

Review

# A systematic review on patient-reported outcomes in cancer survivors of randomised clinical trials: direction for future research

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## Abstract

**Objective:** With increasing expectations of a 5-year survival rate among cancer patients, there is growing interest in patient-reported outcome (PRO) measures, particularly measures of health-related quality of life (HRQOL) in cancer practice. The purpose of this review was to explore the existing interventions for patients coping with cancer in terms of intervention type, PRO measurements and outcomes; and to identify directions for future research.

**Methods:** Systematic review of randomised clinical trials. A systematic search of four databases was conducted to identify articles published in English or Chinese from January 2000 to July 2013. Studies were located using an electronic search, a manual search and an author search.

**Results:** A total of 34 articles corresponding to 33 original studies were identified and included in this review. These interventions were classified under four broad categories according to their approaches: psycho-education (15), case management (13), exercise (4) and feedback of PRO (1). The PRO measures covered different types of PRO measures, including HRQOL, functional status, symptom status, overall well-being and satisfaction with care. Positive outcomes of more than 70% (24) out of these interventions were reported.

**Conclusions:** These findings highlight the significant outcomes of cancer patient interventions that applied PRO measures to evaluate their outcomes. A theory-driven and careful design of the programme should be considered in the whole process of developing, delivering and assessing the programmes. Collaboration among patients, clinicians, researchers and policy makers is crucial to ensure the development of effective and accessible interventions targeting improving cancer survivors' HRQOL.

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Received: 4 September 2013

Revised: 25 January 2014

Accepted: 25 January 2014

## Introduction

With new and advanced medical treatments such as surgery, chemotherapy, radiation and hormonal therapy, 68% of adults diagnosed with cancer today can expect to be alive in 5 years time [1]. These treatments, however, are accompanied by the risk of substantial side effects, either short-term and time-limited or long-term and persistent [2], which raises a claim for long-term outcome assessment.

Recognition has been growing that traditional medical outcomes (i.e. survival, disease-free progression), although remaining indisputably important, do not fully capture the patient's experience of health [2–4]. A comprehensive picture of the patient's health status should include patient-reported outcome (PRO) measures, particularly measures of health-related quality of life (HRQOL) [2,3].

The term PRO is defined as 'outcome measures including any outcome based on data provided by patients or patient proxy, as opposed to data provided by other sources (including providers and care-givers)...' [5].

Evidence showed that the term PRO itself seems to have come into frequent usage since 2000, suggesting a growing interest in bringing the patient's perspective to cancer practice since then [2,4–6]. In cancer practice, PRO measures (PROMs) can supply valuable information on health status, in particular HRQOL, and treatment effects that could not be collected by any other method [7]. Other potential benefits of using PROMs in clinical care may be as prognostic predictors [8] and in facilitating patient–clinician communication, which would promote the model of shared decision-making [9].

Although there are multiple potential uses and benefits of PROMs in cancer practice, the primary area of application has been the use of PROMs in randomised clinical trials (RCTs) to evaluate effectiveness of cancer treatments [10], cancer screening [11,12], prevention [13,14] and management of disease symptoms [2,15,16]. This systematic review focuses on the analysis of the use of PROMs in the measurement of supportive care interventions. These are interventions implemented to help patients with cancer

cope with their illness and complex needs. They are a heterogeneous group of interventions [9,17,18] ranging from interventions such as psycho-educational training to exercise programmes. The aims of this literature review were threefold: (i) to explore the use of PROMs in the measurement of supportive care interventions; (ii) to consider whether the effectiveness of the intervention impacted on global functioning and/or symptom improvement; and (iii) to identify directions for future intervention and PRO research.

## Methods

The PRISMA guideline was followed for this systematic review methodology [19].

