# The effectiveness of nurse-led interventions for cancer symptom management 2000–2018: A systematic review and meta-analysis☆

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## ABSTRACT

*Background:* Evidence for effectiveness of nurse-led interventions for cancer-related symptoms is of variable quality. This study aimed to identify, appraise and evaluate the nature and effectiveness of nurse-led interventions on symptoms for people with cancer.

*Methods:* A systematic review and meta-analysis. Ten major databases were searched (2000 to 2018, no language restrictions). Two reviewers applied *a priori* selection criteria; data extraction included design, population, cancer type, and cancer-related symptoms. Interventions and providers were profiled using TIDieR reporting guidelines, and content analysis of components. Methodological quality was assessed using Cochrane risk of bias. A meta-analysis was performed using mean and standardised mean differences with 95% confidence intervals. Overall certainty was assessed using GRADE.

*Results:* From 29193 records, 149 studies ($n = 107286$ participants) from 22 countries were eligible. Interventions included multiple components; education and psychological approaches dominated. Pooled meta-analyses found evidence of benefit for nurse-led interventions on measures of constipation (MD −4.54, 95% CI −8.08 to −0.99; 645 participants; 6 trials; $I^2 = 0\%$; $P = 0.01$); nausea and vomiting (MD −1.97, 95% CI −3.61 to −0.33; 957 participants; 8 trials; $I^2 = 12\%$; $P = 0.02$) and fatigue (MD −4.63, 95% CI −7.97 to −1.30; 1208 participants; 11 trials; $I^2 = 34\%$; $P = 0.007$). Psychological morbidity (anxiety, depression, mood) also improved. However, few trials used consistent outcome measures, interventions were poorly defined, and certainty of evidence was low or very low.

*Conclusion:* Nurse-led interventions improve specific cancer-related symptoms, including psychological morbidity. Enhanced reporting and collaboration to develop a minimum core dataset would strengthen the quality of evidence.

## Introduction

Cancer is the second leading cause of death worldwide and presents a growing disease burden that requires innovative responses from all health system sectors [85]. An estimated 19.3 million new cancer cases (18.1 million excluding nonmelanoma skin cancer) and almost 10.0 million cancer deaths (9.9 million excluding nonmelanoma skin cancer) occurred in 2020 [72]. However, global surveillance studies also show significant improvements in the 5-year survival rate for the most common cancer types [3]. The impact of living with a cancer diagnosis and the effects of cancer treatment are incalculable, with troublesome symptoms arising from the disease or treatment being a major concern. Although many different cancer clinicians contribute to symptom assessment and management, cancer nurses involved in supportive cancer care tend to work most closely with patients in the assessment and management of their symptoms.

Many cancers result in permanent disability requiring significant long-term care and intervention. Treatment protocols are often physically demanding, potentially life threatening and protracted – lasting months or years in some cases. People living with and beyond cancer commonly experience troublesome symptoms such as fatigue [46,81], pain [1,8,10,69,86], constipation [33,68,90], nausea and vomiting [15,18,23] and sexual dysfunction [2,5,22], even after treatment is complete. The impact of cancer for the individuals, their families and wider society highlights the importance of effective management of these negative sequelae, especially ongoing symptoms which can disrupt everyday life and serve as constant reminders of a cancer diagnosis. As most patients with advanced cancer experience multiple symptoms, symptom management should be approached in a multi-dimensional way [74].

Nurse-led interventions, that is, interventions that are predominantly provided by nurses aim to improve the physical and psychosocial well-being of people living with and beyond cancer. A recent scoping review identified a diverse range of foci, including assessment, direct care, psychological support, teaching, guidance and monitoring, care management and coordination [16]. A variety of novel nurse-led interventions have been described, including supportive interventions to address unmet needs, such as treatment side effects [76], and provision of education and support during complex cancer treatment regimens [41].

Although clinical practice and current guidelines describe the benefit of nurse-led interventions [11,50,54,79], robust evidence of the effectiveness of particular approaches is often lacking [51]. Several systematic reviews and meta-analysis of cancer-specific [25] or symptom-specific nurse-led interventions [37,39,43,73] have been conducted. However, the evidence-base is conflicting [77] and usually focused on a single part of the trajectory [48], one type of cancer [11] or isolated symptoms [39,67]. Reviews focussed on cancer nursing have also been criticised for failing to use innovative review methodology to synthesise the best available evidence with little integration of patient and public involvement in reviews [51].

Despite some promising results, we have little insight about whether and how nurse-led interventions enable symptoms to be managed more effectively in people with cancer across the disease trajectory. These outcomes were prioritised by a wide group of stakeholders, including patient and frontline clinicians, as a key gap in the evidence base. This study aimed to investigate (a) whether cancer nurse-led interventions are more effective than no treatment, usual care or attention control comparisons and (b) whether there is any evidence of benefit post-intervention.

## Methods

### Design

A systematic review and meta-analysis was conducted using established methods described in the Cochrane Handbook for Systematic Reviews (Version 5.1.0) [34], and reported in accordance with the PRISMA statement for reporting on systematic reviews [44]. Selection criteria and analysis were pre-specified and have been published in a protocol [14].

### Search strategy and selection criteria

We defined nurse-led interventions as studies in which nurses had explicitly been involved in delivering the intervention. Trials in which nurses facilitated the intervention as part of a wider multidisciplinary team were excluded.

We searched ten electronic databases and clinical trial registers: CENTRAL, MEDLINE, AMED, CINAHL, EMBASE, Epistemonikos, CDSR, DARE, HTA and clinical trial registers (WHO ICTRP) from 01 January 2000 to 18 January 2018. We conducted backward citation tracking on all included studies and contacted researchers and experts in the field to identify other potentially relevant (published, unpublished and ongoing) randomised controlled trials (RCTs) and controlled before-and-after (CBA) studies of nurse-led interventions. No language restrictions were applied. An example search string is shown in Supplementary Table 1.

### Data collection and extraction

One reviewer (PC) examined searches and eliminated irrelevant titles. Two reviewers (CT and PC) independently screened remaining abstracts and full texts that met selection criteria. Disagreements were resolved through discussion, and a third reviewer (MW) if required. Researchers did not review any studies in which they had any involvement. Data were extracted to a standardised, pre-piloted form based on TIDieR reporting guidelines [35]. Data were extracted by one review author (PC or CT) and independently checked by another review author. Missing information was requested from study authors where possible.

Baseline and follow-up data (mean and standard deviation, or other summary statistics as appropriate) for relevant outcomes for an 'immediate' time point – recorded at the end of the intervention period; and for a 'follow-up' time point were extracted. Where post-intervention follow-up timepoints were not clearly reported, we extracted the final data. Where multiple follow-up time points were clearly reported, data which reflected the following time points were extracted and categorised:

- short-term (<3 months to 6 months post-intervention).
- medium-term (>6 to 12 months post-intervention).
- longer-term (>12 months post-intervention).

### Assessment of methodological quality

### Quality of included studies

Risk of bias (ROB) was independently judged as 'low risk', 'unclear' or 'high risk' by pairs of review authors using the Cochrane risk of bias tool [34]. Trials were assessed for methodological quality, paying attention to whether there was protection from the following types of bias:

- Selection bias (i.e., true random sequencing and true concealment up to the time of allocation).
- Performance bias (i.e., differences in co-interventions between the groups).
- Attrition bias (i.e., withdrawal after trial entry).
- Detection bias (i.e., 'unmasked' assessment of outcome).
- Selective reporting.
- Other types of bias.

Disagreements were resolved by discussion, with involvement of a third review author where necessary.

### Quality of evidence reported in the included studies

Two reviewers (PC, CT) assessed and documented the quality of evidence based on the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach [31].

The quality of a body of evidence was downgraded for a specific outcome based on five factors:

- Limitations of study (e.g., risk of bias due to poor study design or conduct) [30].
- Indirectness of evidence (e.g., variations in participants, interventions, comparisons and outcomes) [27].
- Inconsistency of results (e.g., large $I^2$) [28].
- Imprecision of results (e.g., wide confidence intervals for treatment effect) [26].
- Publication bias [29].

The GRADE approach uses four levels of quality, that is, high, moderate, low, and very low-quality evidence, based on the following definitions:

- High quality: It is unlikely that further research will change our confidence in the estimate of effect.
- Moderate quality: Further research is likely to have an impact and may change the estimates.
- Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect.
- Very low quality: Any estimate of effect is very uncertain.

*Data synthesis and statistical analysis*

Data were tabulated and summarised in a narrative format. Where suitable statistical summary data were available, we combined selected outcome data in pooled meta-analyses using the Cochrane statistical package (Revman v5.4.1) [75]. Mean difference (MD), standardised mean difference (SMD) and 95% confidence intervals were used for continuous data. Where we observed important heterogeneity (based on the $I^2$ value together with significant evidence of heterogeneity as per the $Chi^2$ test P-value), we used a random-effects model [34]. A sensitivity analysis was also conducted for studies with significant heterogeneity by removing studies with high ROB.

We used adjusted data for clustering if provided. However, if no adjustment had been made then the raw data were adjusted using the intracluster correlation coefficient (ICC) and methods described in chapter 23 of the Cochrane Handbook [34]. If the ICC was not reported for a study, then we used the ICC for the study's own sample size calculation instead. For the purposes of this review and the meta-analyses, we have presented and pooled the data within multi-arm RCTs as randomised paired comparisons (indicated as i, ii or iii). As these multi-arm trials present a potential risk for including the same group of participants (usually the control group) twice in a single meta-analysis, we split the number of participants in the control group across the two 'trials' that shared that comparison group [34]. In the case of continuous data, the mean and SD values remained the same.

