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A review on cost-effectiveness and cost-utility of psychosocial care in cancer patients

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ABSTRACT

Several psychosocial care interventions have been found effective in improving psychosocial outcomes in cancer patients. Nowadays there is increasingly being asked for information on the value for money of this type of intervention. This review therefore evaluates current evidence from studies investigating cost-effectiveness or cost-utility of psychosocial care in cancer patients. A systematic search was conducted in PubMed and Web of Science yielding 539 unique records, of which 11 studies were included. Studies were mainly performed in breast cancer populations or mixed cancer populations. Studied interventions included collaborative care (4 studies), group interventions (4 studies), individual psychological support (2 studies) and individual psycho-education (1 study). Seven studies assessed the cost-utility of psychosocial care (based on quality-adjusted life years (QALYs)), while three studies investigated its cost-effectiveness (based on Profile of Mood States (mood), Revised Impact of Events Scale (distress), 12-item Health Survey (mental health) or Fear of Progression questionnaire (fear of cancer progression)). One study did both. Costs included were intervention costs (3 studies), intervention costs and direct medical costs (5 studies) or intervention costs, direct medical costs and direct non-medical costs (3 studies). In general, results indicated that psychosocial care is likely to be cost-effective at different, potentially acceptable, willingness-to-pay thresholds. Further research should be performed to provide more clear information as to which psychosocial care interventions are most cost-effective and for whom. In addition, more research should be performed encompassing potential important cost drivers from a societal perspective, such as productivity losses or informal care costs, in the analyses.

INTRODUCTION

Many cancer patients experience psychosocial problems during or after treatment, including depression, anxiety, fear of cancer progression or problems with coping¹⁻³. The prevalence of depression in cancer patients has been estimated at 8% to 24%¹ and the prevalence of anxiety at 18%². Unmet care needs regarding these psychosocial problems have been reported in up to 89% of cancer patients^{4,5}.

Several psychosocial care interventions have been developed in recent years aiming to target these problems and care needs in cancer patients, ranging from relatively low-intensive interventions (e.g., self-help or group interventions) to high-intensive interventions (e.g., individual cognitive behavioral therapy)⁶. Also stepped care (i.e., an approach in which effective, yet least resource-intensive treatment is delivered first, followed by, when necessary, more resource-intensive treatments) and collaborative care interventions (i.e., a care model in which different healthcare disciplines closely collaborate in order to provide systematic treatment and follow-up) have been developed⁷⁻⁹. In general, psychosocial care interventions have been found effective in improving psychosocial outcomes, such as distress and quality of life, in cancer patients^{6,10}.

Carlson and Bultz^{11,12} hypothesized that providing psychosocial care to cancer patients may not only be effective in improving outcomes, but may also lead to cost savings in the long-term. Cancer patients benefitting from psychosocial care are hypothesized to make less use of other healthcare services (i.e., visits to the general practitioner or oncologist) called cost offset, due to, for example, an increased ability to adhere to demanding treatments or lifestyle recommendations resulting in an improved overall health. In addition, productivity losses may be reduced due to an increased ability to work. Previous studies have indeed found such an association between better psychosocial outcomes and less healthcare utilization or costs¹³⁻¹⁶ and higher rates of return to work^{17,18}. However, other studies did not find such an association^{19,20}.

Whether providing psychosocial care to cancer patients indeed is economically attractive can be assessed by performing economic evaluations, such as cost-effectiveness or cost-utility analyses^{21,22}. The current health care system increasingly asks for this kind of evaluations^{23,24}, since the economic burden of cancer care is high²⁵ and choices have to be made regarding optimal resource allocation.

In cost-effectiveness and cost-utility analyses, the difference in total costs between different interventions or between a new intervention and care-as-usual are weighted against the difference in effectiveness, such as improvement in psychological distress or fear of cancer progression (called cost-effectiveness analyses), or differences in quality-adjusted life years (QALYs) (called cost-utility analyses)^{21,22}. This results in a ratio of the incremental costs for an incremental unit of effect, called incremental cost-effectiveness ratio (ICER). Cost-effectiveness and cost-utility analyses can be performed from different perspectives (e.g., a healthcare perspective or a societal perspective), which determines the cost categories taken into account in the analyses. In a healthcare perspective, costs of the healthcare system are taken into account, while in a societal perspective, a broader spectrum of costs are measured including, for example, productivity losses and informal care costs.

Two systematic reviews^{26,27} on the economic evaluation of psychosocial interventions have been published so far, one of which included studies up to 2013²⁷. This last review revealed that psychosocial care interventions have the potential to be cost-effective²⁷. However, also studies combining exercise interventions and psychosocial support, or on the most optimal follow-up strategy were included²⁷, which hampers firm conclusions on the value for money of psychosocial care among cancer patients. Moreover, because new developments in psychosocial care are ongoing and studies on the cost-effectiveness and cost-utility of psychosocial care are increasingly being published in the past two years, a new search updating current evidence is warranted. The aim of this review was, therefore, to assess current evidence on the cost-effectiveness and cost-utility of psychosocial care interventions in cancer patients.

METHODS

Literature search

A literature search was conducted in two electronic bibliographic databases, namely PubMed (dates of coverage 1950 - present) and Web of Science (1900 - present) from inception to January 2016. Search terms included different terms for economic evaluations (e.g., cost-effectiveness or cost-utility analyses), cancer (e.g., neoplasm), psychosocial care (e.g., psychological care or supportive care) and psychosocial outcomes (e.g., depression or anxiety). Table 1 provides a detailed overview on the combinations of search terms used. In addition to this literature search, reference lists from eligible articles were manually searched and authors were asked for additional studies.