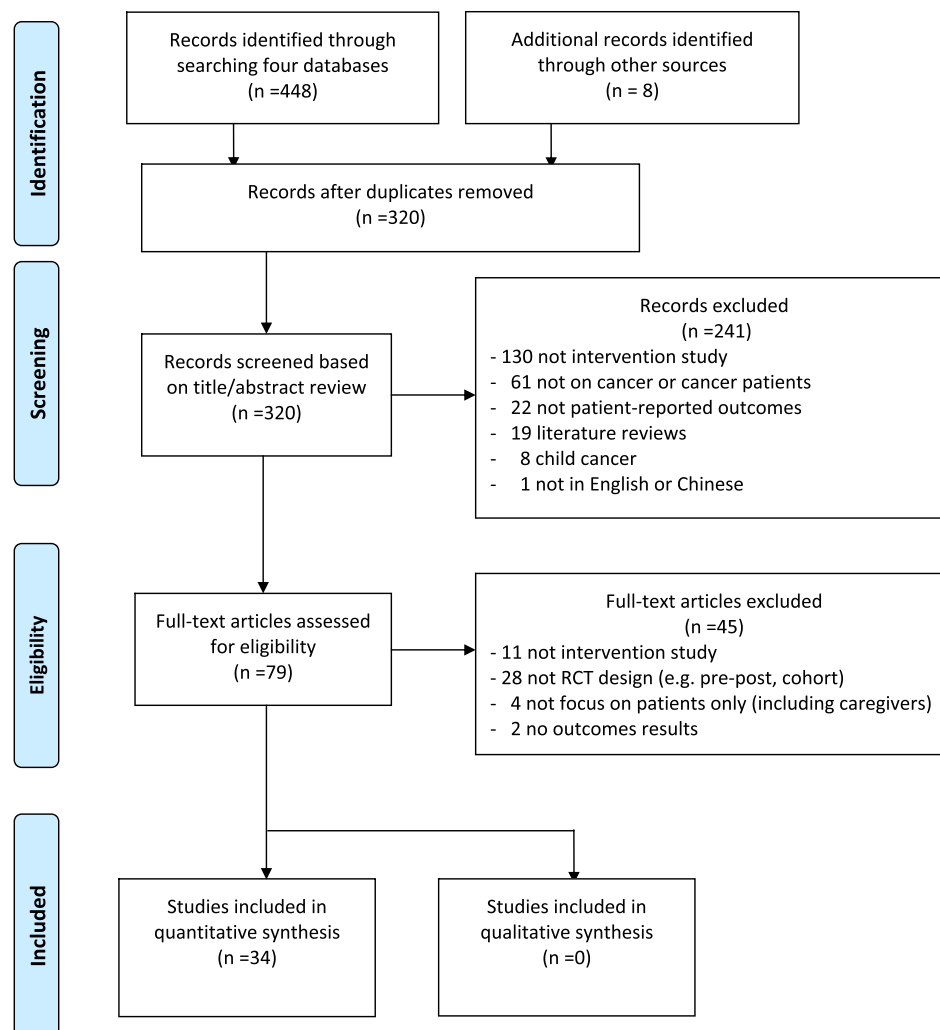
### The process of searching and selecting

Literature related to PRO in cancer of RCT supportive care interventions was searched. The key words used were

as follows: 'intervention' or 'programme' or 'therapy' or 'nursing' or 'care' AND 'cancer' or 'oncology' or 'carcinoma' AND 'patient-reported outcomes' or 'self-reported outcomes'. The four databases searched included Science Citation Index Expanded, PsycINFO, Medline (1950+) via OvidSP and CINAHL database. A manual search of the references to the identified literature from the four databases and an author search were also conducted. The eligibility and selection of the articles were assessed by screening records based on title/abstract review and accessing the full texts according to predefined inclusion and exclusion criteria. The flow diagram of the search and selection process is outlined in Figure 1.

### Criteria for inclusion and exclusion

The studies included in this review met the following criteria: articles published in English or Chinese from January 2000 to July 2013. The focus of the studies was on RCT supportive care interventions for adults



**Figure 1.** The flow diagram on identifying the literature

(age  $\geq 18$  years old) cancer patients, and outcome measures included PROMs. Commentaries, editorials, literature reviews and conference proceedings were not included in this review.

### Data extraction and quality assessment

Data were extracted from each of the included studies using a standard format for the reporting of PROMs in RCTs [20]: information on the literature, study aim, description of interventions, target population, PRO measurements, significant outcomes and methodological quality (Table 1, Supporting information). Quality assessment of the included studies was conducted by using the criteria proposed by the Effective Public Health Practice Project [21]. Six components, including selection bias, study design, confounders, blinding, data collection methods, and withdrawals and dropouts from each study are rated as strong, moderate or weak according to a standardised guide [21]. Studies with no weak ratings and at least four strong ratings were considered strong. Studies with fewer than four strong ratings and one weak rating were considered moderate. Finally, studies with two or more weak ratings were considered weak.

Because of the heterogeneity of the interventions and the PRO measurements identified in this review, a systematic review was adopted to analyse these RCT intervention studies. This is also the reason why a meta-analysis was not possible for this review.