Where feasible, we planned to conduct subgroup analyses [14] using an established method [21] to investigate the effect of:

- Cancer diagnosis.
- Stage of cancer (prevention, early diagnosis, survivor, end-stage cancer).
- Category of cancer nurse involved (general nurse/specialist nurse/oncology nurse specialist).
- Age group as reported by trialists (e.g. "paediatric"/"young adult or young person"/"adult"/"older adult").

*Content analysis*

In a wider scoping review of the literature on nurse-led interventions [16], we had used the OMAHA classification system to summarise whether the interventional approach was: Case Management; Surveillance; Teaching, Guidance and Counselling; or Treatment and Procedures. In this review, two authors (MW, DK) also examined the description (verbatim) of each intervention provided in each included trial, and

based on the content of intervention descriptions, determined whether the intervention included any of the following components: behavioural; psychological; educational; lifestyle (e.g., physical activity, diet, smoking). Details of the treatment components of the active interventions for those trials included within the meta-analyses are provided in Table 1.

## Results

*Study selection*

Our systematic search identified 29193 records, of which 28178 were excluded following review of the title or abstract as they did not meet the selection criteria or were duplicates. 1015 full text papers were reviewed, of which 149 studies were eligible for inclusion in this systematic review. Results of the study flow are displayed in Fig. 1.

*Description of included studies*

Studies employed different designs including quasi-RCT, parallel-RCT, cluster-RCT and multi-arm RCTs (Supplementary File 2). Seventeen studies employed a non-randomised design (Supplementary 2). The studies were conducted in 22 different countries, with most studies carried out in the US ($n = 46$) and in the UK ($n = 22$). The geographical distribution of the included studies is presented in Supplementary File 3.

The number of participants ($n = 107,286$) ranged from 8 to 49,311 in each study with most interventions targeting an adult population. Most trials included less than 500 participants, but there were two screening trials with several thousand participants, hence the wide range [61,63]. Key participant characteristics are summarised in Supplementary File 4. Most trials (77%) were focused on the phase of cancer treatment ($n = 114/149$); but nurse-led cancer interventions were delivered across the entire trajectory. Interventions were mainly hospital-based and usually delivered on an individual basis ($n = 138$) and face-to-face. However, interventions were also delivered to groups ($n = 6$) [7,12,13,42,52,53,64]; three studies included group and individual interventions [32,58,59,65] using a variety of delivery models (telephone $n = 20$; online $n = 5$, combination of face-to-face, telephone and/or online $n = 73$) (Supplementary Table 2).

*Methodological quality*

Overall study quality was variable. Risk of bias is summarised in Fig. 2 and detail of authors judgements are presented in Supplementary file 5. Seventeen studies employed a non-randomised design, so we were unable to draw any conclusions about their randomisation or allocation methods (Supplementary File 2). Of the remaining 132 studies, the methods of randomisation sequence generation were adequately reported in 69/132, but details were not clearly reported in 54/132, and 9/132 trials were judged as potentially high risk of bias (Fig. 2).

Details of the allocation concealment were clearly reported in 32/132 studies; however, most studies (95/132) provided insufficient information and were consequently judged as unclear risk of bias. Because of the nature of nurse-led interventions, blinding of participants and personnel within a trial is challenging and not feasible in most cases. However, avoiding detection bias by blinding of outcome assessors is possible in most trials. Of the 149 included studies, 22 reported blinding of outcome assessors; most studies (97/149) provided insufficient information to allow us to draw any conclusions. Attrition bias was judged as high in 33/149 studies, but most studies ($n = 78/149$) clearly documented numbers of dropouts. Selective reporting was adequately reported in most studies ($n = 93/149$) (Fig. 2).

*Effectiveness of nurse-led interventions on cancer-related symptoms*

Appropriate summary data for nurse-led interventions were available for 41 studies (43 randomised paired comparisons) (Supplementary

**Table 1**

Summary of findings.

| Outcome Measure | | Details of Outcome measures | Participants (Studies) | Statistical method and effect estimate ($I^2$) | Direction of effect | P value | Quality of the evidence (GRADE) |
|---|---|---|---|---|---|---|---|
| Fatigue | Unidimensional measures | *Outcome measurement tools included:* EORTC-QLQ-C30 | 1208 participants ($n$ = 11 trials) | MD −4.63, 95% CI (−7.97 to −1.30) ($I^2$ = 34%) | Favours nurse-led intervention | 0.007 | ⊕⊕⊝⊝ Low[a,b] |
| | Multidimensional Measures | *Outcome measurement tools included:* General fatigue scale, Piper fatigue scale, CIS fatigue scale, BFI scale, Mean (global) fatigue score | 1379 participants ($n$ = 9 trials) | SMD −0.19, 95% CI (−0.35 to −0.03) ($I^2$ = 48%) | Favours nurse-led intervention | 0.02 | ⊕⊝⊝⊝ Very low[a,b,c] |
| Pain | Unidimensional measures | *Outcome measurement tools included:* EORTC-QLQ-C30 | 1229 participants ($n$ = 10 trials) | MD −2.11, 95% CI (−5.52 to 1.31) ($I^2$ = 39%) | No evidence of benefit or harm | 0.23 | ⊕⊕⊝⊝ Low[a,b] |
| | Multidimensional Measures | *Outcome measurement tools included:* Brief pain inventory and one study selected four questions from the BPI | 359 participants ($n$ = 2 trials) | SMD −0.06, 95% CI (−0.37 to 0.25) ($I^2$ = 42%) | No evidence of benefit or harm | 0.70 | ⊕⊕⊝⊝ Low[a,b] |
| Nausea and vomiting | | *Outcome measurement tools included:* EORTC-QLQ-C30 | 957 participants ($n$ = 8 trials) | MD −1.97, 95% CI (−3.61 to −0.33) ($I^2$ = 12%) | Favours nurse-led intervention | 0.02 | ⊕⊕⊝⊝ Low[a,b] |
| Constipation | | *Outcome measurement tools included:* EORTC-QLQ-C30 | 645 participants ($n$ = 6 trials) | MD −4.54, 95% CI (−8.08 to −0.99) ($I^2$ = 0%) | Favours nurse-led intervention | 0.01 | ⊕⊕⊝⊝ Low[a,b] |
| Anxiety | | *Outcome measurement tools included:* State Trait Anxiety Inventory, STAI, Y1, Chinese version of the A-state scale of the State-Trait Anxiety Inventory, HADS, HADS (Korean version), Self-rating anxiety scale, HAMA – Hamilton anxiety scale | 2176 participants ($n$ = 15 trials) | SMD −0.29, 95% CI (−0.48 to −0.10) ($I^2$ = 77%) | Favours nurse-led intervention | 0.003 | ⊕⊝⊝⊝ Very low[a,b,c] |
| Depression | | *Outcome measurement tools included:* CES-D, POMS-D, HADS, HADS (Korean version), Self-rating depression scale | 2589 participants ($n$ = 16 trials) | SMD −0.43, 95% CI (−0.74 to −0.11) ($I^2$ = 93%) | Favours nurse-led intervention | 0.008 | ⊕⊝⊝⊝ Very low[a,b,c] |
| Mood | | *Outcome measurement tools included:* POMS, POMS-K (Korean version) | 1164 participants ($n$ = 7 trials) | SMD −0.18, 95% CI (−0.30 to −0.06) ($I^2$ = 0%) | Favours nurse-led intervention | 0.004 | ⊕⊕⊝⊝ Low[a,b] |

**Key:** CI: confidence interval; MD: mean difference; SMD: standardised mean difference.

[a] Downgraded 1 level as there were serious limitations identified in the risk of bias:

[b] Downgraded 1 level as indirectness

[c] Downgraded 1 level as inconsistency

[d] Downgraded 1 level as Imprecision of results

**Grade Working Group grades of evidence:**

**High quality:** Further research is very unlikely to change our confidence in the estimate of effect.

**Moderate quality:** Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

**Low quality:** Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

**Very low quality:** We are very uncertain about the estimate.

File 6). Studies that did not employ a randomised design were excluded from this stage of analyses. The majority of studies included within the meta-analysis had more than one primary focus ($n$ = 17); the remaining studies focused on improving a single cancer-related symptom including fatigue ($n$ = 8), anxiety ($n$ = 2), pain ($n$ = 3), depression ($n$ = 2), psychological distress ($n$ = 1), uncertainty ($n$ = 3), exercise and diet ($n$ = 1), or aimed to improve quality of life in people living with and beyond cancer ($n$ = 6) (Supplementary File 6). The comparator in 36/43 studies was described as usual care; four studies delivered an attention control intervention, and three studies did not clearly describe the control intervention (Table 1).

Participants within these trials had a range of cancer diagnoses (Supplementary File 6). Interventions were delivered across the cancer trajectory (Supplementary File 6), with most nurse-led interventions ($n$ = 33/43) provided in the treatment phase.

The interventions were all delivered by nurses, however the level of detail provided on experience, training and qualifications of those nurses varied considerably (Supplementary File 6).

