Title: Economic evaluations of psychosocial interventions in cancer: A systematic review

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ABSTRACT

Objective: Although the effectiveness of many psychosocial interventions for people with cancer has been established, one barrier to implementation in routine clinical care is a lack of data on cost-effectiveness. We conducted a systematic review to assess the cost-effectiveness of psychosocial interventions for improving psychological adjustment among people with cancer.

Methods: Systematic review of the literature, study appraisal, and narrative synthesis.

Results: Eight studies involving 1,668 patients were identified. Four of these reported outcomes in a cost per quality adjusted life year (QALY) framework. Six studies reported psychosocial interventions to be cost-effective for improving health-related quality of life, mood, pain, distress, or fear of cancer progression, compared to usual care. Of the six psychosocial interventions identified as cost-effective, three were cognitive behavioural therapy based interventions, one was a nurse-delivered telephone follow-up plus educational group program, one was a group-based exercise and psychosocial intervention, and one was a series of 10 face-to-face or telephone-based individual support sessions delivered by a nurse. The quality of studies according to the CHEC-list criteria was good overall; however, some studies were limited by their choice of outcome measure and omission of important categories of costs.

Conclusions: Several psychosocial interventions, particularly those based on cognitive behavioural therapy, have been demonstrated to represent good value for money in cancer care. Future research should include a clear definition of the economic question, inclusion of all relevant costs, and consideration of utility-based quality of life measures for QALY estimation.

Systematic review registration: PROSPERO Registration Number: CRD42014006370.

Keywords: Psychosocial, cost-effectiveness, economic evaluation, cancer, quality of life

Background

Due to the increasing incidence of and survival from cancer, the psychological burden of cancer continues to rise. One-third of cancer patients experience severe psychological distress and up to 70% will experience some level of anxiety or depression [1, 2]. How well patients live (i.e. quality of life) has long been recognised as important as how long they live (i.e. survival time) [3, 4]. Therefore identification and management of psychological difficulties in people with, or who have survived cancer is an essential part of comprehensive cancer care [5].

Several reviews and meta-analyses have examined the effectiveness of psychosocial interventions for the management of psychological difficulties experienced by cancer patients [3, 6-10]. A meta-analysis by Meyer and Mark [7] found that relaxation and behavioural modification improved functional adaptation and symptom control. Psychosocial interventions have also been used to manage depression in cancer patients. Two systematic reviews [6] [3] reported that psychosocial interventions were effective in improving depression. Moreover, people with cancer who take part in psychosocial interventions have been shown to report lower level of depression and anxiety, and improved quality of life [8] [9].

Although the effectiveness of a range of psychosocial interventions for people with cancer has been established, one barrier to their implementation in routine clinical care is a lack of data on their cost-effectiveness. Given the scarcity of healthcare resources and the increasingly tight funding of healthcare systems, it is vital that psychosocial interventions be evaluated not only in terms of efficacy in symptom reduction, but in economic terms as well [11]. It is important to consider whether conducting psychosocial interventions are worthwhile given the incremental costs and incremental benefits they may generate. A cost-

effective intervention is one that represents good value for money, supporting the additional investment it may require, or the diversion of resources from less effective alternatives. A cost-effective intervention is not necessarily cost-saving, but usually achieves greater benefit than its comparator. The additional cost per health outcome that is considered "worthwhile" is based on explicit or arbitrary willingness to pay thresholds as well as other key criteria, usually defined by government decision makers [12]. In the United States, an intervention is generally considered cost-effective compared to the next best alternative if it costs below US$50,000 per QALY gained [13]. In Australia, although there is not an explicit threshold value, an observation of the decisions of the Pharmaceutical Benefits Advisory Committee between 1994 and 2003 point to a threshold of AU$69,900 per QALY gained [14], while in the UK it is between £20,000-£30,000 per QALY [15].