## Results

A total of 34 quantitative studies were included in this review. We treated two studies that presented the primary [22] and secondary [23] outcomes of the same trial separately as one study. Consequently, the following report was described as 33 studies. Table 1 (Supporting information) summarises the characteristics of the identified RCT supportive care interventions.

### Target population

The sample size of cancer patients in these studies ranged from 45 to 1159, involving a total of 5960 patients. The patients in these studies were coping with breast cancer ( $n=12$ , 36.4%), prostate cancer ( $n=3$ , 9.1%), ovarian cancer ( $n=1$ , 3.0%), oral cancer ( $n=1$ , 3.0%), lung cancer ( $n=1$ , 3.0%), colon cancer ( $n=2$ , 6.1%), gastric or liver cancer ( $n=1$ , 3.0%) and multiple types of cancer ( $n=12$ , 36.4%). Nearly half of the studies (16/33, 48.5%) focused on gender-specific cancers.

The follow-up periods of these studies ranged from immediately post-intervention, to 24 months. They were as follows: 24 months ( $n=1$ , 3.0%), 12 months ( $n=7$ , 21.3%), 6 months ( $n=11$ , 33.3%), 4 months ( $n=1$ , 3.0%), 3 months ( $n=4$ , 12.1%), 2 months ( $n=4$ , 12.1%), 1 months

( $n=1$ , 3.0%), 6 weeks ( $n=1$ , 3.0%), 1 week ( $n=1$ , 3.0%) and immediately post-intervention ( $n=2$ , 6.1%).

The attrition rate ranged from 0 to 47%, with an average rate of 30.0 % (1785/5960). The reasons given by the cancer patients for refusal or dropping out of the study intervention were being too busy, the time of the interventions was not workable, or other time commitments [16,24–27]; lack of interest in research participation or refusal of group assignment [16,22,25,27,28]; change of treatment, too ill or patient mortality [10,16,22,24,26–30]; living too far away from the intervention facilities or transportation issues [16,25–28]; refusal to be followed [10,16,24,28]; and language difficulty [22].

### Quality and characteristics of the selected studies

As shown in Table 1 (Supporting information), five studies had a global rating of 'strong' [10,11,26,31,32], whereas the remaining 28 studies were rated 'moderate'. The most common reason for a study not receiving a 'strong' rating was due to a low response rate from eligible participants and a high withdrawal rate, which led to otherwise 'strong' articles being rated as 'moderate'. Despite different ratings, all 33 studies were included in the review.

It was noted that only one study that focused on evaluating the effects of regular completion of HRQOL, with feedback to physicians on cancer patients' outcomes [22], was identified in this review. Although this point is not included in the criteria for quality assessment proposed by the Effective Public Health Practice Project [21], this may act as one of the downsides in applying PROMs in evaluating the effectiveness of supportive care interventions for cancer patients.

A majority of studies ( $n=32$ , 97.0%) that focused on cancer patients' interventions of RCT design have been conducted in Western countries, namely the USA ( $n=19$ , 57.6%), the UK ( $n=5$ , 15.2%), Denmark ( $n=4$ , 12.1%), Canada ( $n=3$ , 9.1%) and Australia ( $n=1$ , 3.0%). Only one study was conducted in Asia, in Taiwan ( $n=1$ , 3.0%).

### Supportive care intervention approaches and focuses

The interventions reviewed here can be classified under four broad categories according to their approaches: psycho-education ( $n=15$ , 45.5%), case management ( $n=13$ , 39.4%), exercise ( $n=4$ , 12.1%) and feedback of PRO ( $n=1$ , 3.0%).

### Conceptual framework of interventions

There were two studies included in this review that adopted conceptual frameworks to guide their design. The theoretical frameworks applied were cognitive-behavioural theory [31] and social cognitive theory [12].

## PRO measurements and significant outcomes of supportive care interventions

On the basis of the PRO types reported in a review on PRO in cancer [2], PRO measurements applied in these studies were grouped under the following types: HRQOL, symptom status, functional status, global well-being and satisfaction with care (Table 2, Supporting information). The significant outcomes of supportive care interventions were presented by clustering the different supportive care interventions together according to their approaches as psycho-education, case management, exercise and feedback of PRO. The authors opted to describe only the trials with a positive outcome of the intervention, but the potential reasons for a lack of positive results are described in the discussion.