Table 1. Search strategy

PubMed (MedLine)	Web of Science
(Neoplasms[MeSH] OR neoplasm[ti] OR Cancer[ti] OR "chronic cancer patients"[ti] OR "cancer survivors"[ti]) AND (((cost* OR economic[ti]) AND (analysis OR analyses OR effectiveness OR utility OR evaluation OR benefit)) OR (cost-analysis OR cost-analyses OR cost-effectiveness OR cost-utility OR cost-benefit OR cost-evaluation OR cost-effectiv*)) AND ("supportive care"[ti] OR "psychosocial care"[ti] OR "psychological care"[ti] OR "after care"[ti] OR anxiety[ti] OR depression[ti] OR social[ti] OR psychosocial[ti] OR cognitive[ti] OR stress[ti] OR mood[ti] OR pain[ti])	TITLE: (neoplasm OR Cancer OR chronic cancer patients OR cancer survivors) AND TITLE: (supportive care OR psychosocial care OR psychological care OR after care OR anxiety OR depression OR social OR psychosocial OR cognitive OR stress OR mood OR pain) AND TITLE: (cost* OR economic) AND TITLE: (analysis OR analyses OR effectiveness OR utility OR evaluation OR benefit OR cost-analysis OR cost-analyses OR cost-effectiveness OR cost-utility OR cost-benefit OR cost-evaluation OR cost-effectiv*)

Abbreviation: MeSH, medical subject heading; ti, title

Study inclusion and exclusion criteria

Research articles were included if they: (a) presented results on the cost-effectiveness or cost-utility of psychosocial care interventions; (b) used QALYs or a psychosocial outcome measure as outcome; (c) included adult cancer patients only; and (d) full-text was available in English or Dutch. Research articles were excluded if they assessed the cost-effectiveness or cost-utility of an exercise intervention; were not yet published as full-text; or were reviews (although reference lists were checked). No limits were set for year of publication.

Selection procedure and data extraction

Screening of the databases for relevant articles was performed by two of the authors (FJ and VvZ). First, title and abstract of all identified records were screened for potential relevance. Consequently, full-text of potentially relevant articles were assessed for eligibility based on the inclusion and exclusion criteria. Differences in study selection between the two authors were solved by discussion. When needed a third person (IVdL) was consulted.

All studies found eligible for inclusion in this review were thoroughly read and relevant data was extracted. Data extracted included general information (i.e., name of the author, year of publication, country in which the study was conducted), study design, study population (i.e., cancer diagnosis, important eligibility criteria and number of patients), intervention and control treatment (i.e., type of treatment and treatment duration), follow-up period, outcome measure(s), study perspective (e.g., healthcare perspective or societal perspective), included cost categories (i.e., intervention costs, direct medical, direct non-medical, indirect

medical or indirect non-medical costs), and study results. All costs identified were converted to dollar-prices using the exchange rate of the index year reported in the article. In case the index year was not reported, the assumed index year was used.

Main findings of the included studies regarding the cost-effectiveness or cost-utility of psychosocial care interventions were summarized in a permutation matrix with nine possible cost-effectiveness/cost-utility outcomes^[28]. All studies were allocated to one of the nine possibilities based on main evidence for incremental costs (lower costs, equal costs or higher costs) and incremental effects (lower effects, equal effects or higher effects).

Quality assessment

The quality of the included studies was assessed using the 10-item checklist of Drummond et al.^{21,22}. One author (FJ) conducted the quality assessment. When an article referred to previous publications (e.g., design paper or study on effectiveness) for additional information, this study was retrieved as well for quality assessment. A total score per study was calculated by counting the numbers of items scored positively (+ 1) or partly positive (+ 0.5), resulting in a score ranging from 0 - 10. In addition, the percentage of studies that met a particular criterion was calculated.

RESULTS

Identification and selection of the literature

In total 539 records were screened for eligibility based on title and abstract, of which 25 were selected for full-text review (Figure 1). In addition, two articles were added based on reference checking or authors knowledge. After full-text review, 11 studies were included.

Table 2 provides an overview of the selected studies. Studies were published between 2006 and 2015, of which seven recently (i.e., 2014 or 2015)²⁹⁻³⁵. Most studies were conducted in the United Kingdom³⁴⁻³⁶ and the United States^{31,32,37} (both three studies), followed by Canada³⁸, Germany³⁹, Sweden²⁹, the Netherlands³³ and Australia³⁰ (all one study). Nine studies were cost-effectiveness or cost-utility studies conducted alongside a randomized controlled trial (RCT) on effectiveness of psychosocial care^{29,32,35,39}, while two studies used a decision analytic model, in which the cost-utility was estimated based on multiple sources of data^{33,34}.

