [17], with assessors’ agreed judgments presented in Table S4. Full results are provided in Supplementary Material 2. Intervention reporting was considered via the TIDieR checklist [21] and is summarised in Table S2. All published reports provided a clear rationale for the intervention implemented, and key details such as number of sessions and intervention locations were frequently reported. Several common problems were identified, however. Full intervention materials were provided or accessible in very few publications, making replication difficult without collaboration with the original researchers. Furthermore, many publications did not specifically state whether the intervention was modified in way during the course of the study, or whether assessments of intervention fidelity or adherence were planned or actually conducted.

**Outcome Domains and Outcome Measures and their Psychometric Properties**

A wide range of outcomes were assessed for both patients and caregivers, often via established and validated measures (see OSF [31]: <http://tinyurl.com/nc3cjz79>). For patient outcomes, 13 outcome domains were assessed (e.g., emotional functioning, quality of lie), including 76 sub-domains (e.g., anxiety, depression) assessed via numerous outcome measures (ranging from 56 measures of emotional functioning, to 1 measure each of financial well-being and preferred place of care). For caregiver outcomes, 11 outcome domains were assessed (e.g., caregiving experience and attitudes, interpersonal functioning), including 53 sub-domains (e.g., self-efficacy, burden) also assessed via numerous outcome measures (ranging from 53 measures of emotional functioning to 1 measure each of physical well-being, patient pain, preferred place of care and spiritual well-being). It is notable that across patients and caregivers certain potentially important domains were rarely assessed, including spiritual well-being and financial well-being. Tree charts depicting caregiver and patient domains and sub-domains are shown in Supplementary Figures 1 and 2 respectively. Researchers often provided rationale for their choice of specific outcome domains and measures. Table S3 provides the reported psychometric properties of the outcome measures used in each study as computed on the specific samples recruited. Many studies did not compute and report psychometric properties, although when performed was most frequently internal consistency via Cronbach’s alpha. While internal consistency was acceptable or better in many cases, several studies reported Cronbach's alpha values <.70, indicating questionable reliability. Test-retest reliability was less commonly assessed, although most would be considered good or better (< .70).

**Narrative Review Summary**

A narrative review providing a summary of the 84 studies is provided on the OSF [31] (<http://tinyurl.com/nc3cjz79>). Interventions varied widely in their aims and design, although most reported one or more statistically significant beneficial outcomes. Many interventions were aimed at caregivers caring for adult patients with cancer and which report beneficial outcomes for patients and caregivers, although individual studies also typically report numerous outcomes which did not show statistically significant improvements. Fewer interventions were aimed at caregivers of patients with other medical conditions, although at least some benefits have been reported by caregivers or patients with dementia, AIDS/HIV, end stage renal failure, stroke, Parkinson’s disease, and idiopathic pulmonary fibrosis. Only six studies provided interventions to support informal caregivers of paediatric patients with LLCs. One reported significant increases in knowledge and attitudes towards pain medication from pre- to post-intervention in parents managing pain after their child’s cardiac surgery [32]. Another reported significant reduction in caregiver burden and improvements in social adjustment were reported by caregivers in the intervention group compared to caregivers in the control group, along with significant decreases in patient acute pain and bleeds [33]. The remaining four studies explored interventions for children with sickle cell disease, all of which reported some positive outcomes [34-37].

**Meta-Analyses of Patient Outcomes**

**Within-group Analyses**

Statistical analyses for within-groups analyses are provided in Table S5 and overall pooled effect sizes in Figure 3. Full written analyses are provided in Supplementary Material 3, and individual forest plots in Supplementary Figure 3. The only significant effects were for cancer and dementia populations. Cancer patients whose caregivers received an intervention reported significant improvements in pain and fatigue pre- to post-intervention. Cancer patients whose caregivers were allocated to a control group also showed significant reductions in pain pre- to post-intervention, but this was only after a sensitivity analysis removed one study with a large effect size that could be considered an outlier and should be interpreted with caution. Caregivers of cancer patients receiving an intervention showed significant improvements pre- to post-intervention in burden, self-efficacy, anxiety and depression, and decreases in avoidant coping. The improvement in self-efficacy was no longer statistically significant however after a sensitivity analysis was performed removing one study with a large effect size that could be considered an outlier. Dementia patients whose caregivers received an intervention showed significantly reduced pain intensity and improvements in quality of life from pre- to post-intervention. Caregivers of patients with dementia showed significantly reduced distress from pre- to post-intervention.

**Between-groups Analyses – Patient Outcomes**

Full statistical results are presented in Table S6, overall pooled effect sizes in Figure 4, and forest plots for individual analyses in Supplementary Figure 4.