### Psycho-education

Psycho-education included interventions that focus on offering information to patients, including written or printed materials [11,12,25,26,30,33,34], and video or audio materials [10,12,30,34]; decision support system [35,36]; and psycho-education of cancer-related symptoms [16,30,31,37–39]. Of the 15 psycho-education studies, 12 studies reported significant outcomes [10–12,16,26,30,34–39].

There were five psycho-education interventions that mainly focus on pain management [16,30,34,37,38]. Bulter *et al.* [16] examined whether a group education intervention, including hypnosis, can reduce cancer pain using the pain and suffering rating scale and self-rating scale of pain. The result showed that patients in the intervention group experienced significantly less of an increase in the intensity of pain and suffering over time, compared with those in the control group [16].

A study tested the effectiveness of a pain training intervention with watching the videotape and reviewing the content of the handbook on patients' ratings of pain using the Memorial Symptom Assessment Scale, the Brief Pain Inventory (BPI) and Barriers Questionnaire (BQ) [30]. Findings indicated that physician and nurse ratings were closer to patients' pain ratings in the intervention group versus the control group ( $p=0.04$  and  $<0.001$ ) [30]. The outcomes also showed that patients in the intervention group reported reduced barriers to pain relief ( $p<0.001$ ), lower than usual pain ( $p=0.03$ ) and greater opioid use ( $p<0.001$ ) compared with those in the control group. No patients in the intervention group reported severe pain ( $>6$  on a 0–10 scale) at 1-month outcomes ( $p=0.03$ ) [30].

The findings of a pain management intervention [34] in offering video and booklet information to patients with a variety of cancer patients showed that mean average pain and worst pain scores improved significantly in patients receiving both the video and booklet information. The addiction subscale of the barriers questionnaire score was improved by 0.44 (SE=0.19) for participants receiving any part of the intervention ( $p=0.03$ ) [34].

To examine the impact of a brief pain education/communication skills training on patient outcomes in breast cancer [37] found that patients in the pain education/communication skills group reported a significant decrease in pain barriers assessed by BQ. Overall, patients with lower barrier scores reported less distress (Mental Health Inventory) and better emotional well-being (SF-12). Patients who scored higher in active communication (e.g. asking questions, giving information) reported fewer barriers and better pain relief (BPI's 'degree of pain relief'). Findings of satisfaction with care measured by the Patient Satisfaction Questionnaire showed that although there was just a marginally significant ( $t=1.83$ ;  $p=0.07$ ) increase in satisfaction with care over time, significant ( $z=1.73$ ;  $p=0.04$ ) individual differences in satisfaction with health care that changed over time were evident. Individuals who perceived their physicians as being both more receptive and facilitative were more satisfied with their health care [37].

Thomas and colleagues [38] tested the effectiveness of two interventions compared with usual care in decreasing attitudinal barriers to cancer pain management, decreasing pain intensity, and improving functional status and quality of life (QOL) using the BPI, the BQ and the SF-36. The two intervention arms were an education group and a coaching group. In an education group, participants viewed a video and received a pamphlet on managing cancer pain, whereas in a coaching group, apart from what was included in the education group, there were also four telephone sessions within a 6-week period, with an advanced practice nurse interventionist using motivational interviewing techniques to decrease attitudinal barriers to cancer pain management. The findings showed that patients in the coaching group reported a significant improvement in their ratings of pain-related interference with function, as well as general health, vitality, mental health and mental component summary [38].

Among the three studies that focused on controlling other cancer-related symptoms, a study examined the efficacy of providing men with prostate cancer with an audiotape of their primary treatment consultation [10]. The findings from the Satisfaction Questionnaire showed that patients receiving an audiotape reported having been provided with significantly more disease and treatment information in general ( $p=0.04$ ), more information about treatment alternatives ( $p=0.04$ ) and treatment side effects ( $p=0.01$ ) than patients who did not receive the audiotape. Patients also rated the audiotape intervention positively, with an average score of 83.0 out of 100, indicating a highly positive regard for the intervention [10].

Another study that tested the efficacy of a combined written and verbal expression group programme for psychological distress in colorectal cancer showed that patients in the intervention group experienced significantly greater changes in distress compared with those in the control group



at month 2 on the Brief Symptom Inventory (Global Severity Index, GSI) and the Center for Epidemiologic Studies—Depression Scale (CES-D) scores ( $p < 0.05$  for each) [26]. The European Organization for Research and Treatment of Cancer QOL questionnaire (EORTC QOL) differences in the EORTC global QOL scores approached significance ( $p = 0.063$ ) at month 2 and significance in emotional functioning at month 4 ( $p < 0.05$ ) [26].