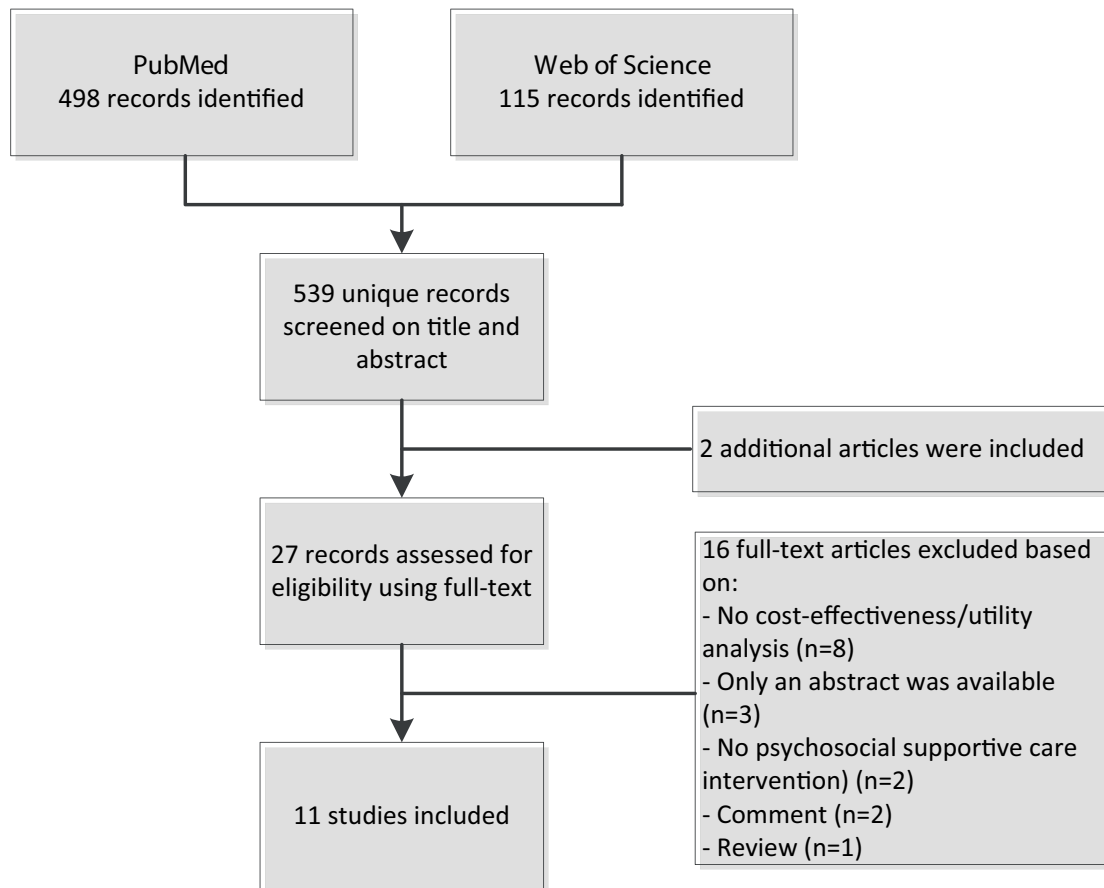


Figure 1: Flow diagram

Study populations and psychosocial care interventions

Of all nine studies that were performed alongside an RCT, four studies were conducted in breast cancer patients^{29,32,37,38}, and five studies were conducted in a mixed cancer population^{30,31,35,36,39}, which also consisted mainly of breast cancer patients. The two model studies used a hypothetical cohort of 1,000 breast cancer patients³³ or one hypothetical female cancer patient³⁴. In six studies all patients were included regardless of baseline scores on psychosocial outcomes^{29,32,34,37,38}, while in five studies selection criteria for psychosocial outcomes were set^{30,31,35,36,39}. In Strong et al. and Duarte et al.^{35,36} patients were included when they had a diagnosis of major depressive disorder (based on screening followed by a structured clinical interview). In Choi Yoo et al.³¹ patients screened with clinical significant depression or pain were included. Sabariego et al.³⁹ included patients screened with increased fear of cancer progression. Finally, Chatterton et al.³⁰ included patients with elevated levels of distress measured using the distress thermometer.

Table 2. Characteristics of the included studies

	Design	Study population	Treatment
Lemieux (2006)³⁸ Canada	RCT	Women with metastatic breast cancer (n = 125).	1) Weekly supportive-expressive psychosocial group therapy plus standard care. Patients were asked to attend group sessions for at least one year. Control: Care-as-usual, which comprised of educational materials and psychosocial treatment when deemed necessary.
Mandelblatt (2008)³⁷ United States	RCT	Women treated with surgery for invasive breast cancer four to six weeks ago (n = 389).	1) An educational video addressing re-entry challenges in physical health, emotional well-being, interpersonal relations and life perspectives plus the control-booklet. 2) Individual psycho-educational counselling (one face-to-face and one telephone session) plus the educational video and control-booklet. Control: A booklet-control condition.
Strong (2008)³⁶ United Kingdom	RCT	Mixed cancer patients with a prognosis > 6 months and screened for major depressive disorder (HADS \geq 15 and major depressive disorder assessed in a Structured Clinical Interview) (n = 200).	1) Nurse-delivered collaborative care intervention (DCPC) comprising of education about depression and its treatment (including antidepressant medication), problem-solving therapy, and communication with each patient's oncologist and general practitioner. A maximum of 10 individual sessions of 45 minutes were provided over 3 months followed by additional sessions when necessary. Control: Care-as-usual. Each patient's general practitioner was informed about the major depression diagnosis and was provided with advice on antidepressant drug, if requested.
Sabariego (2010)³⁹ Germany	RCT	Mixed cancer patients with increased fear of cancer progression and treated with a 3-week inpatient rehabilitation program (n = 174).	1) Four sessions of 90 minutes of cognitive behavioral group therapy (CBT) in addition to the standard rehabilitation program. Control: Four sessions of 90 minutes of supportive-experiential group therapy (SET) in addition to the standard rehabilitation program.