*Content analysis of intervention components*

In our protocol, we planned to conduct subgroup analyses when there were sufficient studies included in a single analysis. However, we had no opportunity to conduct subgroup analyses for age, category of cancer nurse, trajectory, or cancer type, as there was inadequate information to determine these subgroups and/or insufficient data available within meta-analyses. Further discussions within the research team centred on how best to pool the data from what appeared on the face of it to be some very diverse nurse-led interventions, so that we could conduct meaningful analyses to answer our key research question (i.e., whether nurse-led interventions were more effective than no treatment, or usual
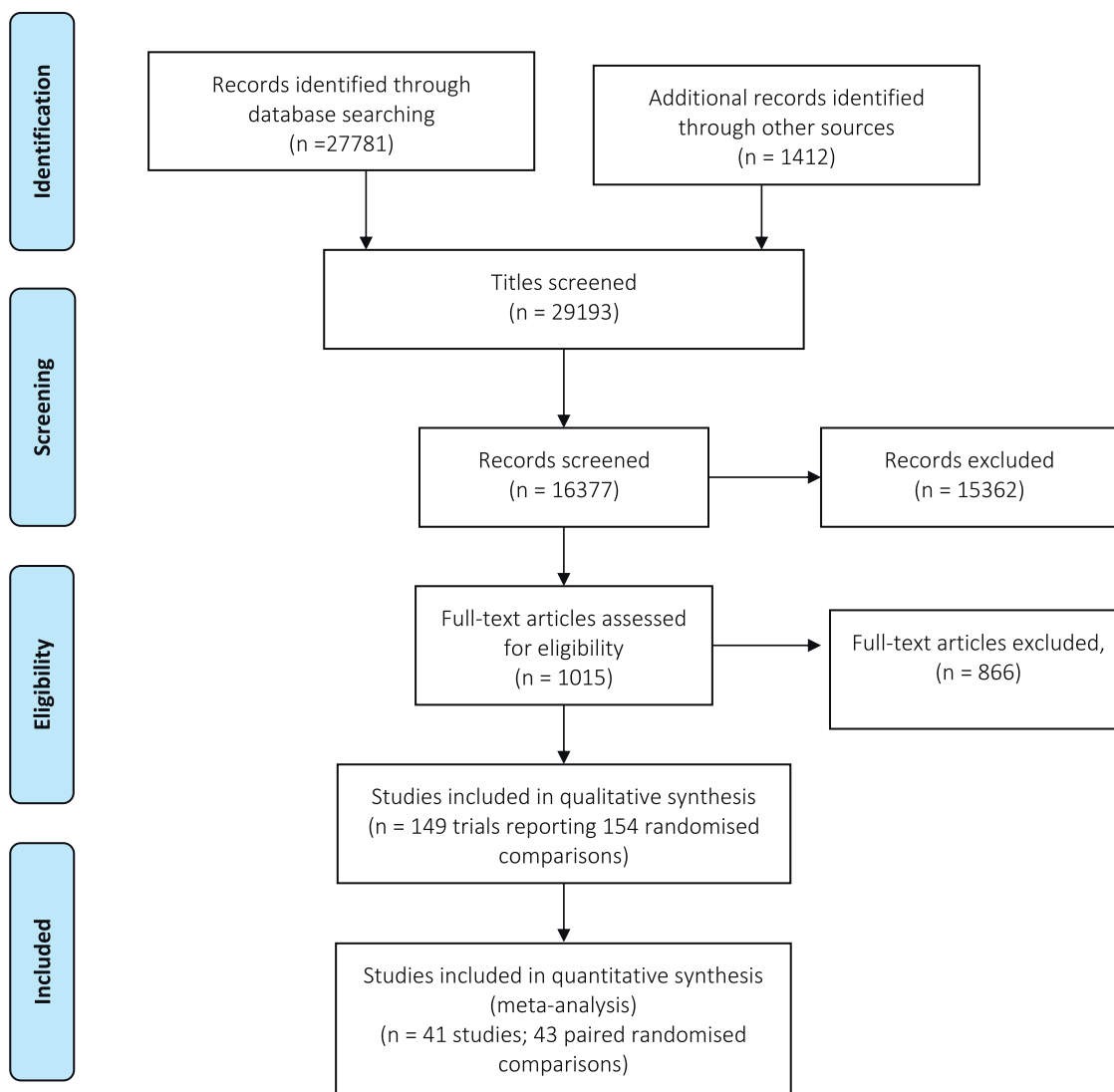
**Fig. 1.** PRISMA flow diagram.

care). Consequently, it was decided to conduct a content analysis of each intervention as previously described in the methods section.

The number of intervention components across trials included in the meta-analysis are summarised in a stacked bar plot (Fig. 3). Most of the nurse-led interventions (41/43) were classified as multicomponent, with the number of components described within each intervention ranging from two components in 13, three components in 14 studies, and four components in 7 studies. Only one multi-arm study was considered to be a single component intervention, although a different component was attributed to each arm [62]. Most interventions were coded as including an educational component (38/43); whereas lifestyle components were described in only 14 trials (Fig. 3).

*Outcome measures*

A total of 15 different outcome measures were used across the 43 trials (Table 1). Many interventions that focused on a specific symptom e.g., fatigue, also included measures related to other symptoms, as well as to the symptom targeted by the same intervention.

*Cancer related symptoms*
*Fatigue.* Eleven trials reported data from unidimensional measures of fatigue ($n = 1208$ participants; 1 outcome tool). Pooling data from

these trials showed evidence of effectiveness of nurse-led interventions when compared to control groups (MD −4.63, 95% CI −7.97 to −1.30; $I^2 = 34\%$; $P = 0.007$, low quality evidence) (Table 1, Supplementary File 7). Four studies reported unidimensional fatigue follow-up post-intervention data: at 3 weeks [40], 6 months in two studies [36,78] and up to 9 months (post-recruitment) in one study [4]. Fatigue symptoms were still reduced in participants at 3 weeks follow-up [40] (MD −15.20, 95%CI −25.31 to −5.09; 60 participants; $P = 0.003$), but there was no evidence of a difference in fatigue symptoms when measured short-term post-intervention (MD −3.52, 95% CI −9.52 to 2.47; 358 participants; $I^2 = 41\%$; $P = 0.25$). Suitable statistical data at medium or long-term post-intervention time points were unavailable.

Nine trials reported data from multidimensional measures of fatigue ($n = 1379$ participants; 5 outcome tools used). Participants receiving nurse-led interventions had significantly improved multidimensional fatigue symptom scores compared with controls (SMD −0.19, 95% CI −0.35 to −0.03; 1379 participants; 9 trials; $I^2 = 48\%$; $P = 0.02$; very-low quality evidence) (Table 1, Supplementary File 7). Pooled data showed no difference by 3 months in pain symptoms on multidimensional fatigue measures in two trials [6,89] (SMD −0.48 95% CI −0.98 to 0.01; 463 participants; $I^2 = 72\%$; $P = 0.06$). Suitable statistical data at medium or long-term post-intervention time points were unavailable.
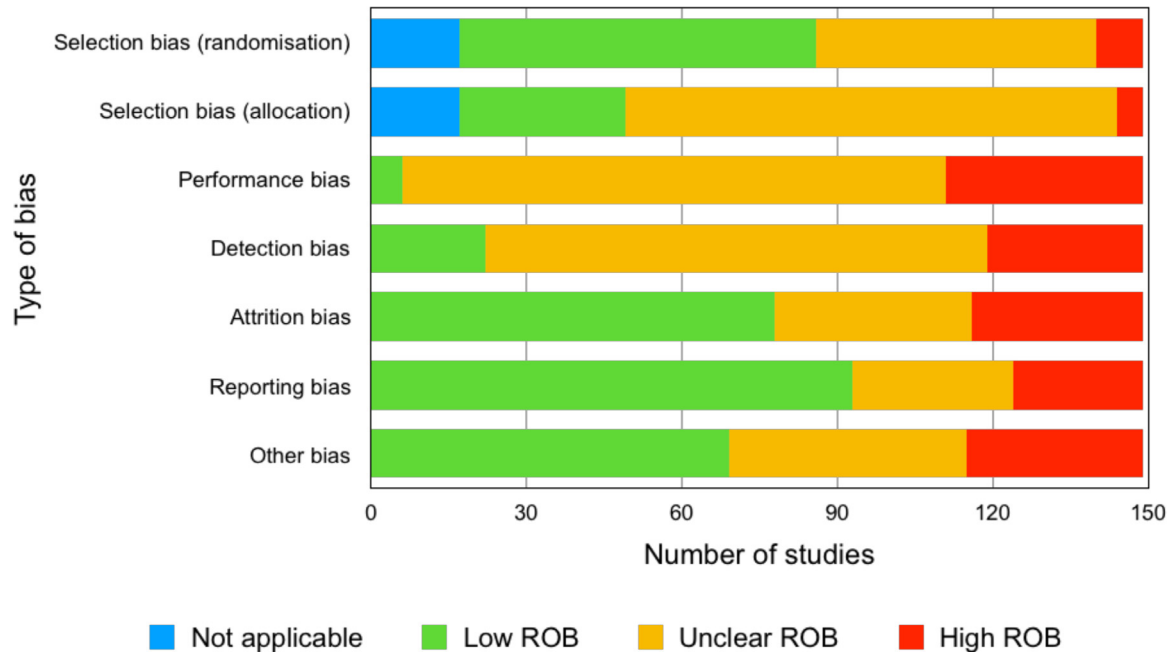
**Fig. 2.** Review of authors' judgements about each risk of bias item presented as percentages across all included studies.
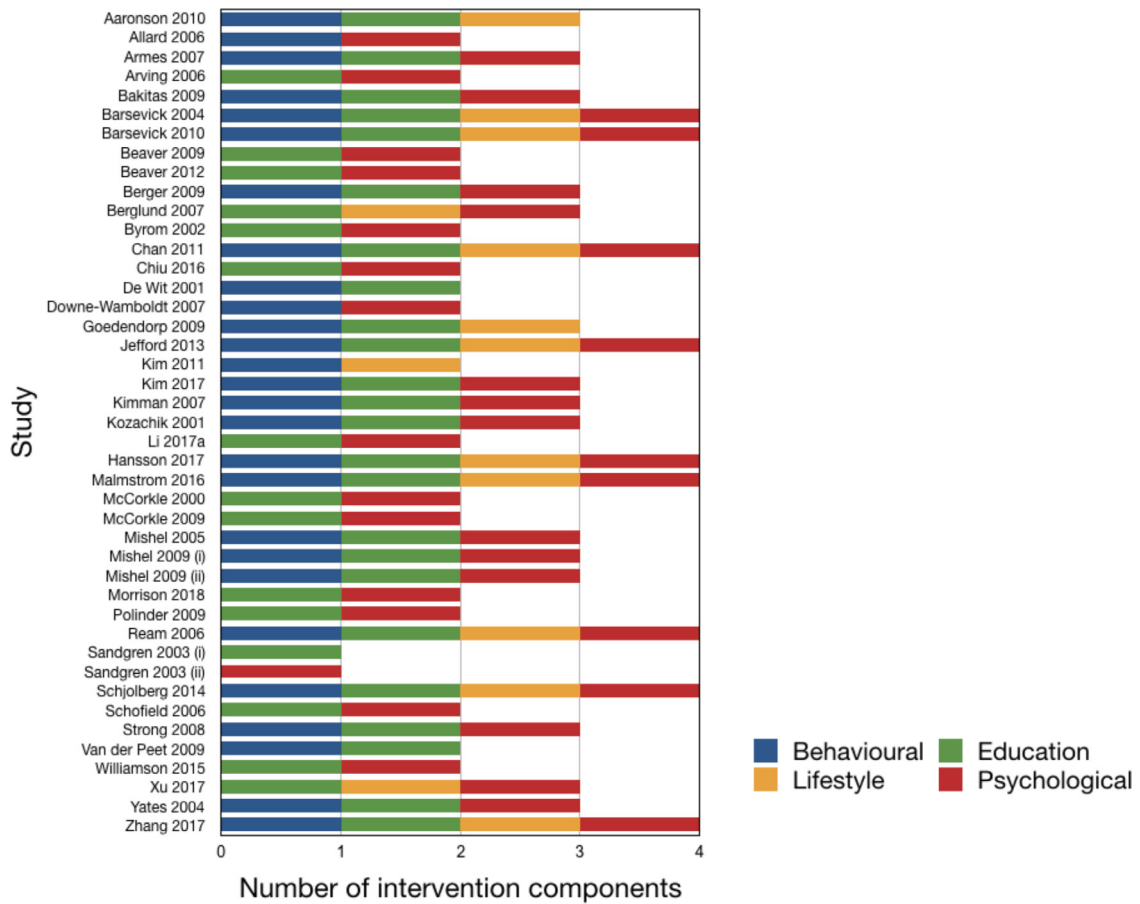