Thornton and colleagues [39] designed a study to test whether a psychological intervention reduces depression-related symptoms and markers of inflammation among breast cancer patients [39]. The PROMs used in this study included CES-D, fatigue and bodily pain subscales of SF-36. The results revealed that the intervention significantly reduced depressive symptoms, pain, fatigue and inflammation markers. Moreover, the intervention effect on inflammation was mediated by its effect on depressive symptoms [39].

Of the two studies targeting on improving knowledge [11,12], Boundouki and colleagues investigated the influence of a patient information leaflet on patients with oral cancer to improve knowledge, reduce distress and increase intention to accept a mouth screen over a 2-month period [11]. Three questionnaires made for this study were applied to assess the outcomes: the knowledge of mouth cancer scale, the mouth screen distress scale and the intention to accept a mouth cancer screen scale. The findings indicated that all measures showed some benefit of immediate exposure to the leaflet at follow-up. The introduction of a mouth cancer patient information leaflet into dental practice could help to inform patients about oral cancer, moderate distress and encourage acceptance of an oral health screen [11].

Another study assessed the effect of video and pamphlet interventions on patient prostate cancer screening knowledge using a 10-item index for patients' screening knowledge [12]. The results indicated that patients in the intervention group reported significantly higher mean knowledge index scores and a higher percentage of correct responses to questions on cancer natural history, treatment efficacy and expert disagreement than those in the control group [12].

Two studies focusing on decision support reported significant outcomes [35,36]. One study assessed the effect of a decision support system based on the Internet-based Personal Patient Profile—Prostate on decisional conflict associated with decision making, plus explored time-to-treatment, and treatment choice using the Decisional Conflict Scale, and the Acceptability E-scale. The findings reported that the patients in the intervention group had reduced adjusted decisional conflict in uncertainty score and values clarity over time, compared with those in the control group [35]. Acceptability and usefulness were also highly rated in the intervention group [35].

The other study that evaluated the long-term psychological impact of a decision aid intervention on breast cancer patients showed that patients in the intervention group

experienced less decisional conflict (DCS,  $p = 0.047$ ) [36]. Although no significant findings were found between groups [36], subgroup analyses revealed that patients in the intervention group showed better long-term body image outcomes ( $p = 0.009$ ) assessed by the Body Image Scale, which were mediated by reduced depressive coping ( $p = 0.049$ ). Coping was assessed using the Freiburg Questionnaire of Coping with Illness [36].

In summary, the significant outcomes of the 12 psychoeducation interventions included relieving symptoms, such as pain, distress and depression; offering cancer-related information to patients, which could benefit patients' satisfaction and acceptance of health care; and supporting decision-making.

### Case management

There were 13 case management interventions focusing on single-skill training or symptom management, including hypnosis [13], foot reflexotherapy [15], cognitive behavioural stress management (CBSM) [40] and energy and sleep enhancement [24]; and multiple dimensional HRQOL or holistic case management [14,29,32,41–46]. Of that total, eight studies reported significant findings [13–15,32,40,41,44,45].

Among the three studies focusing on single-skill training or symptom management [13,15,40], a study was designed to test the hypotheses that a brief presurgery hypnosis intervention would decrease intraoperative anaesthesia and analgesic use and side effects associated with breast cancer surgery using visual analogue scale (0–100). The findings showed that patients in the intervention group not only required less propofol and lidocaine but also reported less pain intensity, pain unpleasantness, nausea, fatigue, discomfort and emotional upset than those in the control group [13].

Another study conducted in Taiwan designed a foot reflexotherapy for pain alleviation and anxiety in patients with cancer undergoing major abdominal surgery, using the Short-form McGill Pain Questionnaire, visual analogue scale for pain and the hospital anxiety and depression scale [15]. Findings showed that patients in the intervention group reported less pain ( $p < 0.05$ ) and less anxiety ( $p < 0.05$ ) over time compared with those in the control group [15].

The effects of a 10-week group-based CBSM intervention on psychosocial adaptation in patients with breast cancer was tested using the Hamilton rating scale for anxiety, Impact of Event Scale and the Affects Balance Scale [40]. The findings showed that the omnibus group\* time interaction test for both anxiety and Impact of Event Scale-Intrusive thoughts were statistically significant,  $F(2, 81) = 3.86$ ,  $p < 0.05$ , and  $F(2, 83) = 3.24$ ,  $p < 0.05$ , respectively [40].