Follow-up	Outcome(s) ¹	Perspective	Results
2-year (mean)	Mood (POMS)	Healthcare perspective, including intervention costs and direct medical costs.	<p>Intervention costs were on average \$1,394 per patient.</p> <p>Psychosocial group therapy was more costly (\$+3,526, NS) and more effective (POMS effect size of 0.32, sig) than care-as-usual. ICER was \$5,550 for an effect size of 0.5 in mood.</p>
6-month	Distress (IES-R)	<p>Societal perspective, including intervention costs (which includes patient opportunity costs) and direct medical costs.</p> <p>Only intervention costs were included in the CEA analyses.</p>	<p>Intervention costs were \$11 (control), \$26 (video) and \$134 (video plus counseling) per participant.</p> <p>Individual counselling was most costly, while equally effective as the educational video condition and therefore dominated. The educational video condition was more costly (\$+15) and more effective (IES-R incremental effect -0.002, NS) than a booklet-control condition. ICER was \$7,275 per unit improvement in IES-R.</p>
6-month	QALYs (EQ-5D)	Healthcare perspective, including intervention costs and direct medical costs.	<p>Intervention costs were on average \$487 (£262) per patient.</p> <p>DCPC was more costly (\$+623 (£335), sig) and more effective (incremental QALYs +0.063, sig) than care-as-usual. ICER was \$9,818 (£5,278) per QALY gained.</p>
1-year	Fear of progression (FoP-Q); Mental health (SF-12 mental).	<p>Societal perspective, including intervention costs, direct medical costs, direct non-medical and indirect non-medical costs.</p> <p>Indirect non-medical costs were not included in the CEA analyses.</p>	<p>Incremental intervention costs were on average \$57 (€47) per patient (or \$345 (€282) per group).</p> <p>CBT was less costly (\$-2,889 (€-2,362) or \$-3,322 (€-2,716) depending on analyses, both NS), while almost equal in effectiveness (FoP-Q incremental effect +0.03, NS and SF-12 incremental effect +0.16, both NS) compared to SET.</p> <p>ICER was \$-96,309 (€-78,742) per unit improvement in FoP-Q. ICER was \$-20,763 (€-16,976) per unit improvement in SF-12.</p>

Table 2. Continued

	Design	Study population	Treatment
Arving (2014)²⁹ Sweden	RCT	Breast cancer patients about to start adjuvant treatment (n = 168).	1) Individual psychological support from a nurse trained in psychological techniques (INS). 2) individual psychological support from a psychologist (IPS). No maximum number of sessions were set. Control: Care-as-usual including referral to a psychiatrist or social worker when needed.
Choi Yoo (2014)³¹ United States	RCT	Mixed cancer patients with clinical significant depression (PHQ-9 \geq 10 and endorsement of depressed mood and/or anhedonia) or pain (definitely or possibly cancer-related and BPI worst pain score \geq 6) (n = 405).	1) Centralized telecare management for pain and depression coupled with automated home-based symptom monitoring. Control: Care-as-usual, which comprised of informing patients on their depressive and pain symptoms and providing screening results to the oncologist.
Walker (2014)³⁴ United Kingdom	Decision analytic model	Hypothetical patient diagnosed with cancer (female 63-years) attending specialist cancer outpatients services (base-case).	1) Systematic identification for major depressive disorder (HADS \geq 15 and major depressive disorder assessed in a Structured Clinical Interview), followed by a nurse-delivered collaborative care intervention (DCPC). DCPC comprised of education about depression and its treatment (including antidepressant medication), problem-solving therapy, and communication with each patient's oncologist and general practitioner, in addition to care-as-usual. A maximum of 10 individual sessions of 45 minutes were provided over 4 months, followed by additional sessions when necessary. Control: Care-as-usual, consisting of identification and treatment of major depression by patient's general practitioner.
Mewes (2015)³³ The Netherlands	Decision analytic model	Hypothetical cohort of 1,000 breast cancer patients with matched clinical characteristics as in the RCT.	1) A 6-week cognitive behavioral group therapy (CBT) program of 90 minutes each 2) A 12-week home-based exercise program, individually tailored during an intake with a physiotherapist ² . Control: A care-as-usual, waiting-list control group.

Follow-up	Outcome(s) ¹	Perspective	Results
2-year	QALYs (EORTC QLQ-C30 mapped into EQ-5D)	Healthcare perspective, including intervention costs and direct medical costs.	<p>Intervention costs were per patient on average \$690 (€560) for the INS group and \$805 (€653) for the IPS group.</p> <p>INS as well as IPS were less costly (\$-8,786 (€-7,130) and \$-6,630 (€-5,381), both sig) and more effective (incremental QALYs +0.09, NS and +0.16, both NS) compared to care-as-usual.</p> <p>INS and IPS were dominant compared to care-as-usual.</p>
1-year	QALYs (disease free days; SF-12 converted to SF-6D; modified EQ-5D and a VAS scale)	Healthcare perspective, including intervention costs.	<p>Intervention costs were on average \$953 (all patients) or \$1189 (depressed patients only) per patient.</p> <p>Centralized telecare management was more costly (\$+953) and more effective (incremental QALYs +0.088, sig (EQ-5D) or +0.013 (SF-12)) than care-as-usual.</p> <p>ICER was \$10,826 or \$73,287 per QALY gained.</p> <p>In depressed patients (n=309) the ICER ranged from \$19,72 to \$26,95 per disease-free day gained or from \$18,018 to \$49,549 per QALY gained.</p>
5-year	QALYs	Healthcare perspective, including intervention costs.	<p>Intervention costs were per patient \$676 (£464) for the intervention group and \$532 (£365) for the control group.</p> <p>DCPC was more costly (\$+144 (£99)) and more effective (incremental QALYs +0.009) than care-as-usual.</p> <p>ICER was \$17,132 (£11,765) per QALY gained.</p>
5-year	QALYs (SF-36 converted to EQ-5D).	Healthcare perspective, including intervention costs and direct medical costs.	<p>Intervention costs were \$247 (€190) per patient.</p> <p>CBT was more costly (\$239 (€+184)) and more effective (incremental QALYs +0.008) than the weight-list control group.</p> <p>ICER was \$29,266 (€22,502) per QALY gained.</p>