**Cancer – Patient-reported pain and fatigue outcomes.** Six studies provided data comparing pain outcomes in patients whose caregivers received an intervention to patients whose caregivers were in a control group [38-43]. Patient pain intensity was significantly lower in the intervention group than the control group (Hedges’ *g*= -0.421 (95% CI = -0.783, -0.059), *p* < .023). A sensitivity analysis was conducted removing studies which provided attentional control or enhanced treatment-as-usual comparison conditions [41-43], with the results remaining significant (*g*= -0.404 (95% CI = -0.709, -0.098), *p* = .010).

Four studies provided data comparing fatigue outcomes in patients whose caregivers received an intervention to patients whose caregivers were in a control group [39, 42-44], one of which randomised patients and caregivers to either reflexology or meditative practice intervention groups [44]. Patients in the intervention group reported significantly lower fatigue post-intervention than patients in the control group when data was included from the reflexology group (*g*= -0.278 (95% CI = -0.466, -0.091), *p* = .004), and meditative practice group (*g*= -0.232 (95% CI = -0.421, -0.044), *p* = .016).

**Between-groups Analyses – Caregiver Outcomes**

 **Cancer – Caregiver burden**. Five studies provided burden data for caregivers of cancer patients who received an intervention compared to caregivers in a control group [39, 41, 42, 45, 46], one of which included reflexology and meditative practice intervention groups [46]. No significant difference was found in caregiver burden post-intervention between intervention and control groups, either when data was included from the reflexology group (*g*= -0.286 (95% CI = -0.748, 0.176), *p* = .225) or the meditative practice group (*g*= -0.309 (95% CI = -0.763, 0.145), *p* = .182). The analyses were repeated removing studies which included control groups featuring a sixty minute reading session to the patient [42] or enhanced treatment-as-usual [41]. The results remained non-significant when data was included from the reflexology group (*g*= -0.278 (95% CI = -1.226, 0.671), *p* = .566) or the meditative practice group (*g*= -0.316 (95% CI = -1.230, 0.598), *p* = .498).

**Cancer – Caregiver self-efficacy**. Six studies provided self-efficacy data for caregivers of cancer patients who received an intervention compared to caregivers of cancer patients who received usual care [40, 41, 47-50], one of which included extensive FOCUS and brief FOCUS intervention groups [49]. With data from the extensive FOCUS group included, caregivers receiving the intervention reported significantly greater self-efficacy post-intervention compared to caregivers in the usual care condition (*g*= 0.301 (95% CI = 0.036, 0.565), *p* = .026). No significant effect was found when data from brief FOCUS group was included [49] (*g*= 0.289 (95% CI = -0.017, 0.595), *p* = .064).

These analyses were repeated excluding one study which included an enhanced treatment-as-usual control condition [41]. The result remained significant when including the extensive FOCUS group (*g*= 0.378 (95% CI = 0.025, 0.732), *p* = .036), and non-significant when including the brief FOCUS group (*g*= 0.365 (95% CI = -0.048, 0.777), *p* = .083).The analysis was repeated with data from three studies recruiting patients with prostate cancer specifically [47, 48, 50], with no significant difference found between groups (*g*= 0.356 (95% CI = -0.086, 0.798), *p* = .114).

**Cancer – Caregiver anxiety**. Five studies provided anxiety data for caregivers of cancer patients who received an intervention compared to caregivers of cancer patients who received usual care [41, 45-47, 51]. No significant difference was found in caregiver anxiety post-intervention between caregivers receiving interventions and those in a control group, either when data from the reflexology group (*g*= 0.105 (95% CI = -0.260, 0.470), *p* = .572) or the meditative practice group (*g*= 0.072 (95% CI = -0.269, 0.413), *p* = .679) was included from one study [46]. The analyses were repeated removing one study which included an enhanced treatment-as-usual control condition [41]. The results remained non-significant when data was included from the reflexology group (*g*= 0.268 (95% CI = -0.068, 0.604), *p* = .118) or the meditative practice group (*g*= 0.226 (95% CI = -0.104, 0.556), *p* = .180).

**Cancer – Caregiver depression**. Six studies provided depression data for caregivers of cancer patients who received an intervention compared to caregivers of cancer patients who received usual care [41, 45-47, 51, 52]. No significant difference was found in caregiver depression post-intervention between caregivers receiving interventions and those in a control group, either when data from the reflexology group (*g*= 0.002 (95% CI = -0.289, 0.292), *p* = .992) or the meditative practice group (*g*= -0.108 (95% CI = -0.300, 0.084), *p* = .270) was included [46]. The analyses were repeated removing one study which included an enhanced treatment-as-usual control condition [41]. The results remained non-significant when data was included from the reflexology group (*g*= 0.081 (95% CI = -0.254, 0.416), *p* = .636) or the meditative practice group (*g*= -0.034 (95% CI = -0.283, 0.215), *p* = .789).