Of the five studies that focused on multiple dimensional HRQOL or holistic case management [14,32,41,44,45], Temel *et al.* [14] examined the effect of introducing

palliative care early, after a new diagnosis, among patients with lung cancer on PRO and end-of-life care using Functional Assessment of Cancer Therapy Scale—Lung (FACT-L). The findings showed that patients in the intervention group had a better HRQOL than did patients in the control group (98.0 vs 91.5;  $p=0.03$ ) [14].

Strong *et al.* designed a nurse-delivered complex intervention to treat major depressive disorders in cancer patients [32]. The findings showed that the intervention improved anxiety, which was assessed by a 10-item subscale of the Symptom Checklist-90 questionnaire [32]. The intervention also improved depression, in that the adjusted difference in mean Symptom Checklist-20 depression score, between patients in the intervention group and those in the control group was 0.34 (95% CI 0.13–0.55) at 3, 6 and 12 months follow-up [32].

This study also analysed the cost-effectiveness of the intervention using the Euroqol-5D questionnaire (EQ-5D) [32]. The findings showed that the incremental cost associated with the intervention was £334 (US\$668) over 6 months. The cost per quality-adjusted life-year gain of £5278 (\$10 556) was better when compared with a median cost per quality-adjusted life-year of at least £10 000 (\$20 000) for anticancer treatments [32]. It is stated that the intervention would probably be a relatively cheap and acceptable model for effective treatment of depression in cancer patients undergoing medical services [32].

Another study assessed the effectiveness of a collaborative model of depression care on cancer patients by using the Patient Health Questionnaire—9 (PHQ-9) and FACT-General [41]. The findings showed that patients in the intervention group were more likely than those in the control group to show improvement in depression symptoms (50% reduction in PHQ-9 score), and their PHQ-9 score was significantly more likely to have decreased by 5 points since baseline (54% compared with 37%; OR=2.07) [41]. This study also reported that patients in the intervention group had significantly better social ( $p=0.03$ ) and functional ( $p=0.01$ ) well-being, which was assessed by FACT-General [41].

McCorkle and colleagues [44] tested the effect of a nursing intervention on QOL in women with gynaecological cancer using CES-D, the Symptom Distress Scale, the ambiguity subscale of the Mishel Uncertainty in Illness Scale and SF-12 [44]. Intervention contents included symptom management and monitoring, emotional support, patient education, coordination of resources, referrals and direct nursing care. The findings showed that the nursing intervention contributed to a significant improvement over time in depression (CES-D), symptom distress (Symptom Distress Scale) and uncertainty (Mishel Uncertainty in Illness Scale) [44]. Patients in the intervention group had better SF-12 mental and physical QOL over time [44].

The remaining study tested the effects of a shared care programme on the attitudes of cancer patients towards

the health care system, their HRQOL and performance status using a self-developed questionnaire of patients' attitudes towards health care services, EORTC QLQ-C30 and Eastern Cooperative Oncology Group Scale of Performance Status [45]. The care programme included transfer of knowledge from the oncologist to the general practitioner (GP), improved communication between the parties and active patient involvement. The outcomes revealed that the shared care programme had a positive effect on patient evaluation of cooperation between the primary and secondary health care sectors. The effect was particularly significant in men and in younger patients (18–49 years), who felt they received more care from the GP and were left in limbo less often. Young patients in the intervention group rated the GP's knowledge of disease and treatment significantly higher than those in the control group [45].

To summarise, there were multiple significant effects in these case management studies, including improved symptoms, such as pain, nausea, fatigue, discomfort, emotional upset, intrusive thoughts, anxiety, depression and uncertainty; HRQOL, such as general QOL, social and functional well-being, and mental and physical QOL; and the attitudes of cancer patients towards the health care system.

### Exercise

Exercise included interventions focusing on home-based exercise [28,47] and group exercise [27,48]. Of the four studies that focused on exercise intervention, three articles reported significant outcomes [27,28,48]. One study evaluated the impact of a home-based walking intervention on self-reported physical function in cancer patients using the Role Limitations Due to Physical Health subscale of SF-36 (MOS-RLPS) and the Physical Functioning subscale of SF-36 (MOS-PFS) [28]. The results showed that exercise patients undergoing chemotherapy reported worsening MOS-RLPS by the end of cancer treatment ( $p=0.037$ ). A younger age was associated with improved MOS-PFS ( $p=0.048$ ) [28].