Table 2. continued

	Design	Study population	Treatment
Lengacher (2015)³² United States	RCT	Breast cancer patients who completed treatment within 2 years prior to study enrollment (n = 104).	1) A 6-week mindfulness stress reduction program, which consisted of 2-hour group sessions once a week. Control: A care-as-usual, waiting-list control group. Care-as-usual comprised of standard post-treatment clinic visits.
Chatterton (2015)³⁰ Australia	RCT	Mixed cancer patients with elevated levels of distress (score \geq 4 on the distress thermometer) (n = 336).	1) Psychologist-led, individual cognitive behavioral intervention (PI) (max. 5 sessions). Control: Nurse-led, single-session self-management intervention (NI).
Duarte (2015)³⁵ United Kingdom	RCT	Mixed cancer patients with a prognosis > 12 months and screened for major depressive disorder (HADS \geq 15 and major depressive disorder assessed in a Structured Clinical Interview) (n = 500).	1) Nurse-delivered collaborative care intervention (DCPC) comprising of education and its treatment (including antidepressant medication), problem-solving therapy, and communication with each patient's oncologist and general practitioner, in addition to care-as-usual. A maximum of 10 individual sessions of 45 minutes were provided over a 4 month-period, followed by some additional sessions when necessary. Control: Care-as-usual, patient's general practitioner and oncologist were informed about the major depression diagnosis and ask to treat their patients as they normally would.

Abbreviations: RCT, randomized controlled trial; POMS, Profile of Mood States; NS, not significant; sig, significant; ICER, incremental cost-effectiveness ratio; IES-R, Revised Impact of Events Scale; CEA, cost-effectiveness analyses; HADS, Hospital Anxiety and Depression Scale; DCPC, Depression Care for People with Cancer; QALYs, quality-adjusted life years; EQ-5D, EuroQol 5-dimensions; CBT, cognitive behavioral therapy; SET, supportive-experiential therapy; FoP-Q, Fear of Progression Questionnaire; SF-12, 12-item Health Survey; INS, individual psychosocial support from a trained nurse; IPS, individual psychosocial support from a psychologist; EORTC QLQ-C30, The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30-questions; PHQ, Patient Health Questionnaire; BPI, Brief Pain Inventory; SF-6D, Short-Form 6-dimensions;

Follow-up	Outcome(s) ¹	Perspective	Results
12-week	QALYs (SF-12)	Societal perspective, including intervention costs and direct non-medical costs (i.e., patient opportunity costs).	Intervention costs were \$666 per patients. The mindfulness program was more costly (\$+666 (intervention costs) and \$+592 (patient opportunity costs)) and more effective (incremental QALYs +0.03, sig) than care-as-usual. ICER was \$22,200/QALY for the direct costs and \$19,733/QALY for the patient opportunity costs.
12-month	QALYs (AQOL-8D)	Healthcare perspective, including intervention costs, direct medical costs and direct non-medical costs (e.g., costs of support services).	Intervention costs were on average \$60 (NI) and \$181 or \$202 (PI) per patient. In patients with low distress (BSI < 63) the psychologist-led intervention was more costly (+\$335, NS) and more effective (incremental QALYs +0.016, NS) than the nurse-led intervention. In patients with high levels of distress (BSI > 63) the psychologist-led intervention was less costly (-\$332, NS) and more effective (incremental QALYs +0.037, NS) than the nurse led intervention.
48-week	QALYs (EQ-5D)	Healthcare perspective, including intervention costs and direct medical costs.	Intervention costs were on average \$935 (£642) per patient. Including only depression-related healthcare costs, DCPC was more costly (\$+919 (£631), sig) and more effective (incremental QALYs +0.066, sig) than care-as-usual. ICER was \$13,905 (£9,549) per QALY gained.

VAS, Visual Analog Scale; SF-36, Medical Outcomes Study 36-Item Short-Form Health Survey; CBT, cognitive behavioral therapy; PI, psychologist-led, individual cognitive behavioral intervention; NI, nurse-led, single-session self-management intervention; AQOL-8D, quality of life – eight dimension-; BSI, Brief Symptom Index.

¹ Only those outcomes (i.e., psychosocial outcomes or quality adjusted life years) that were used in this systematic review are presented.

² Only results of the cognitive behavioral therapy group are presented (i.e., results regarding the exercise program are not presented).