**Fig. 3.** Stacked bar graph showing intervention components across trials included in the meta-analyses.

*Pain.* Ten trials reported data from unidimensional measures of pain ($n$ = 1229 participants; 1 outcome tool used). Pooled data from these 10 trials showed no significant differences in pain outcomes between groups receiving nurse-led interventions or usual care (MD −2.11, 95% CI −5.52 to 1.31; 1229 participants; $I^2$ = 39%; $P$ = 0.23; low-quality evidence). Three trials reported follow-up data from unidimensional pain outcomes: at 3 weeks post-intervention [40] and two trials at 6 months [36,78]. Pain was still reported as significantly reduced in the [40] trial [40] at 3 weeks (MD −12.70, 95%CI −24.48 to −0.92; 60 participants; $P$ = 0.03). There was no evidence of a difference in pain symptoms when measured at 6 months post-intervention follow-up (MD −3.67, 95% CI −9.68 to 2.35; 358 participants; $I^2$ = 36%; $P$ = 0.23). Suitable statistical data at medium or long-term post-intervention time points was unavailable.

Two trials used multi-dimensional measurement pain outcome tools. Pooled data from these trials also failed to show a difference in pain outcomes between groups (SMD −0.06, 95%CI −0.37 to 0.25; 359 participants; $I^2$ = 42%; $P$ = 0.70; low quality evidence) (Table 1, Supplementary File 7). Suitable statistical data at short, medium, or long-term post-intervention time points were unavailable.

*Nausea and vomiting.* Eight trials reported data about nausea and vomiting symptoms that were measured using the same EORTC-QLQ-C30 tool ($n$ = 957 participants). Pooled data from the eight trials showed that participants who received a nurse-led intervention reported a significant improvement in their nausea and vomiting symptoms compared with participants in the control groups (MD −1.97, 95%CI −3.61 to −0.33; 957 participants; $I^2$ = 12%; $P$ = 0.02; low quality evidence) (Table 1, Supplementary File 7). Short-term follow-up data were available for three studies ranging from 3 weeks follow-up [40] to 6 months [36,78]. Nausea and vomiting symptoms were significantly reduced in participants at 3 weeks follow-up (MD −13.30, 95%CI −25.05 to −1.55; 60 participants; $P$ = 0.03), but there was no evidence of a difference between nurse-led intervention and usual care groups at 6 months (MD −0.82, 95% CI −2.40 to 0.77; 322 participants; $I^2$ = 0%; $P$ = 0.31). Suitable statistical data at medium or long-term post-intervention time points were unavailable.

*Constipation.* Six trials reported data about constipation symptoms using the same EORTC-QLQ-C30 tool ($n$ = 645 participants). Data pooled from these six trials demonstrated that nurse-led interventions had a significantly beneficial effect on constipation in people with cancer compared with usual care (MD −4.54, 95% CI −8.08 to −0.99; 645 participants; $I^2$ = 0%; $P$ = 0.01; low quality evidence) (Table 1, Supplementary File 7). There was no evidence of a significant difference in constipation scores at short term follow-up (at 3 weeks, [40]) (MD −7.70, 95% CI −24.77 to 9.37, 60 participants), or at 6 months follow-up (MD −2.80, 95% CI −8.19 to 2.59, 60 participants) [78]. Suitable statistical data at medium or long-term post-intervention time points were unavailable.

*Anxiety.* Fifteen trials reported anxiety symptoms measured using multiple tools ($n$ = 2176 participants, Table 1). Pooled data demonstrated a significant benefit in nurse-led care for anxiety (SMD −0.29, 95% CI −0.48 to −0.10, 2176 participants; 15 trials; $I^2$ = 77%; $P$ = 0.003; very-low quality evidence) (Table 1, Supplementary File 7). However, there was considerable heterogeneity within this analysis. Conducting sensitivity analysis made little difference on the overall $I^2$ and we concluded that this represented clinical heterogeneity and downgraded the evidence accordingly (Table 1). Five trials reported post-intervention follow-up data at 3 weeks [40], 8 weeks [87], and one trial at 6 months [65]. No difference in depression symptoms were seen at short-term post-intervention follow-up (SMD −0.14, 95% CI −0.45 to 0.17; 495 participants; $I^2$ = 60%; $P$ = 0.36). Suitable statistical data at medium or long-term post-intervention time points were unavailable.

*Depression.* Information relating to depression was available for 16 trials ($n$ = 2589 participants, Table 1). Multiple outcome tools were used to measure depression including CES-D, HADS, POMS-D, SCL-20 depression, and self-rating depression scale (Table 1). Participants that had received nurse-led interventions were significantly better on measures of depression than those who had not received the nurse-led intervention (SMD −0.43, 95% CI −0.74 to −0.11; $I^2$ = 93%; $P$ = 0.008 very-low quality evidence) (Table 1, Supplementary File 6). There was considerable heterogeneity within this analysis and the evidence was downgraded twice (Table 1). Five trials reported post-intervention follow-up data at 3 weeks [40], 8 weeks [87], and three trials up to 6 months [47,65,89]. No difference in depression symptoms were seen at short-term post-intervention follow-up (SMD −0.29, 95% CI −0.67 to 0.08; 869 participants; $I^2$ = 85%; $P$ = 0.13). Suitable statistical data at medium or long-term post-intervention time points were unavailable.

*Mood.* Data relating to mood was available for five studies (7 randomised paired comparisons). Pooled analysis showed that nurse-led interventions had a significant effect on mood (SMD −0.18, 95% CI −0.30 to −0.06, $I^2$ = 0%; $P$ = 0.004; low quality evidence) (Table 1, Supplementary File 7). Short-term follow-up data were only available for one trial [40], and showed that nurse-led interventions significantly improved mood in women with breast cancer at 3-week follow-up (MD −12.80, 95% CI −21.97 to −3.63, 60 participants, $P$ = 0.006). Suitable statistical data at medium or long-term post-intervention time points were unavailable.

## Discussion

Given that our aims were: (a) to determine whether cancer nurse-led interventions are more effective than no treatment, usual care or attention control comparisons, and (b) to see whether there is any evidence of benefit post-intervention, in nurse-led studies published between 2000 and 2018, we identified 149 trials (154 randomised paired comparisons) of nurse-led interventions of which 41 trials (43 randomised paired comparisons) were included in this meta-analyses.

Nurse-led interventions showed evidence of effectiveness across several common but cancer-related symptoms including fatigue, constipation, nausea and vomiting, anxiety, depression, and mood when compared with usual care or attention control. Only pain did not show any evidence of effectiveness, a finding that is surprising given how fundamental the assessment and management of pain is to cancer nursing practice. Interestingly, a recent review concluded that nurse-led, non-pharmacological, interventions for pain are effective both in the short and longer term [57]. Possible explanations for our finding may include differences in analgesia prescribing practices in different countries, as well as limitations in outcome measures commonly used to assess pain outcomes.