Danhauer and colleagues [27] examined the effectiveness of a 10-week 75-min long restorative yoga class on self-reported emotional, HRQOL and symptom outcomes in patients with breast cancer using SF-12; the Functional Assessment of Cancer Therapy Scale—Breast Cancer (FACT-B); FACT-Fatigue; the functional assessment of chronic illness therapy—spiritual well-being scale (FACIT-Sp); CES-D; Pittsburgh Sleep Quality Index/Inventory; and Positive And Negative Affect Schedule (PANAS). The findings showed that patients in the intervention group reported better mental health (FACT-B), depression (CES-D), positive affect (PANAS) and spirituality (peace/meaning, FACIT-Sp) compared with those in the control group. HRQOL (FACT-B) showed a borderline difference between the two groups ( $p=0.052$ ) [27].

Mutrie *et al.* [48] conducted a study to determine functional and psychological benefits of a 12-week supervised

group exercise programme during treatment for early stage breast cancer [48]. The study reported that the intervention had an effect at 12 weeks on FACT-B general, social domain (FACT-GS), and positive mood (PANAS). Findings of physical status, which was measured by a Scottish physical activity questionnaire [48], showed that the intervention had effect at 12 weeks on metres walked in 12 min, minutes of moderate intensity activity reported in a week, and shoulder mobility [48].

Overall, three out of four exercise interventions had significant effectiveness in cancer patients, including improved physical function, mental health, depression, positive mood, spirituality (peace/meaning), social health and FACT-B general.

### Feedback of PRO

Only one study focused on feedback of PRO in this review, which referred to regular completion of HRQOL with feedback to physicians, and concluded two separated reports on primary [22] and secondary outcomes [23]. The primary aims were designed to examine the effects of the regular collection and use of HRQOL data on process of care and patient well-being in oncology practice. The findings indicated that patients in the intervention group and attention control group (completion of HRQOL without feedback) enjoyed better HRQOL than those in the control group ( $p=0.006$  and  $p=0.01$ , respectively), but the intervention group and attention-control group were not significantly different ( $p=0.80$ ). The same pattern of results was observed for physical well-being and functional well-being, with the main differences being between the intervention and control arms, but not between the intervention and attention-control arms. The emotional well-being of the intervention group of patients was better than that of the control group ( $p=0.008$ ) [22].

The trial's secondary aims were to measure any impact on patient satisfaction and patients' perspectives on continuity and coordination of their care. The outcomes showed that patients' evaluation of the intervention was positive. Patients in the intervention group rated their continuity of care as better than that of the control group for the 'Communication' subscale ( $p=0.03$ ) [23]. To the end, the regular completion of HRQOL with feedback to physicians benefited not only patient well-being but also patient-physician communication in oncology practice.

### Discussion

This systematic review has found that the RCTs using PROMs to measure the effectiveness of supportive care interventions have used all but one to the different types of PROM measures as defined by Lipscomb and colleagues [2]—HRQOL, functional status, symptom status, overall well-being and satisfaction with care. The only

measure not covered in these studies was treatment adherence. Although all 33 studies included in this review applied PROMs to evaluate the effectiveness of the intervention, only one study was identified to evaluate the effectiveness of feedback on the HRQOL data to physicians [22]. This is also the only study using a touch-screen computer to collect HRQOL data [22].

These studies provided valuable suggestions on interventions to be developed for patients with cancer, including offering information to patients [10,12,30,34], decision support system [16,35,36], CBSM [40], group exercise [27,48] and feedback of PRO information to physicians [22]. It was noted that although most of these supportive care interventions had significant findings, nearly a quarter of the interventions did not report positive outcomes as hypothesised [24,25,31,33,42,43,46,47]. A reverse outcome was reported in one study in that the participants in the control group experienced a greater decrease in total mood disturbance and more improvement in emotional, cognitive and social functioning than those in the intervention group [29].

The potential reasons for lack of positive results were as follows: (1) target population: choice of target population [24,43], as well as confounding effects, including gender [24] and commuting times [25]; (2) intervention: insufficient dose and intensity of the intervention [24,29], or intervention not well-matched to improving outcomes in the target population [42], as well as compliance with intervention instructions [25]; (3) PROMs: the choice of outcome measures [31], the PROM may not have been sensitive enough to capture some intervention effects [43]; and (4) time: incorrect timing of measures [24] and insufficient observation period [42].