Studies were heterogeneous regarding the psychosocial care intervention investigated. Four studies investigated a collaborative care intervention^{31,34-36}, of which three studies investigated the intervention called “Depression Care for People with Cancer”, consisting of a nurse-delivered intervention comprising of depression education and its treatment, problem-solving therapy, and communication with each patient’s oncologist and general practitioner³⁴⁻³⁶. The other study investigated a centralized telecare management intervention for pain and depression coupled with automated home-based symptom monitoring³¹. Four studies investigated a group intervention: cognitive behavioral group therapy^{33,39}, supportive-expressive psychosocial group therapy³⁸, and a mindfulness program in groups³². Mandelblatt et al.³⁷ investigated a psycho-education intervention (an educational video addressing re-entry challenges) or a psycho-education intervention combined with individual psycho-educational counselling. Finally, in Arving et al. and Chatterton et al.^{29,30} the cost-utility of individual psychological support incorporating cognitive behavioral therapy was studied.

Most studies compared the intervention group(s) with care-as-usual^{29,31-36,38}, which comprised of informing the patient’s general practitioner on major depressive disorder diagnosis^{35,36}, identification and treatment of major depressive disorder diagnosis by patient’s general practitioner³⁴, referral to a psychiatrist or social worker when needed²⁹, provision of educational materials and psychosocial treatment when deemed necessary³⁸, informing patients on their depressive and pain symptoms and providing screening results to the oncologist³¹, or standard post-treatment clinic visits³². In one study it was not entirely clear what care-as-usual encompassed³³. Three studies compared the intervention group(s) with a booklet-control condition³⁷, supportive-experiential group therapy³⁹ or a nurse-led self-management intervention³⁰.

Methods of the cost-effectiveness and cost-utility studies

Seven studies performed cost-utility analyses^{29,30,32-36} using the EuroQol 5-dimensions (EQ-5D)^{35,36}, the 12-item Health Survey (SF-12)³², quality of life - eight dimension - (AQOL-8D)³⁰, mapping of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) or the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) into EQ-5D scores^{29,33}, or using estimates based on previous studies³⁴. Three studies performed cost-effectiveness analyses using Profile of Mood States (mood)³⁸, Revised Impact of Events Scale (distress)³⁷, 12-item Health Survey (mental health) or Fear of Progression questionnaire (fear of cancer progression)³⁹ as outcome measure. One study performed both cost-utility and cost-effectiveness analyses with

depression-free days gained (calculated using the 20-item Hopkins Symptoms Checklist) as the outcome in the cost-effectiveness analyses³¹.

Follow-up period for measurement of effects and costs was mostly 6 to 12 months after the intervention^{30,31,35-39}. One study had a follow-up period of 12 weeks³², one study of 2 years²⁹ and the two model studies had a follow-up period of 5 years^{33,34}.

The majority of studies used the healthcare perspective for measuring costs^{29-31,33-36,38}, while three studies used a societal perspective^{32,37,39}, although cost inputs were not always consistent with the perspective taken. In the actual cost-effectiveness analyses, three studies included intervention costs only^{31,34,37}, five studies included intervention costs and direct medical costs (e.g., hospitalization or visit to the general practitioner)^{29,33,35,36,38}, and three studies included intervention costs, direct medical costs and direct non-medical costs (e.g., cost for support services)^{30,32,39}. One study measured indirect non-medical costs (e.g., productivity losses), however, these costs were not included in the actual analyses³⁹.

Cost-effectiveness of the included psychosocial care interventions

Information on the cost-effectiveness or cost-utility of the different psychosocial care interventions is presented in Table 2. In Figure 2 these findings are summarized using a permutation matrix. Two studies found evidence that costs were lower, while the intervention was more effective, indicating dominance of psychosocial care^{29,30}. Arving et al.²⁹ found that individual psychological support provided by a nurse or psychologist was significantly less costly (\$-8,786 or \$-6,630, respectively) and more effective in gaining QALYs (non-significant incremental QALYs of +0.09 and +0.16, respectively) compared to care-as-usual. Chatterton et al.³⁰ found that in highly-distressed cancer patients treated with cognitive behavioral group therapy, total costs were on average \$332 non-significantly lower, while more QALYs were gained (non-significant incremental QALYs of +0.037) compared to a nurse-led self-management intervention. However, in less-distressed patients less strong evidence in favor of cognitive behavioral group therapy compared to the self-management intervention was found (i.e., costs were \$335 higher and incremental QALYs were +0.016).

		Incremental effectiveness		
		More effective	Equal effective	Less effective
Incremental costs	More costly	Lemieux et al. ³⁸ (supportive expressive psychosocial group therapy) Mandelblatt et al. ³⁷ (educational video or educational video combined with psycho-educational counselling) Strong et al. ³⁶ (nurse-delivered collaborative care) Choi Yoo et al. ³¹ (centralized telecare management) Walker et al. ³⁴ (nurse-delivered collaborative care) Mewes et al. ³³ (cognitive behavioral group therapy) Lengacher et al. ³² (mindfulness stress reduction program) Duarte et al. ³⁵ (nurse-delivered collaborative care)		
	Equal in costs			
	Less costly	Arving et al. ²⁹ (individual psychological support from a nurse or psychologist) Chatterton et al. ³⁰ (psychologist-led, individual cognitive behavioral intervention)	Sabariego et al. ³⁹ (cognitive behavioral group therapy)	

Figure 2: Permutation matrix

One study showed lower costs in the psychosocial intervention group compared to the control group, while effectiveness was almost equal³⁹. This study by Sabariego et al.³⁹ found on average \$2,889 to \$3,322 non-significantly lower costs in the cognitive behavioral group therapy group compared to the supportive-experiential group therapy. No major difference in effects were found on fear of progression or mental health. The probability that cognitive behavioral therapy was more cost-effective compared to supportive-experiential group therapy without additional costs was 92%, indicating that cognitive behavioral group therapy is likely to be cost-effective.