**Cancer – Caregiver coping.** Three studies provided data for caregivers of cancer patients who received an intervention compared to caregivers of cancer patients who received usual care [49, 50, 53], one of which included extensive FOCUS and brief FOCUS interventions [49]. Significantly higher active coping was reported by caregivers in the intervention group than the usual care group when data was included from the extensive FOCUS group (*g*= 0.214 (95% CI = 0.054, 0.374), *p* = .009) and brief FOCUS group (*g*= 0.249 (95% CI = 0.088, 0.409), *p* = .002). Analysis with data from the extensive FOCUS group included revealed significantly lower avoidant coping reported by caregivers in the intervention group than the usual care group (*g*= -0.215 (95% CI = -0.405, -0.024), *p* = .027). When data from the brief FOCUS group was included, no significant difference was found (*g*= -0.080 (95% CI = -0.241, 0.080), *p* = .325).

 **Heart failure.** Two studies provided data for caregivers who received an intervention compared to caregivers who received usual care [54, 55]. No significant difference was found between the intervention and usual care conditions for anxiety (*g*= 0.170 (95% CI = -0.181, 0.521), *p* = .342), depression (*g*= 0.036 (95% CI = -0.315, 0.386), *p* = .841), burden (stress) (*g*= -0.095 (95% CI = -0.433, 0.243), *p* = .582), or quality of life (*g*= 0.211 (95% CI = -0.316, 0.738), *p* = .433).

**Discussion**

 Interventions targeting family caregivers can improve both patient symptoms and caregiver outcomes. Cancer patients whose caregivers received an intervention reported significantly lower pain and fatigue post-intervention compared to patients whose caregivers were allocated to a usual care control group with small to medium effect sizes, and also compared to pre-intervention scores with small effect sizes. Caregivers of cancer patients receiving an intervention reported significantly greater self-efficacy and active coping, and significantly lower avoidant coping, post-intervention compared to caregivers allocated to a usual care condition. Caregivers receiving an intervention also reported significant increases in self-efficacy (although this effect was no longer statistically significant after a sensitivity analysis was performed), and significant decreases in caregiver burden, anxiety, depression and avoidant coping, pre- to post-intervention. These results were associated with small effect sizes and align with previous reviews which report a range of beneficial outcomes for caregivers (e.g., [10, 11, 56-58]), although former reviews assessing patient outcomes produced mixed results and conclusions (e.g., [12, 59, 60]).

Dementia patients whose caregivers received an intervention experienced significant reduction in pain intensity and improvements in quality of life post-intervention with medium effect sizes. Additionally, caregivers of these patients reported significantly less distress post-intervention with a medium effect size. These preliminary results are promising considering the high prevalence of pain in individuals with dementia living in the community and its impact on both patients and caregivers [61]. Indeed, family members wish for more involvement in pain management, but fear analgesics' side effects (61). It is crucial to develop pain management interventions for patients with dementia, facilitated by caregivers [62]. Most current research on pain evaluation and management in people with dementia focuses on those in advanced stages of the disease residing in long-term care facilities however [63], and as such we were able to conduct only a few analyses.

With appropriate clinical support, family caregivers can assist in the management of patient pain and other symptoms at home. While meta-analyses did not show significant improvements for caregivers for patients with Parkinson’s disease or heart failure, only limited analyses could be conducted on data from a small number of studies. Inspection of individual studies does show, in certain instances, beneficial outcomes in patients with Parkinson’s disease and their caregivers [64] and patients with heart disease and their caregivers [65], although not in all studies [54, 66, 67]. Beneficial outcomes have also been reported in individual studies exploring interventions for other LLCs that we were unable to meta-analyse, including for example stroke [68], HIV/AIDS [69], and end-stage renal disease [70]. Overall, these findings are especially important as, due in part to rapidly aging populations, many Western countries aim to meet the needs of long-term care via informal/family caregivers [71]. Many individuals who are dying also express a wish to die at home [72]. Appropriate support is therefore vital for the patient. As family caregivers are not professionally trained however, they may experience clinically significant levels of distress and impairments in quality of life [73], and associations between caregiver distress and patient outcomes are frequently reported (e.g., [74-76]).