Based on the GRADE approach, the quality of the evidence identified was judged to be low and very low grade; suggesting that more high-quality research is needed to improve confidence in these findings. Many of the included studies delivered an intervention over lengthy time intervals and reported data from multiple assessments taking place while the intervention was being delivered (i.e., post-recruitment). However, our review also found limited short-term follow-up data, and identified no medium-to-longer term follow-up studies (>6 months post-intervention), comparing nurse-led interventions with usual care or attention control that could be included within our meta-analyses. This is a limitation of the evidence base. In addition, most interventions were focussed on the cancer treatment phase, whilst many symptoms may endure beyond this period. Thus, the impact of post-intervention cancer nursing interventions on the quality of the survival experience is an important consideration not addressed in published trials in the period covered by this study.

Other reviews of interventions for cancer symptom management have also found the quality of evidence to be low [57,60]. A recent

Cochrane review of telephone interventions, which was not specifically focussed on those delivered by nurses, found, in fact, that the majority were nurse-led [60]. Although Ream et al's review found evidence of benefits for fatigue, depression, anxiety, and emotional distress, the authors commented on the significant heterogeneity and low certainty of this evidence. It could be argued that, at present, nurse-led interventions differ too widely to compare effects using traditional systematic review and meta-analysis techniques. Noyes [51] has pointed out the need for nurse researchers to utilise novel and mixed-methods approaches to synthesise published evidence, particularly for complex interventions, such as those delivered by cancer nurses [51].

We had intended to conduct subgroup analyses for the 'type' of nurse-led intervention delivered in our included studies, to determine whether one 'type' of intervention was better than another. However, several challenges were faced when categorising trials in this way. Our content analysis of the descriptions of each intervention revealed that most interventions included several different components, each of which were difficult to separate. This has, however, provided new insights into the complexity of interventions which seek to address complex cancer symptoms; for example, education about symptom management may be combined with behavioural support for lifestyle changes, as well as the introduction of psychological skills to enhance coping and motivation. Cancer nurses clearly require a complex set of skills in practice to address symptoms experienced by patients because of their disease or treatment, which are multi-dimensional in nature. As with many complex interventions, it is often difficult to determine which component is the most important or effective, or indeed whether it is the subtle combination of components, as well as how they are delivered, that can make the difference.

This suggests that those responsible for disseminating evidence concerning effectiveness of cancer nursing interventions should ensure that they describe the component elements in sufficient detail to allow for replication studies, or the building by others on the available data [70,71]. Moreover, it is important that researchers communicate sufficient information concerning the theoretical basis and rationale for their chosen intervention [35], so that it can clearly be understood how a particular approach is expected to lead to an improvement, not only in terms of the key symptom that is the focus of the intervention, but also when considered alongside other symptoms, and the impact overall.

*Strengths and limitations*

The review followed the recommended approach for high quality reviews. A sensitive search strategy was employed for the years chosen, and an extensive range of databases were accessed without language restrictions. The review process followed the Cochrane Handbook for Systematic Reviews (Version 5.1.0) [34] and the PRISMA statement for reporting on systematic reviews [44]. Selection criteria and analysis were pre-specified and documented in a protocol [14]. However, we may not have identified all cancer nurse-led trials, as not all profiled the professional background of the lead interventionist. It was not possible to include non-English language papers which may have altered the findings.

This is the first meta-analysis of its kind to capture the range and quality of nurse-led trials, over an 18-year period, and published at a global level and to demonstrate the evidence on the effectiveness of nurse-led interventions on common cancer symptoms. In this review we compared nurse-led interventions with a range of comparison groups including no treatment, attention control and 'usual care'. Usual care, however, is highly variable in reality [88] and it is not always clear what is meant by this at a national, let alone an international, level. Without this information it is not always possible to consider the comparative benefits of nurse-led interventions. The introduction of reporting guidelines such as TIDieR [35], provides a framework to improve the reporting of interventions such as those described here, however, as our review

also has demonstrated, there is room for significant improvement in the description of interventions led by nurses.

This meta-analysis was further challenged by different outcome measures used to judge trial effectiveness. Nurse-specific outcomes are needed with more specificity, and agreed at an international level, so that large scale comparative trials can be developed. Small sample sizes and variable quality of reporting were encountered commonly in this study. Although we sought to highlight the impact of nurse-led interventions on symptoms, only 41 studies reported findings in a way that could be included in the meta-analysis. Our selection stopped in 2018, meaning that new interventions may have appeared since (although the COVID1-19 pandemic may have had an impact on reducing research such as this) and future researchers will be best able to judge whether our findings remain relevant over time. Each of these limitations should be addressed to enhance the quality of published evidence to determine any benefit from nursing interventions that address symptoms experienced by people diagnosed with cancer.

*Implications for practice*

The evidence presented here highlights the benefits of nurse-led interventions for cancer-related symptoms and confirms that trials have focussed on those especially problematic for patients and families. Our findings support the benefits that cancer nurses, and nurse-led interventions, bring to cancer care, and reinforce the need for wider access to evidence-based symptom management [45,50,79]. This review has identified a range of diverse interventions, and the in-depth nature of our analysis highlighted that many of the components are, arguably, already delivered by cancer nurses in their daily practise. For instance, cancer nurses routinely provide education, psychological support, and lifestyle advice to people living with a cancer diagnosis. These skills are often the result of years of training and clinical experience, but they may not have been subjected to scrutiny. This evidence clearly shows that nurse-led interventions do make a difference to symptoms. Importantly, however, we must question the components of the most effective interventions that comprise multiple components, especially as some may be more helpful than others.

However, all of this relies on a well-trained cancer nursing workforce being available to contribute to effective supportive cancer care. To ensure improvements in cancer symptom management and enhance the quality of future symptom-focused interventions, cancer nurses need to be prepared appropriately and highly skilled in terms of undertaking assessment, patient education, behavioural and lifestyle management, as well as psychological support. Unfortunately, not all patients have access to specialist cancer nurses at present, and the education, scope, and recognition of the value of these roles varies significantly across different countries and health systems, even in Europe alone [17,38,66].

*Implications for further research*

This review has confirmed that cancer nurse researchers should be recognized for addressing troublesome symptoms for people with cancer, but that they also need to address weaknesses in trial design and reporting. Interventions need to be more fully described, including study context (e.g., specialist hospital, home, or outpatient clinic) and personnel involved in delivery (e.g., level of nursing qualification, cancer training, expertise and time available) [84]. One of the challenges also faced when conducting this meta-analysis was the lack of clear reporting about the length (or dose) of interventions or at what intervals outcomes were being assessed. Trial methods also need to be more clearly articulated, and recent extensions to CONSORT (Consolidated Standards of Reporting) for social and psychological interventions [24], as well as other non-pharmacological interventions [9] will be particularly relevant for future nurse-led intervention studies. Robust economic evaluations, another important requirement, will only be possible when suf-

ficient details are provided that allow comparisons based on actual or estimated costs.

This meta-analysis also demonstrates that some areas of cancer nursing practice have attracted more attention than others. Most of the evidence focusses on common cancers and on the treatment phase [16], which means that rarer cancers and other phases of the cancer trajectory remain open for further research. As nurses continue to extend their roles and scope of practice into the diagnostic and survivorship phases of cancer, there will be an ongoing need for well-designed research to underpin symptom-focused interventions. Supportive care interventions are also needed for patients with rarer, but highly symptomatic, disease such as pancreatic cancer [80]. Future research should address the needs of cancer patient groups that may have been neglected, including those with rarer cancers or poorly understood supportive care needs, to ensure that benefits are shared more widely [19].

The challenge for cancer nurses now is to secure funding to undertake large-scale, high quality, international trials. Funding at national and international levels will be required to secure more findings that can be implemented in more than one health system. Recent MRC guidance for developing and evaluating complex interventions – such as those identified in this review – now recommend adopting a broader perspective, and moving beyond the question of 'does the intervention work' to deeper understanding of *how* it works and in *what* context? [71].

*Implications for policy*

Despite the advances outlined here into the effectiveness and development in nurse-led interventions, cancer nurses continue to lack sufficient recognition for the part they play in the design, development and delivery of interventions that may enhance patient experience, reduce cost, and improve outcomes for those living with cancer. Better recognition of the current contribution, and future potential, of cancer nurses (and cancer nursing interventions), is part of the solution for the provision of more effective care in the future [17].

The impetus for this project arose out of the European Oncology Nursing Society's Recognising Cancer Nursing (RECaN) initiative. This had sought to advance recognition of the contribution that an educated and specialist nursing workforce make to enhancing the quality of cancer care (https://www.cancernurse.eu/research/recan.html). This study has revealed the contribution that nurse researchers made between 2000–2018 to address symptoms commonly experienced by people with cancer. As demand for cancer treatment grows, there will be a need for even more evidence-based interventions that improve the cancer experience, including innovations designed by nurses. This paper has provided a baseline position from which to consider how best to strengthen the quality of nurse-led intervention reporting, as well as illustrating the role that standardized cancer nursing outcome measures could play in helping to gauge the effectiveness of novel symptom management interventions. The benefit of nursing innovation has long been clear in improving cancer practise. The challenge now is to further improve the design and quality of novel interventions that will, in time, make further valuable contributions to improving the lives of those experiencing cancer-related symptoms.

## Declarations of sources of funding

SUPPLEMENTARY FILES: Supplementary File 1. Search string developed in MEDLINE (Ovid) (complete). Supplementary File 2. Key characteristics of nurse-led interventions delivered across included studies. Supplementary File 3. Geographical distribution of included studies. Supplementary File 4. Key participant characteristics. Supplementary File 5. Risk of bias judgements for individual studies. Supplementary File 6. Content analysis. Supplementary File 7. Forest plots of cancer-related symptoms immediately post-intervention.