### Study gap identified

It is worth noting that the majority of these interventions were conducted in Western countries; only one study was identified that was conducted in an Asian country. It is recommended that similar studies be conducted in different cultures to help cancer patients in different cultures gain a better understanding of the PRO measurements. Additionally, although it has been reported that an explicit conceptual model is needed to maximise the information value of PRO assessment in cancer trials [2], only two RCT studies included in this review reported that there were conceptual frameworks to guide their study design [12,31]. A theory-driven approach should be adopted in future intervention study design and outcome assessment for using PRO in clinical practice [17].

Although many different kinds of PROMs were applied across these studies, the main focus for the majority of these studies was to evaluate the effectiveness of the (supportive care) interventions. It was noted that only one study focused on evaluating the effects of regular completion of HRQOL with feedback to physicians on cancer patients' outcomes [22].



Among the variety of PRO measurements applied in this review, EQ-5D was the only PRO measurement used to analyse the cost-effectiveness of the intervention. EQ-5D was also the only 'preference-based' PRO measurement applied in this review.

### Limitations of this review

It is essential to acknowledge several limitations of this review. Although both English and Chinese literature were searched, no literature published in Chinese on cancer patients' supportive care interventions was identified. Supportive care intervention studies other than RCT study design, other languages, conference abstracts, dissertations and book chapters were not included. In addition, unpublished studies in this area were also not included in this review.

Given that PRO was one of the focuses of this review, 'patient-reported or self-reported outcomes' were applied as search keywords. However, this led to the narrow search method of this review, which may act as a major limitation of this review and exclude articles in that 'self-reported' or 'patient-reported' are not used as keywords from the databases [49]. Although a manual search of the references to the identified literature from the four databases was conducted, this may also be restricted by the narrow search method used in this review. A manual search from previous systematic reviews and meta-analyses [50,51] should be conducted to identify eligible studies.

### Recommendations for future intervention programme

The attrition rate in these studies ranged from 0 to 47%, with an average rate of 30%. The barriers to taking part in these interventions, as reported by the participants, point to the need for greater flexibility in the content and delivery of interventions for patients coping with cancer. Moreover, careful study design and execution are also needed for preventing missing data [2,20], including target population choice, good intervention design, considered choice of the PROMs, correct timing assessment, a reasonable follow-up period and effective methods of data collection.

In cancer practice, PROMs can supply valuable information on health status, in particular HRQOL, and treatment effects that could not be collected by any other method that is different from PROMs [7]. However, only with the considered choice of the PROMs, correct timing assessment and a reasonable follow-up period, as well as a good fit with the study purpose and design, can PROMs information benefit cancer practice [2]. In addition, future

research in supportive care interventions and assessment of their effectiveness using PROMs should highlight the importance of providing feedback on valuable PROMs information to physicians, which will benefit the day-to-day use of PROMs in patient-provider decision-making [2].

More studies on cost-effective analyses of cancer interventions and preference-based measures of HRQOL are required. To enhance the application of PROMs in oncology practice, it is urged that new information infrastructures, technologies and cancer care delivery systems be adopted. Such changes could lower data collection costs, ensure confidentiality, facilitate cost-effective analyses of cancer interventions and benefit the day-to-day use of PRO information in patient-provider decision-making [2].

### Conclusion

These findings highlight the significant outcomes of cancer patient interventions that applied PROMs to evaluate their outcomes. Future studies on cancer patient interventions and PROMs can be conducted in different cultures, such as those in Asia. A theory-driven, careful design should be considered in the entire process of developing, delivering and assessing the programmes. Collaboration among patients, clinicians, researchers and policy makers is crucial to ensure the development of effective and accessible interventions targeting improving cancer survivors' HRQOL in PROMs.

### Acknowledgements

Financial support of this study was provided by the National Nature Science Foundation (No. 81072393). The funders had no role in study design, data collection and analysis, decision to publish or preparation of the manuscript.

### Author contributions

Qiuping Li: study conception/design, literature search/analysis, drafting of manuscript and final approval of the version to be published; Yi LIN: literature search/analysis and drafting of manuscript; Xiwen LIU: literature search/analysis, drafting of manuscript and critical revisions of the manuscript; Yongyong XU: supervision and critical revisions for important intellectual content.

### Conflict of interest

The authors declare no conflicts of interest.

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