In 2004, Carlson and Bultz reported that many psychosocial interventions for cancer resulted in a reduction of subsequent healthcare use and savings in medical expenditure, particularly related to ongoing treatment for depression [11]. In 2011, Gordon et al. [16] published a review investigating the cost-effectiveness of interventions specifically designed to treat depression and anxiety in cancer patients. This review was not able to make a firm recommendation about whether particular types of interventions were cost-effective, possibly due to a small number of relevant studies. Thus, the aim of the present review was to systematically search the literature to assess the total costs and health benefits of psychosocial interventions for all types of psychological conditions in people with cancer, compared to usual care, from either a societal or health system perspective.

Methods

The protocol for this review was registered in the PROSPERO register (Registration number: CRD42014006370; http://www.crd.york.ac.uk/PROSPERO) in January 2014. The preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines [17] were followed to identify and screen publications, extract data, and describe the systematic review process.

Inclusion criteria

Economic evaluations based on psychosocial interventions aiming to improve quality of life and/or psychological outcomes for people with, or survivors of, cancer were included. We included all economic evaluation study types that aggregated monetary costs and psychological health outcomes. The total cost will take into account the costs of the intervention plus the costs of downstream care as the result of an intervention. Economic evaluations are comparative analyses of alternative interventions in regards to costs, resource use, and health outcomes [18]. There are three main types of full economic evaluations and they differ in the approach taken to measure the health benefits of the intervention. *Cost-effectiveness analysis* measures costs and benefits of interventions with costs expressed in monetary units (e.g. $) and effects in clinical outcome units (e.g. years of life); *cost-utility analysis* measures costs in monetary units and benefits in Quality Adjusted Life Years (QALYs); *cost-benefit analysis* measures costs and benefits with both expressed in monetary units.

Exclusion criteria

We excluded:

- Cost consequence studies, where costs and effects were presented in a disaggregated format;

- Studies that assessed costs only and included no measures of benefits;

- Studies that made claims of cost-effectiveness but did not quantify or report cost and effectiveness outcomes;

- Methodological papers that did not present health economic outcomes;

- Review articles and case studies;

- Commentaries, letters, editorials, and conference abstracts; and

- Studies not published in a peer-reviewed journal.

Search strategy

Relevant international electronic bibliographic databases were searched from 1980 to May 2015, including Medline, Medline In-Process, Embase, PsycINFO, Cumulative Index to Nursing and Allied Health Literature (CINHAL), Econlit, Cost Effectiveness Analysis Registry (CEA Tufts), and the National Health Service Economic Evaluation Database (NHS EED). We also searched the reference lists of retrieved publications to identify any additional relevant articles. Medical Subject Heading (MeSH) terms and text words for the population (cancer, neoplasms), the intervention (cognitive and behavioural intervention, psychotherapy, cognitive therapy, psycho-education, psychosocial), and the outcomes or study design (Quality-Adjusted Life Years, cost, Cost-Benefit Analysis, cost-effectiveness, cost utility, economic evaluation) were combined. Supplementary Table 1 shows the search strategy used for Medline. The search strategies for other databases were similar but tailored slightly to fit each specific database. Auto-alerts were installed to provide continual literature updates.

Study Selection

The first author (MD) screened all manuscripts, titles and abstracts for non-research articles, duplicates and irrelevant references, such as single case reports, letters, commentaries, conference abstracts, or those focused on clinical issues. Then the selected, screened manuscripts were fully assessed by two reviewers (MD, RM). Disagreement was resolved through discussion until a consensus was reached. We extracted the following information using a predefined data form: study location, publication year, type of cancer, type of psychosocial intervention, type of economic evaluation (i.e. cost-effectiveness, cost-utility or cost–benefit analysis), economic evaluation methods used (e.g. modelled or within-trial analysis), perspective of analysis (health system or societal), time horizon of analysis, reference year for costs, discount rate (i.e. the rate of adjustment of the value of costs or benefits that occur at different points of time in the future) [19], psychological outcomes, quality of life, QALYs, survival, costs included, incremental cost effectiveness ratios (ICERs) or net benefit reported; and type of sensitivity analysis conducted. "Traditional techniques of meta-analysis are not appropriate for pooling results of many economic analyses because of the different outcome measures used, multiple country perspectives, different interventions and comparators."