## Declaration of Competing Interest

DK, PC, CT, AC, ME, ML, IN, CO, UÖ, EP, MS, LS, TW: none Two reviewers (WO and MW) were involved in trials that were included in this study. WO was involved in two trials (see Oldenmenger et al. [55,56] and de Raaf et al. [20]); MW was involved in three trials (see entries for Moore et al. [49] and Wells et al. [82,83]). Neither reviewer was involved in the assessment or interpretation of either of these studies

The work presented here represents the view of the review authors and not necessarily those of the funding body.

## CRediT authorship contribution statement

**Daniel Kelly:** Visualization, Methodology, Writing – original draft, Writing – review & editing. **Pauline Campbell:** Investigation, Formal analysis, Data curation, Methodology, Writing – original draft, Writing – review & editing. **Claire Torrens:** Investigation, Formal analysis, Data curation, Methodology, Writing – review & editing. **Andreas Charalambous:** Writing – review & editing. **Ulrika Östlund:** Methodology, Writing – review & editing. **Manuela Eicher:** Writing – review & editing. **Maria Larsson:** Writing – review & editing. **Iveta Nohavova:** Methodology, Writing – review & editing. **Cecilia Olsson:** Writing – review & editing. **Mhairi Simpson:** Writing – review & editing. **Elisabeth Patiraki:** Methodology, Writing – review & editing. **Lena Sharp:** Methodology, Writing – review & editing. **Theresa Wiseman:** Methodology, Writing – review & editing. **Wendy Oldenmenger:** Methodology, Writing – review & editing. **Mary Wells:** Visualization, Methodology, Writing – original draft, Writing – review & editing.

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## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.hsr.2022.100052.

## References

[1] A.A. Abahussin, R.M. West, D.C. Wong, L.E. Ziegler, PROMs for pain in adult cancer patients: a systematic review of measurement properties, Pain Pract. 19 (2019) 93–117.

[2] Y. Afiyanti, I.N. Rachmawati, A. Milanti, Evaluating sexual nursing care intervention for reducing sexual dysfunction in indonesian cervical cancer survivors, Asia Pac. J. Oncol. Nurs. 3 (2016) 266–271.

[3] C. Allemani, T. Matsuda, V. Di Carlo, R. Harewood, M. Matz, M. Niksic, A. Bonaventure, M. Valkov, C.J. Johnson, J. Esteve, O.J. Ogunbiyi, E.S.G. Azevedo, W.Q. Chen, S. Eser, G. Engholm, C.A. Stiller, A. Monnereau, R.R. Woods, O. Visser, G.H. Lim, J. Aitken, H.K. Weir, M.P. Coleman, C.W. Group, Global surveillance of trends in cancer survival 2000–14 (CONCORD-3): analysis of individual records for 37 513 025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries, Lancet 391 (2018) 1023–1075.

[4] J. Armes, T. Chalder, J. Addington-Hall, A. Richardson, M. Hotopf, A randomized controlled trial to evaluate the effectiveness of a brief, behaviorally oriented intervention for cancer-related fatigue, Cancer 110 (2007) 1385–1395.

[5] H. Baker, S. Wellman, V. Lavender, Functional quality-of-life outcomes reported by men treated for localized prostate cancer: a systematic literature review, Oncol. Nurs. Forum 43 (2016) 199–218.

[6] A.M. Barsevick, W. Dudley, S. Beck, C. Sweeney, K. Whitmer, L. Nail, A randomized clinical trial of energy conservation for patients with cancer-related fatigue, Cancer 100 (2004) 1302–1310.

[7] G.P.L.M. Berglund, K.C. Eriksson, I. Wallenius, A. Roshanai, K.M. Nordin, P.O. Sjödén, M. Häggman, Between Men": a psychosocial rehabilitation programme for men with prostate cancer, Acta Oncol. 46 (2007) 83–89 (Stockholm, Sweden).

[8] L.M. Blackburn, S. Abel, L. Green, K. Johnson, S. Panda, The use of comfort kits to optimize adult cancer pain management, Pain Manag. Nurs. 20 (2019) 25–31.

[9] I. Boutron, D.G. Altman, D. Moher, K.F. Schulz, P. Ravaud, C.N. Group, CONSORT statement for randomized trials of nonpharmacologic treatments: a 2017 update and a CONSORT extension for nonpharmacologic trial abstracts, Ann. Intern. Med. 167 (2017) 40–47.

[10] S. Bouya, A. Balouchi, A. Maleknejad, M. Koochakzai, E. AlKhasawneh, A. Abdollahi-mohammad, Cancer pain management among oncology nurses: knowledge, attitude, related factors, and clinical recommendations: a systematic review, J. Cancer Educ. 34 (2019) 839–846.

[11] T. Brown, S. Cruickshank, M. Noblet, Specialist breast care nurses for support of women with breast cancer, Cochrane Database Syst. Rev. 2 (2021) CD005634.

[12] W.C.H.C.N. Budin, J. Haber, D.W. Sherman, G. Maislin, J.R. Cater, F. Cartwright-Alcarese, M.O. Kowalski, C.B. McSherry, R. Fuerbach, S. Shukla, Breast cancer: education, counseling, and adjustment among patients and partners: a randomized clinical trial, Nurs. Res. 57 (2008) 199–213 115p.

[13] J. Byrom, T. Clarke, J. Neale, P.D. Dunn, G.M. Hughes, C.W. Redman, M. Pitts, Can pre-colposcopy sessions reduce anxiety at the time of colposcopy? A prospective randomised study, J. Obstet. Gynaecol. 22 (2002) 415–420.

[14] P. Campbell, C. Torrens, D. Kelly, A. Charalambous, N. Domenech-Climent, I. Nohavova, U. Ostlund, E. Patiraki, D. Salisbury, L. Sharp, T. Wiseman, W. Oldenmenger, M. Wells, Recognizing european cancer nursing: protocol for a systematic review and meta-analysis of the evidence of effectiveness and value of cancer nursing, J. Adv. Nurs. 73 (2017) 3144–3153.

[15] S. Carnio, D. Galetta, V. Scotti, D.L. Cortinovis, A. Antonuzzo, S. Pisconti, A. Rossi, O. Martelli, F.L. Cecere, A. Lunghi, A. Del Conte, E.S. Montagna, J. Topulli, D. Pelizzoni, S.G. Rapetti, M. Gianetta, M.V. Pacchiana, V. Pegoraro, N. Cataldo, E. Bria, S. Novello, Chemotherapy-induced nausea and vomiting (CINV) in patients with advanced lung cancer during the first-line treatment: assessment by physicians, nurses, and patients from an Italian multicenter survey, Support. Care Cancer 26 (2018) 1841–1849.

[16] A. Charalambous, M. Wells, P. Campbell, C. Torrens, U. Ostlund, W. Oldenmenger, E. Patiraki, L. Sharp, I. Nohavova, N. Domenech-Climent, M. Eicher, C. Farrell, M. Larsson, C. Olsson, M. Simpson, T. Wiseman, D. Kelly, A scoping review of trials of interventions led or delivered by cancer nurses, Int. J. Nurs. Stud. 86 (2018) 36–43.

[17] A.K.D. Charamlambous, Promoting a safety culture through effective nursing leadership in cancer care, Eur. J. Oncol. Nurs. 36 (2018) 6–7.

[18] R.A. Clark-Snow, C. Vidall, S. Borjeson, P. Jahn, Fixed combination antiemetic: a literature review on prevention of chemotherapy-induced nausea and vomiting using netupitant/palonosetron, Clin. J. Oncol. Nurs. 22 (2018) E52–E63.

[19] J. Cockle-Hearne, F. Charnay-Sonnek, L. Denis, H.E. Fairbanks, D. Kelly, S. Kav, K. Leonard, E. van Muilekom, P. Fernandez-Ortega, B.T. Jensen, S. Faithfull, The impact of supportive nursing care on the needs of men with prostate cancer: a study across seven European countries, Br. J. Cancer 109 (2013) 2121–2130.

[20] P.J. de Raaf, C. de Klerk, R. Timman, J.J. Busschbach, W.H. Oldenmenger, C.C. van der Rijt, Systematic monitoring and treatment of physical symptoms to alleviate fatigue in patients with advanced cancer: a randomized controlled trial, J. Clin. Oncol. 31 (2013) 716–723.

[21] J.J. Deeks, J.P. Higgins, D.G. Altman, Chapter 10: Analysing data and undertaking meta-analyses, Cochrane Handbook for Systematic Reviews of Interventions Version 6.1 Higgins Jpt, T.J.C.J.C.M.L.T.P.M.J.W.V.A., Cochrane Collaboration, 2020 (Updated September 2020) www.training.cochrane.org/handbook .

[22] J.L. Depke, A.A. Onitilo, Sexual health assessment and counseling: oncology nurses' perceptions, practices, and perceived barriers, J. Community Support Oncol. 13 (2015) 442–443.

[23] P. Fox, A. Darley, E. Furlong, C. Miaskowski, E. Patiraki, J. Armes, E. Ream, C. Papadopoulou, L. McCann, N. Kearney, R. Maguire, The assessment and management of chemotherapy-related toxicities in patients with breast cancer, colorectal cancer, and Hodgkin's and non-Hodgkin's lymphomas: a scoping review, Eur. J. Oncol. Nurs. 26 (2017) 63–82.

[24] S. Grant, E. Mayo-Wilson, P. Montgomery, G. Macdonald, S. Michie, S. Hopewell, D. Moher, o.b.o.t.C.-S.P.I. Group, CONSORT-SPI 2018 explanation and elaboration: guidance for reporting social and psychological intervention trials, Trials 19 (2018) 406.