Despite an increasing prevalence of LLCs in children and adolescents (67), only six studies in this review involved interventions targeting caregivers of paediatric patients. Although some positive outcomes were reported in all studies, it was not possible to perform any meta-analyses. Pain is a common symptom reported in children with LLCs, management of which is essential [77]. A recent review [19, 78] explored barriers and facilitators of paediatric pain and other symptom management at end of life, and providing medication was viewed as helpful by family caregivers in improving or managing the child’s symptoms. Barriers included inadequate assistance with administering or managing treatment, and treatment side effects. Additional fears when caring for their child at home included failure to control symptoms such as pain, or potentially making their child worse if they gave too much medication. Symptom management was facilitated when parents received information, advice or education from healthcare professionals or disease-specific organisations. Overall, it was concluded families would benefit from increased education and training, along with social and practical support.

Methodological quality assessment of the reviewed studies revealed several important limitations. First, not all studies reported following an intervention development framework such as the Medical Research Council’s framework for the development and evaluation of complex interventions [79, 80]. Second, while interventions were well-described in most reports, access to the actual intervention material such as treatment manuals, websites, videos or audio recordings were not provided. Full details are necessary to comprehend, replicate, and expand upon the reported interventions [81, 82]. Third, not all studies collected data at multiple follow-up points. While most studies provided evidence for some beneficial patient or caregiver outcomes following the intervention, it is important to ascertain whether these are maintained across time. Fourth, the use of heterogeneous outcomes across interventions can lead to research waste, restricting the comparison and combination of results in meta-analyses [83, 84]. The development of a core outcome set for caregivers is now timely, and this systematic review provides a comprehensive foundation of outcome domains and measures used to date [85]. Certain outcomes such as quality of life and self-esteem were frequently assessed by studies, although other important outcomes such as spiritual well-being, financial functioning and even intervention feedback were much less commonly assessed. Furthermore, while most studies used validated outcome measures with established psychometric properties, they often failed to report specific properties like Cronbach's alpha. We recommend that all studies—particularly those using modified versions of established measures or bespoke outcome measures—should report psychometric properties as standard practice.

**Strengths and Limitations.**  Strengths of this review include the breadth of focus on all life-limiting conditions and the inclusion of informal caregivers of both adult and paediatric patients. Additionally, this review included both RCTs and observational studies, enabling us to comment on both the effectiveness and efficacy of interventions respectively. RCTs with a low risk of bias are undoubtedly the most methodologically robust design for evaluating health interventions due to random allocation and causal inference. Meta-analysis of RCTs is vital but limited by strict patient selection criteria, generally short follow-ups, and high costs for the identification of rare events. Non-randomised studies of interventions (NRSIs) may better represent real-world clinical practice and can complement or replace RCTs, especially when RCTs are impractical or unethical. Both RCTs and NRSIs are valuable, and efforts exist to integrate them to enhance evidence certainty (e.g., [86-89]). Unlike other recent reviews (e.g., [9, 10, 57, 58, 90, 91]), this review provides a comprehensive list of patient and caregiver outcome domains and measures, including their psychometric properties. This represents a crucial first step toward developing a core outcome set. A limitation of this review is that many of the meta-analyses conducted were based on a small number of studies, many of which showed high statistical heterogeneity. While we acknowledge the limitations of such analyses which warrant caution in their interpretation, we believe it is important to perform and report meta-analyses where they are conceptually and theoretically meaningful.

**Future Research.** Research is needed to elucidate which individual components of a successful intervention are the most important in terms of overall observed effects, as it is possible that time-consuming and expensive components may contribute very little to the beneficial outcomes observed [92]. Several different approaches may help address this. Involving patients in intervention design and development is crucial for identifying appropriate research questions and assessment outcomes, and we suggest including family caregivers as well wherever possible. [93, 94]. Furthermore, following a framework such as the multiphase optimization strategy (MOST) would allow researchers to evaluate and optimise their interventions [92, 95]; none of the interventions described in the present review reported following a framework such as MOST. Many interventions include ‘bundled’ content, which is typically compared to a comparator in an RCT to determine overall efficacy. Such an approach cannot definitively guide subsequent steps to improve the effectiveness, efficiency, economy, or scalability of the intervention [95].