All of the eight other studies found evidence that psychosocial care is more effective albeit at higher costs³¹⁻³⁸. Whether the psychosocial care interventions investigated in

these studies can be seen as cost-effective depends on the willingness-to-pay for an incremental unit of effect. Of the eight studies, four studies investigated a collaborative care intervention compare to care-as-usual^{31,34-36}. These studies found that incremental costs were \$144 to \$953 higher, while incremental QALYs were 0.009 to 0.088 higher. The corresponding incremental costs for an incremental QALY gained (i.e., ICER) were respectively \$9,818/QALY³⁶, \$13,905/QALY³⁵, \$17,132/QALY³⁴ or ranged from \$10,826/QALY to \$73,287/QALY, depending on the method used to measure QALYs³¹.

Three of the other four studies that found higher effects and higher costs investigated the cost-effectiveness of psychosocial group interventions^{32,33,38}. Lemieux et al.³⁸ found that supportive-expressive psychosocial group therapy was significantly more effective in improving mood than care-as-usual. However, total costs were higher (\$+3,526), resulting in incremental costs of \$5,550 for an effect size of 0.5 mood. Mewes et al.³³ who investigated the cost-effectiveness of cognitive behavioral group therapy found \$239 higher costs and an incremental QALY gain of 0.008 in the intervention group compared to the waiting-list care-as-usual group. The ICER was \$29,266/QALY. In addition, Lengacher et al.³² found that a mindfulness program in groups was more costly (\$+666), while significantly more effective in gaining QALYs (incremental QALY gain of +0.03) than a waiting-list care-as-usual group. This resulted in an ICER of \$22,200/QALY.

The last study that reported higher effects although at higher costs was a study by Mandelblatt et al.³⁷. This study only included intervention costs in the actual cost-effectiveness analyses. They reported that a psycho-education intervention (which consisted of an educational video addressing re-entry challenges) was more costly (\$+15), while marginally more effective (non-significant incremental effect in distress of -0.002) compared to a booklet-control condition. A psycho-education intervention combined with individual psycho-educational counseling was not more effective than the booklet-control condition or psycho-education alone, while total costs were higher. Psycho-education combined with individual psycho-educational counseling can therefore be seen as dominated. In additional analyses, direct medical costs between the three groups were compared, which showed no significant differences.

Table 3: Quality assessment of the included studies

	Lemieux (2006)³⁸	Mandelblatt (2008)³⁷	Strong (2008)³⁶
1. Was a well-defined question posed?	No	Yes	No
2. Was a description of the alternatives given? And were all relevant alternatives omitted?	Yes	Partly	Yes
3. Was the effectiveness established?	Partly	Partly	Yes
4. Were all relevant and important costs and consequences identified for each alternative?	No	No	No
5. Were costs and consequences measured accurately in appropriate units?	Partly	No	Partly
6. Costs and consequences valued credibly?	Yes	Yes	Partly
7. Were costs and consequences adjusted for differential timing?	No	NA	NA
8. Was an incremental analysis of costs and consequences of alternatives performed?	Yes	Yes	Yes
9. Was allowance made for uncertainty for the estimates of costs and consequences?	Yes	Yes	Yes
10. Did the presentation and discussion of study results include all relevant issues?	No	No	Yes
Total	5	6	7

Quality of the included studies

The quality of the included studies was in general moderate; total score ranged from 5 to 9 (Table 3). Lemieux et al.³⁸ scored lowest, while Arving et al, Walker et al. and Duarte et al.^{29,34,35} scored highest. It was remarkable that in four studies the cost-effectiveness or cost-utility of a psychosocial care intervention was investigated, while the effectiveness was not yet properly established^{30,32,37,38}. Another major concern was the inclusion of all relevant costs and consequences; three studies only included intervention costs^{31,34,37}, hampering the measurement of a potential cost offset. In addition, only two studies measured informal care costs^{30,39} and only one study measured productivity losses³⁹. Another concern was the measurement of costs and consequences; three studies did not provide clear information regarding the source of data^{32,36,38}, and two studies omitted costs from the actual cost-effectiveness analyses without giving clear arguments^{37,39}. Furthermore, four studies did not give sufficient information on the valuation of costs and consequences, lacking for instance information on index year^{31-33,36}. A positive point was that the studies, except for one³⁹, performed sensitivity analyses. In addition, all of the studies provided information on incremental costs and incremental effects.

Sabariego (2010) ³⁹	Arving (2014) ²⁹	Choi Yoo (2014) ³¹	Walker (2014) ³⁴	Mewes (2015) ³³	Lengacher (2015) ³²	Chatterton (2015) ³⁰	Duarte (2015) ³⁵	% yes or NA
Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	73%
Partly	Yes	Yes	Yes	Yes	Yes	Partly	Yes	73%
Yes	Yes	Yes	Yes	Yes	Unclear	Partly	Yes	64%
Yes	No	No	No	No	No	No	No	9%
No	Yes	Yes	Yes	Yes	Partly	Yes	Yes	55%
Yes	Yes	Partly	Yes	No	Partly	Yes	Yes	64%
NA	NA	NA	Yes	Yes	NA	NA	NA	91%
Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	100%
No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	91%
Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	73%
7,5	9	7,5	9	8	6	8	9	

DISCUSSION

In this study we aimed to assess current evidence on the cost-effectiveness and cost-utility of psychosocial care interventions in cancer patients. Eleven studies were included in this review, of which seven in recent years (2014 or 2015). Two of the included studies, both on individual psychological support, found lower costs and higher effects compared to the control group^{29,30}, while one study on cognitive behavioral group therapy found lower costs and equal effects compared to the control group³⁹. These findings support the hypothesis of Carlson and Bultz^{11,12} that psychosocial care can improve outcomes, but also lead to cost savings. However, eight other studies on collaborative care, group interventions and psycho-education, found higher effects and higher costs compared to the control group³¹⁻³⁸, indicating that psychosocial care is likely to be effective, although at additional costs.