[25] S. Grant, A. Motala, J.G. Chrystal, R. Shanman, J. Zuchowski, L. Zephyrin, K.M. Cordasco, Describing care coordination of gynecologic oncology in western healthcare settings: a rapid review, Transl. Behav. Med. 8 (2018) 409–418.

[26] G.H. Guyatt, A.D. Oxman, R. Kunz, J. Brozek, P. Alonso-Coello, D. Rind, P.J. Devereaux, V.M. Montori, B. Freyschuss, G. Vist, R. Jaeschke, J.W. Williams Jr., M.H. Murad, D. Sinclair, Y. Falck-Ytter, J. Meerpohl, C. Whittington, K. Thorlund, J. Andrews, H.J. Schunemann, GRADE guidelines 6. Rating the quality of evidence–imprecision, J. Clin. Epidemiol. 64 (2011) 1283–1293.

[27] G.H. Guyatt, A.D. Oxman, R. Kunz, J. Woodcock, J. Brozek, M. Helfand, P. Alonso–Coello, Y. Falck-Ytter, R. Jaeschke, G. Vist, E.A. Akl, P.N. Post, S. Norris, J. Meerpohl, V.K. Shukla, M. Nasser, H.J. Schunemann, G.W. Group, GRADE guidelines: 8. Rating the quality of evidence–indirectness, J. Clin. Epidemiol. 64 (2011) 1303–1310.

[28] G.H. Guyatt, A.D. Oxman, R. Kunz, J. Woodcock, J. Brozek, M. Helfand, P. Alonso–Coello, P. Glasziou, R. Jaeschke, E.A. Akl, S. Norris, G. Vist, P. Dahm, V.K. Shukla, J. Higgins, Y. Falck-Ytter, H.J. Schunemann, G.W. Group, GRADE guidelines: 7. Rating the quality of evidence–inconsistency, J. Clin. Epidemiol. 64 (2011) 1294–1302.

[29] G.H. Guyatt, A.D. Oxman, V. Montori, G. Vist, R. Kunz, J. Brozek, P. Alonso-Coello, B. Djulbegovic, D. Atkins, Y. Falck-Ytter, J.W. Williams Jr., J. Meerpohl, S.L. Norris, E.A. Akl, H.J. Schunemann, GRADE guidelines: 5. Rating the quality of evidence–publication bias, J. Clin. Epidemiol. 64 (2011) 1277–1282.

[30] G.H. Guyatt, A.D. Oxman, G. Vist, R. Kunz, J. Brozek, P. Alonso-Coello, V. Montori, E.A. Akl, B. Djulbegovic, Y. Falck-Ytter, S.L. Norris, J.W. Williams Jr.,

D. Atkins, J. Meerpohl, H.J. Schunemann, GRADE guidelines: 4. Rating the quality of evidence–study limitations (risk of bias), J. Clin. Epidemiol. 64 (2011) 407–415.

[31] G.H. Guyatt, A.D. Oxman, G.E. Vist, R. Kunz, Y. Falck-Ytter, P. Alonso-Coello, H.J. Schunemann, G.W. Group, GRADE: an emerging consensus on rating quality of evidence and strength of recommendations, BMJ 336 (2008) 924–926.

[32] C. Häggmark, L. Bohman, K. Ilmoni-Brandt, I. Näslund, P. Sjödén, B. Nilsson, Effects of information supply on satisfaction with information and quality of life in cancer patients receiving curative radiation therapy, Patient Educ. Couns. 45 (2001) 173–179 177p.

[33] C. Hagmann, A. Cramer, A. Kestenbaum, C. Durazo, A. Downey, M. Russell, J. Geluz, J.D. Ma, E.J. Roeland, Evidence-based palliative care approaches to non-pain physical symptom management in cancer patients, Semin. Oncol. Nurs. 34 (2018) 227–240.

[34] J.P.T. Higgins, J. Thomas, J. Chandler, M. Cumpston, T. Li, M.J. Page, Cochrane Handbook for Systematic Reviews of Interventions, 6.0 ed., Cochrane Collaboration, 2019.

[35] T.C. Hoffmann, P.P. Glasziou, I. Boutron, R. Milne, R. Perera, D. Moher, D.G. Altman, V. Barbour, H. Macdonald, M. Johnston, S.E. Lamb, M. Dixon-Woods, P. McCulloch, J.C. Wyatt, A.W. Chan, S. Michie, Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide, BMJ 348 (2014) g1687.

[36] M. Jefford, K. Gough, A. Drosdowsky, L. Russell, S. Aranda, P. Butow, J. Phipps-Nelson, J. Young, M. Krishnasamy, A. Ugalde, D. King, A. Strickland, M. Franco, R. Blum, C. Johnson, V. Ganju, J. Shapiro, G. Chong, J. Charlton, A. Haydon, P. Schofield, A randomized controlled trial of a nurse-led supportive care package (survivorcare) for survivors of colorectal cancer, Oncologist 21 (2016) 1014–1023.

[37] J.Y. Joo, M.F. Liu, Effectiveness of nurse-led case management in cancer care: systematic review, Clin. Nurs. Res. 28 (2019) 968–991.

[38] D. Kelly, A. Lankshear, T. Wiseman, P. Jahn, H. Mall-Roosmae, K. Rannus, W. Oldenmenger, L. Sharp, The experiences of cancer nurses working in four European countries: a qualitative study, Eur. J. Oncol. Nurs. 49 (2020) 101844.

[39] J.M. Kiernan, J. Conradi Stark, A.H. Vallerand, Chemotherapy-induced nausea and vomiting mitigation with music interventions, Oncol. Nurs. Forum 45 (2018) 88–95.

[40] Y.H. Kim, K.S. Choi, K. Han, H.W. Kim, A psychological intervention programme for patients with breast cancer under chemotherapy and at a high risk of depression: a randomised clinical trial, J. Clin. Nurs. (2017) 572–581.

[41] H. Komatsu, K. Yagasaki, The power of nursing: guiding patients through a journey of uncertainty, Eur. J. Oncol. Nurs. 18 (2014) 419–424.

[42] H. Lee, Y. Lim, M.-S. Yoo, Y. Kim, Effects of a nurse-led cognitive-behavior therapy on fatigue and quality of life of patients with breast cancer undergoing radiotherapy: an exploratory study, Cancer Nurs. 34 (2011) E22–E30 21p.

[43] P. Li, Y.J. Guo, Q. Tang, L. Yang, Effectiveness of nursing intervention for increasing hope in patients with cancer: a meta-analysis, Rev. Lat. Am. Enferm. 26 (2018) e2937.

[44] A. Liberati, D.G. Altman, J. Tetzlaff, C. Mulrow, P.C. Gotzsche, J.P. Ioannidis, M. Clarke, P.J. Devereaux, J. Kleijnen, D. Moher, The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration, PLoS Med. 6 (2009) e1000100.

[45] MacmillanQuality in Nursing. Excellence in Cancer Care: The contribution of the Clinical Nurse Specialist, Macmillan Cancer Support, UK, 2010.

[46] M. Maqbali, C. Hughes, L. Dunwoody, J.P. Rankin, E.D. Hacker, J. Gracey, Exercise interventions to manage fatigue in women with gynecologic cancer: a systematic review, Oncol. Nurs. Forum 46 (2019) 71–82.

[47] R. McCorkle, N.E. Strumpf, I.F. Nuamah, D.C. Adler, M.E. Cooley, C. Jepson, E.J. Lusk, M. Torosian, A specialized home care intervention improves survival among older post-surgical cancer patients, J. Am. Geriatr. Soc. 48 (2000) 1707–1713.

[48] L. Monterosso, V. Platt, M. Bulsara, M. Berg, Systematic review and meta-analysis of patient reported outcomes for nurse-led models of survivorship care for adult cancer patients, Cancer Treat. Rev. 73 (2019) 62–72.

[49] S. Moore, J. Corner, J. Haviland, M. Wells, E. Salmon, C. Normand, M. Brada, M. O'Brien, I. Smith, Nurse led follow up and conventional medical follow up in management of patients with lung cancer: randomised trial, BMJ 325 (2002) 1145.

[50] NICELung Cancer: Diagnosis and Management: Clinical Guideline [ng122], National Institute for Health and Care Excellence, UK, 2019.

[51] J. Noyes, The value of synthesizing evidence to inform cancer nursing, Cancer Nurs. 43 (2020) 173–176.

[52] E. Ohlsson-Nevo, B. Andershed, U. Nilsson, Psycho-educational intervention on mood in patients suffering from colorectal and anal cancer: a randomized controlled trial, Nord. J. Nurs. Res. 37 (2016) 135–142.

[53] E. Ohlsson-Nevo, J. Karlsson, U. Nilsson, Effects of a psycho-educational programme on health-related quality of life in patients treated for colorectal and anal cancer: a feasibility trial, Eur. J. Oncol. Nurs. 21 (2016) 181–188.

[54] W.H. Oldenmenger, J.I. Geerling, I. Mostovaya, K.C.P. Vissers, A. de Graeff, A.K.L. Reyners, Y.M. van der Linden, A systematic review of the effectiveness of patient-based educational interventions to improve cancer-related pain, Cancer Treat. Rev. 63 (2018) 96–103.

[55] W.H. Oldenmenger, P.A.E. Sillevis Smitt, C. van Montfort, P.J. de Raaf, C.C.D. van der Rijt, A combined pain consultation and pain education program decreases average and current pain and decreases interference in daily life by pain in oncology outpatients: a randomized controlled trial, Pain 152 (2011) 2632–2639.

[56] W.H. Oldenmenger, C.C. van der Rijt, Feasibility of assessing patients' acceptable pain in a randomized controlled trial on a patient pain education program, Palliat. Med. 31 (2017) 553–558.