Costs in economic evaluations of health care interventions can be divided into direct medical costs, direct non-medical costs, and indirect non-medical costs [20]. Direct medical costs refer to medical costs borne by patients and payers as a consequence of disease, intervention, side effects (e.g. drug costs, costs of healthcare personnel, hospital costs) [20]. Direct non-medical costs refer to costs that accrue to patients and their families while receiving health care (e.g. travelling to hospital for treatment) [20]. Indirect non-medical costs refer to costs

indirectly associated with the illness or the intervention of interest (e.g. family caregiver time, lost work time) [20].

Appraisal and Quality Assessment

Traditional techniques of meta-analysis are not appropriate for pooling results of many economic analyses because of the different outcome measures used and multiple country perspectives [21]. For this reason, we used a narrative approach to summarise the findings as recommended by the Campbell and Cochrane Economics Methods Group [22]. We also constructed a permutation matrix [23] to categorise the cost-effectiveness results to inform decision making. The methodological quality and risk of bias of the included studies were assessed using the Consensus Health Economic Criteria (CHEC) list [24]. The CHEC-list is suitable for evaluating within-trial economic evaluations [24], and consists of 19 yes-or-no questions. Two authors (MD and RM) used the CHEC-list to independently assess the quality of each individual study with a consensus reached through discussion.

Results

Literature search

Results of the literature search are summarised in Figure 1. The initial search yielded 2,083 records; after removing duplicates and applying the inclusion and exclusion criteria to the titles and abstracts, 22 articles remained. After assessment of the full text, eight economic evaluations of psychosocial interventions for cancer care were included in this review (see Table 1). Supplementary Table 2 lists the 14 excluded studies along with the reasons for their exclusion.

Of the eight identified studies, two were undertaken in the USA [25, 26], and one each from Australia [27], the United Kingdom [28], Canada [29], Sweden [30], the Netherlands [31] and Germany [32]. Five studies [26, 27, 29-31] were undertaken with breast cancer patients, two among people with a range of cancers [32] [28], and one with melanoma patients [25]. Of the 12 interventions tested in the eight studies reviewed, half (6) were individual therapies and half tested the effect of group-based therapies.

Study Design

All eight included studies were within-trial economic evaluations, where economic data (e.g. resource utilisation, quality of life) were collected alongside a single clinical study, usually a controlled clinical trial [33]. Five studies were two-arm randomised controlled trials (RCT) [25, 28-30, 32], two studies [26, 30] were three-arm RCTs, and one study by Kimman et. al was a four-arm RCT [31]. Five of the studies had usual care as the comparator [25, 28-31]; whereas Sabriego et al. [32] used another psychosocial intervention as the comparator, Mandelblatt and colleagues [26] used an information booklet as the comparator, and Gordon et al. [27] chose an external comparator sample from another study concurrently undertaken at the same university. Five of the studies were cost-effectiveness analyses (CEA) [25-27, 31, 32], two studies performed cost-utility analyses (CUA) [28, 30], and one undertook both cost minimisation and cost-effectiveness analyses [29]. Half of the studies [25, 29, 30, 32] stated the reasons for choice of study type. The sample size of the economic evaluations ranged from 30 to 389 participants. The majority of the studies were not powered to detect a difference in cost-effectiveness, as power calculations had been based on the primary clinical outcome [25, 28-30, 32]. Three studies did not include information on sample size

calculations [26, 27, 31]. The follow-up period ranged from 6 to 24 months, with only one study [30] including a two-year follow-up.

Costs

Four studies were conducted from a societal perspective [26, 27, 31, 32] and four from a healthcare system perspective [25, 28-30]. None of the studies included a discussion of the rationale for the choice of perspective. Resource use and unit costs were reported by five of the studies [25-27, 31, 32]. Three studies reported mean costs only [28-30] (Table 1).

Direct medical costs

All studies reported direct medical costs, including treatment costs, outpatient hospital visits, and hospitalisation costs (Table 2). For all studies, direct medical costs were estimated from self-reported healthcare services use, hospital records and medical databases. All studies calculated costs related to the intervention and presented costs separately for the intervention and comparator(s). In one study [30], the intervention costs comprised 3% of total costs. Despite that intervention costs, the total health care costs were lower in the intervention groups than in the usual care group. The authors concluded that unmet psychological needs in the usual care group resulted in additional healthcare resource use.