Young carers are increasingly included in caregiving tasks [96] which is perceived as challenging and complex [97]. This review did not find any interventions specifically targeted to young people however, which is a critical area for future research. Additionally, to develop, evaluate and implement interventions that address the complex network of direct and indirect factors impacting the health and well-being of caregivers and patients, future research needs to be guided by caregiving theoretical frameworks [98, 99]. Regardless of whether the primary goal is to improve patient symptoms or caregiver coping, we recommend outcome measures for both patients and caregivers are standardized. A reciprocal relationship exists between the wellbeing of patients with LLCs and the wellbeing of their family caregivers (e.g., [100, 101]). We also recommend more studies add qualitative components to their intervention evaluations, interviewing both patients and caregivers regarding their thoughts and experiences. Only eight studies used a mixed-methods approach in this review (and one used qualitative methods only), although methods such as interviews and focus groups can help identify factors affecting outcomes such as variation in intervention delivery and engagement, contexts helping or hindering intervention delivery, and participants’ interactions with different intervention components [102, 103].

Researchers should also carefully consider data collection points and provide clear theoretical or clinical justifications for their decisions. In this meta-analysis post-intervention data collection points varied between studies, and also within some studies (e.g., [39, 40]). While this was a source of heterogeneity between studies, heterogeneity statistics were not always significant/high in the meta-analyses conducted. Furthermore, the first follow-up point utilised in the analyses was the one the authors expected to see results from their intervention, and even though they are not chronologically the same across studies they are conceptually equivalent. Finally, long-term follow-ups are needed, although cost-effectiveness is a pragmatic constraint to their implementation [104, 105].

 **Conclusion.** Interventions targeting family caregivers of patients with LLCs such as cancer and dementia are effective at improving patient symptoms and caregiver outcomes. Future research using mixed-method methodologies should aim to collect data from patient and caregiver dyads, identifying key components of complex interventions, and involving patients and caregivers in the design and evaluation of interventions as equal partners with researchers and clinicians. There is also an urgent need for studies on paediatric patients and their caregivers.

**Declarations**

**Ethical approval**: This study does not involve human participants

**Consent for publication**: All authors contributed to the final written manuscript and have provided approval for publication.

**Availability of data and materials**: Data and materials are available from the corresponding author on reasonable request. Additional supplementary material is available on the Open Science Framework (<http://tinyurl.com/nc3cjz79>).

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**Author contributions**: CL is the Chief Investigator of the PARAMOUNT study and conceived the project, designed the protocol and takes overall responsibility for the conduct of this systematic review and meta-analysis. CL is responsible for the overall content and is the guarantor. DES and SH planned and designed the study protocol, planned and performed the data extraction and statistical analyses and wrote drafts of the manuscript. ELS performed data extraction, contributed to data analysis and interpretation, and assisted in manuscript write-up. KR, SSJ, MJ and EH provided critical insights. All authors have approved and contributed to the final written manuscript.

**Competing interests**: The authors declare that they have no competing interests.

**Figures**

Figure 1. PRISMA 2020 flow of records for inclusion in the systematic review and meta-analyses of home-based physical symptom management interventions for family caregivers of patients with life limiting conditions

Figure 2. Traffic light plots of the domain-level judgements for each individual randomised controlled study assessed via the Cochrane Risk of Bias 2 tool

Figure 3. Forest plot showing overall pooled effect sizes for each patient and caregiver within-group analysis conducted in a meta-analysis of home-based physical symptom management interventions for family caregivers of patients with life limiting conditions

Figure 4. Forest plot showing overall pooled effect sizes for each patient and caregiver between-groups analysis conducted in a meta-analysis of home-based physical symptom management interventions for family caregivers of patients with life limiting conditions

**Supplementary Materials**

Supplementary Material 1. Search strategy.

Supplementary Material 2. Study Quality Assessment Tools, Procedures and Results

Supplementary Material 3. Within-groups analyses

Supplementary Figure 1. A tree chart showing outcome domains (inner circle) and where applicable sub-domains (outer circle) assessed in caregivers of patients with life-limiting conditions

Supplementary Figure 2. A tree chart showing outcome domains (inner circle) and where applicable sub-domains (outer circle) assessed in patients with life-limiting conditions

Supplementary Figure 3. Within-group forest plots for individual analyses

Supplementary Figure 4. Between-groups forest plots for individual analyses

Table S1. Characteristics of eligible studies included in the systematic review

Table S2. Description of the intervention used in each study, comments on Template for Intervention Description and Replication (TIDieR) review and results

Table S3. Reported psychometric properties of patient and parent outcome variables used in each study included in a systematic review and meta-analysis of home-based physical symptom management interventions for family caregivers of patients with life limiting conditions.

Table S4. Methodological quality assessments for pre-post single group interventions included in a systematic review and meta-analysis of home-based physical symptom management interventions for family caregivers of patients with life limiting conditions.

Table S5. Within-groups meta-analyses of pre- to post-intervention change scores for patient and caregiver outcomes

Table S6. Between-groups meta-analysis effect sizes for patient and caregiver outcomes

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