[57] Y.J. Park, M.K. Lee, Effects of nurse-led nonpharmacological pain interventions for patients with cancer: a systematic review and meta-analysis, J. Nurs. Scholarsh. (2021) 397–528.

[58] C. Paterson, C. Primeau, G. Nabi, A multimodal supportive care intervention in men and their partners/carers affected by metastatic prostate cancer: a randomised controlled feasibility study, European urology, supplements, in: Proceedings of the 32nd Annual European Association of Urology Congress, EAU 2017, United Kingdom, 2017, p. e1641.

[59] C. Paterson, C. Primeau, G. Nabi, A randomised controlled feasibility study: a multimodal supportive care intervention in men and their partners/carers affected by metastatic prostate cancer, in: Proceedings of the 112th Annual Meeting of the American Urological Association, AUA 2017, United States, 2017, p. e195.

[60] E. Ream, A.E. Hughes, A. Cox, K. Skarparis, A. Richardson, V.H. Pedersen, T. Wiseman, A. Forbes, A. Bryant, Telephone interventions for symptom management in adults with cancer, Cochrane Database Syst. Rev. 6 (2020) CD007568.

[61] P.G. Ritvo, R.E. Myers, L.F. Paszat, J.M. Tinmouth, J. McColeman, B. Mitchell, M. Serenity, L. Rabeneck, Personal navigation increases colorectal cancer screening uptake, Cancer Epidemiol. Biomark. Prev. 24 (2015) 506–511.

[62] A. Sandgren, K. McCaul, Short-term effects of telephone therapy for breast cancer patients, Health Psychol. 22 (3) (2003) 310–315.

[63] R. Sankaranarayanan, P.O. Esmy, R. Rajkumar, R. Muwonge, R. Swaminathan, S. Shanthakumari, J.M. Fayette, J. Cherian, Effect of visual screening on cervical cancer incidence and mortality in Tamil Nadu, India: a cluster-randomised trial, Lancet 370 (2007) 398–406 (London, England).

[64] T.K. Schjolberg, M. Dodd, N. Henriksen, K. Asplund, M. Cvancarova Smastuen, T. Rustoen, Effects of an educational intervention for managing fatigue in women with early stage breast cancer, Eur. J. Oncol. Nurs. 18 (2014) 286–294.

[65] P. Schofield, K. Gough, K. Lotfi-Jam, R. Bergin, A. Ugalde, P. Dudgeon, W. Crellin, K. Schubach, F. Foroudi, K.H. Tai, G. Duchesne, R. Sanson-Fisher, S. Aranda, Nurse-led group consultation intervention reduces depressive symptoms in men with localised prostate cancer: a cluster randomised controlled trial, BMC Cancer 16 (2016) 637.

[66] L. Sharp, K. Rannus, A. Olofsson, D. Kelly, W. Oldenmenger, Patient safety culture among European cancer nurses—an exploratory, cross-sectional survey comparing data from Estonia, Germany, Netherlands, and United Kingdom, J. Adv. Nurs. (2019) 3535–3543.

[67] J. Shaw, S. Sethi, L. Vaccaro, L. Beatty, L. Kirsten, D. Kissane, B. Kelly, G. Mitchell, K. Sherman, J. Turner, Is care really shared? A systematic review of collaborative care (shared care) interventions for adult cancer patients with depression, BMC Health Serv. Res. 19 (2019) 120.

[68] J. Shin, H. Park, Effects of auricular acupressure on constipation in patients with breast cancer receiving chemotherapy: a randomized control trial, West. J. Nurs. Res. 40 (2018) 67–83.

[69] S. Shin, C. Mitchell, K. Mannion, J. Smolyn, S.H. Meghani, An integrated review of cannabis and cannabinoids in adult oncologic pain management, Pain Manag. Nurs. 20 (2019) 185–191.

[70] K. Skivington, L. Matthews, S.A. Simpson, P. Craig, J. Baird, J.M. Blazeby, K.A. Boyd, N. Craig, D.P. French, E. McIntosh, M. Petticrew, J. Rycroft-Malone, M. White, L. Moore, Framework for the development and evaluation of complex interventions: gap analysis, workshop and consultation-informed update, Health Technol. Assess. 25 (2021) 1–132.

[71] K. Skivington, L. Matthews, S.A. Simpson, P. Craig, J. Baird, J.M. Blazeby, K.A. Boyd, N. Craig, D.P. French, E. McIntosh, M. Petticrew, J. Rycroft-Malone, M. White, L. Moore, A new framework for developing and evaluating complex interventions: update of medical research council guidance, BMJ 374 (2021) n2061.

[72] H. Sung, J. Ferlay, R.L. Siegel, M. Laversanne, I. Soerjomataram, A. Jemal, F. Bray, Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries, CA Cancer J. Clin. 71 (2021) 209–249.

[73] L.H. Tay, A.K.W. Ong, D.S.P. Lang, Experiences of adult cancer patients receiving counseling from nurses: a qualitative systematic review, JBI Database Syst. Rev. Implement. Rep. 16 (2018) 1965–2012.

[74] S.C. Teunissen, W. Wesker, C. Kruitwagen, H.C. de Haes, E.E. Voest, A. de Graeff, Symptom prevalence in patients with incurable cancer: a systematic review, J. Pain Symptom Manag. 34 (2007) 94–104.

[75] T.C.C. The Nordic Cochrane Centre, Review Manager (RevMan). 5.3. The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, 2014.

[76] L. Traeger, T. McDonnell, C. McCarty, J. Greer, A. El-Jawahri, J. Temel, Nursing intervention to enhance outpatient chemotherapy symptom management: patient-reported outcomes of a randomized controlled trial, Cancer 121 (2015) 3905–3913.

[77] L. Tuominen, M. Stolt, R. Meretoja, H. Leino-Kilpi, Effectiveness of nursing interventions among patients with cancer: An overview of systematic reviews, J. Clin. Nurs. 28 (2019) 2401–2419.

[78] H. van Waart, M.M. Stuiver, W.H. van Harten, E. Geleijn, J.M. Kieffer, L.M. Buffart, M. de Maaker-Berkhof, E. Boven, J. Schrama, M.M. Geenen, J.M. Meerum Terwogt, A. van Bochove, V. Lustig, S.M. van den Heiligenberg, C.H. Smorenburg, J.A. Hellendoorn-van Vreeswijk, G.S. Sonke, N.K. Aaronson, Effect of low-intensity physical activity and moderate- to high-intensity physical exercise during adjuvant chemotherapy on physical fitness, fatigue, and chemotherapy completion rates: results of the PACES randomized clinical trial, J. Clin. Oncol. 33 (2015) 1918–1927.

[79] K. Vissers, M. Van den Beuken-van Everdingen, D. Dijstra, G. MJMM, A. de Graeff, F. Jansman, et al., Dutch guideline: Diagnostics and treatment of pain in patients with cancer, Netherlands.

[80] F.M. Walter, K. Mills, S.C. Mendonca, G.A. Abel, B. Basu, N. Carroll, S. Ballard, J. Lancaster, W. Hamilton, G.P. Rubin, J.D. Emery, Symptoms and patient factors associated with diagnostic intervals for pancreatic cancer (SYMPTOM pancreatic study): a prospective cohort study, Lancet Gastroenterol. Hepatol. 1 (2016) 298–306.

[81] K. Wang, S. Qi, H. Lai, X. Zhu, G. Fu, Clinical massage therapy for patients with cancer-related fatigue protocol of a systematic review, Medicine 97 (2018) e13440 (Baltimore).

[82] M. Wells, P.T. Donnan, L. Sharp, C. Ackland, J. Fletcher, J.A. Dewar, A study to evaluate nurse-led on-treatment review for patients undergoing radiotherapy for head and neck cancer, J. Clin. Nurs. 17 (2008) 1428–1439.

[83] M. Wells, A. Harrow, P. Donnan, P. Davey, S. Devereux, G. Little, E. McKenna, R. Wood, R. Chen, A. Thompson, Patient, carer and health service outcomes of nurse-led early discharge after breast cancer surgery: a randomised controlled trial, Br. J. Cancer (2004) 651–658.

[84] M. Wells, B. Williams, S. Treweek, J. Coyle, J. Taylor, Intervention description is not enough: evidence from an in-depth multiple case study on the untold role and impact of context in randomised controlled trials of seven complex interventions, Trials 13 (2012) 95.

[85] WHOCancer, World Health Organisation, 2017.

[86] M. Yamanaka, A concept analysis of self-management of cancer pain, Asia Pac. J. Oncol. Nurs. 5 (2018) 254–261.

[87] P. Yates, H. Edwards, R. Nash, S. Aranda, D. Purdie, J. Najman, H. Skerman, A. Walsh, A randomized controlled trial of a nurse-administered educational intervention for improving cancer pain management in ambulatory settings, Patient Educ. Couns. 53 (2004) 227–237 211p.

[88] E. Yorganci, C.J. Evans, H. Johnson, S. Barclay, F.E. Murtagh, D. Yi, W. Gao, A. Pickles, J. Koffman, Understanding usual care in randomised controlled trials of complex interventions: a multi-method approach, Palliat. Med. 34 (2020) 667–679.

[89] Q. Zhang, F. Li, H. Zhang, X. Yu, Y. Cong, Effects of nurse-led home-based exercise & cognitive behavioral therapy on reducing cancer-related fatigue in patients with ovarian cancer during and after chemotherapy: a randomized controlled trial, Int. J. Nurs. Stud. (2017) 52–60.

[90] H. Zhe, The assessment and management of constipation among patients with advanced cancer in a palliative care ward in China: a best practice implementation project, JBI Database Syst. Rev. Implement. Rep. 14 (2016) 295–309.