Whether these additional costs are acceptable, depends on the willingness-to-pay for an incremental unit of effect. Several willingness-to-pay thresholds have been suggested in the literature, with higher thresholds for more serious diseases⁴⁰. An often used

threshold is the National Institute for Health and Clinical Excellence (NICE) threshold of about \$28,992 – \$43,488 per QALY (£20,000 - £30,000 per QALY)^{41,42}. Based on these thresholds, six of the eight studies in the present study that found higher costs and higher effects are likely to be cost-effective (ICER ranged from \$9,818 to \$29,266 per QALY, with one outlier at \$73,287 per QALY)³¹⁻³⁶. The other two studies found incremental costs of \$5,550 for an effect size of 0.5 in mood³⁸ or marginal higher costs (\$+15) for a marginal incremental effect in distress of -0.002³⁷. No clear willingness-to-pay thresholds exist for these outcome measures, although the incremental costs for an effect size 0.5 in mood may be judged as acceptable³⁸.

In summary, findings thus showed that psychosocial care is likely to be cost-effective at potentially acceptable willingness-to-pay thresholds, with three interventions^{29,30,39} even cost-effective at a willingness-to-pay threshold of zero. It was remarkable that of these three studies^{29,30,39}, two studies investigated individual psychological support^{29,30}. However, no clear conclusions can be drawn regarding the dominance of individual psychological support compared to other psychosocial care interventions, since there was considerable heterogeneity among studies. Studies differed regarding psychosocial care intervention investigated, care provided in the control group, study population targeted, used outcome measure and included cost categories, which hampers comparability of the results. Further research is therefore called for.

Several recommendations can be formulated for these further studies. At first, more studies should be performed to investigate which psychosocial care interventions are most likely to be cost-effective and for whom these psychosocial care interventions are most likely to be cost-effective. It may be assumed that in line with findings on effectiveness⁶, psychosocial care interventions are especially cost-effective in preselected patients who suffer from psychosocial problems. Five of the 11 studies included in this review preselected patients based on psychosocial outcomes. However, no clear conclusion can be drawn as to whether these studies were more cost-effective than studies that did not preselect patients, since studies that did and did not preselect patients differed regarding the type of intervention provided.

In addition, further studies should focus on the cost-effectiveness or cost-utility of psychosocial care from a societal perspective as recommended in several guidelines^{22,43,44}. In this review, no study included productivity losses in the actual analyses (although one study measured productivity losses³⁹), and only two studies^{30,39} measured informal

care costs. Productivity losses and informal care costs have been shown to provide an important contribution to the overall economic burden of cancer²⁵. Since, it can be hypothesized that the provision of psychosocial care can reduce both productivity losses and costs of providing informal care^{11,12,17,18}, further studies should take these costs into account, especially when healthcare is being paid for by the society.

Moreover, additional research should be performed using the QALY as outcome measure as also recommended in pertinent guidelines^{42,43}, which will enhance comparability of results among different psychosocial interventions as well as enhance comparability to cost-effectiveness or cost-utility of other (supportive) care interventions. Although the more recent studies included in this review already used the QALY as outcome measure, the strategies to calculate QALYs widely differed. Different measurement instruments were used to calculate QALYs, such as the EQ-5D, SF-6D and the AQOL-8D. In addition, different strategies were used for mapping outcomes of other instruments, such as the EORTC QLQ-C30 or SF-36, into EQ-5D scores. A more uniform approach is recommended to enhance comparability.

Some limitations of this review are evident. At first, included studies were in general of moderate quality. Several studies lacked sufficient information on the effectiveness of the studied intervention, the source of data, the reasons for data omission, the valuation of costs and consequences, or did not include all relevant costs and consequences, which may limit validity of findings. In addition, studies showed considerable heterogeneity in studied psychosocial care interventions and study methods, hampering the formulation of clear conclusions. Furthermore, most studies were conducted among breast cancer patients and may therefore not be representative for other patient groups. Finally, all studies were conducted in Western countries, hampering generalizability to other non-western countries. A clear strength of this review is that it encompassed an up to date literature search, which included seven studies published in 2014 or 2015, which were not yet included in the most recent review²⁷. This reflects the fast growing number of studies that are conducted on the cost-effectiveness or cost-utility of psychosocial care. Also, several protocol papers of currently ongoing studies were identified⁴⁵⁻⁵¹, which will provide new evidence on the cost-effectiveness or cost-utility of psychosocial care in the coming years.

In conclusion, results of this review revealed that psychosocial care is likely to be cost-effective at different, potentially acceptable, willingness-to-pay thresholds. Heterogeneity

of studies, however, hampered the comparison of findings and consequently the formulation of clear conclusions regarding the most cost-effective psychosocial care interventions. New studies providing insight on which psychosocial care interventions are most likely to be cost-effective and for whom are therefore called for. In these new studies potential important cost drivers from a societal perspective, such as productivity losses or informal care costs, should be taken into account.

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