One study [27] found that health service expenditure was higher in the psychosocial intervention (STRETCH) group. One study [31], on the other hand, found that participation in a nurse-led intervention was associated with fewer hospital follow-up visits, laboratory tests, other diagnostics, and fewer contacts with specialised health professionals. Contrary to their expectation, one study [29], found that radiation and psychotropic drug utilisation was

significantly higher in the intervention arm. One study [26] were not able to show that an effective intervention for meeting patient needs (i.e. improvement in distress) would decrease direct medical costs. One study [32] reported that patients in the intervention group had fewer general practice visits and inpatient days, and less outpatient treatment in hospital, which resulted in lower direct medical costs at 12 months. One study [28] reported that patients in the intervention group had a moderate incremental per patient cost for healthcare costs and antidepressant medication compared to the usual care group. Bares et al. [25] reported direct medical costs of the psychosocial intervention (i.e. cognitive behavioural therapy), but not the subsequent cost of healthcare. (Table 2)

Direct non-medical costs

Only three studies [27, 31, 32] reported direct non-medical costs.(Table 2) In one study [27], the evaluation included travel costs and other out-of-pocket expenses; they found that these costs were much higher in the STRETCH intervention group. In another study [31] included paid help, informal care received by patients and out-of-pocket costs, and found no significant difference in direct non-medical costs between groups. Another study [32] included costs associated with self-help groups and relatives' time and found the direct non-medical costs for the supportive-experimental group therapy were nearly double the costs of cognitive-behavioral group therapy (CBT).

Indirect non-medical costs

Three studies reported the indirect non-medical costs [27, 31, 32](Table 2). In one study [27], the indirect non-medical costs included patient time, leisure time forgone, loss of productivity, and program volunteers; they found the STRETCH intervention group incurred the highest indirect non-medical cost. One study [31] included the costs of lost production in

terms of both paid work and domestic tasks, and found that the costs of lost production were substantially higher in the hospital follow-up plus educational group program (EGP) and in the nurse-led telephone follow-up compared to nurse-led telephone follow-up plus EGP and to usual hospital follow-up. Another study [32] reported that the costs related to sick leave were lower in the cognitive-behavioral group therapy than in the supportive-experimental group therapy.

Six of eight studies [26, 28-32] reported missing data and the statistical methods used to adjust for this. Discounting of costs was only relevant for one study that had 2 years of follow-up, but this was not applied. [30]

Drivers of costs

We analysed the drivers of costs in the included studies. Direct medical costs appeared to be the most apparent cost driver. For Gordon et al. the cost of health services expenditures was estimated to be 40% of the total cost of the intervention {Gordon, 2005 #182}. The study by Sabariego et al.{Sabariego, 2011 #453} reported direct medical cost as the most important cost. For two studies inpatient hospital care {Arving, 2013 #599} and hospitalisation costs {Lemieux, 2006 #308} were found to be the drivers of costs. Only one study reported direct non medical cost including the cost of lost production as the main cost category {Kimman, 2011 #1046}. The study by Bares et al.{Bares CB, 2013 #585} reported staffing cost as the most important cost category however, they did not include the medical costs. In the contrary Mandelblatt et al.{Mandelblatt, 2008 #330} excluded staffing costs and they also reported the cost of health care utilisation as the most important costs.

Cost of the psychosocial interventions were not considered as drivers of costs in the studies. They were found to be inexpensive compared to the others costs.

Outcomes

Many psychological outcomes were reported by the primary studies, including distress, coping style, anxiety, fear of cancer progression, mood, pain, and health functioning. (Table 2) Four studies [27, 28, 31, 32] reported utility-based health-related quality of life (HRQOL) outcomes used in the calculation of QALYs. One study [30] used the EORTC-QLC-C30 questionnaire to obtain quality of life scores which were then transformed into utilities using a published algorithm [34]. One study [27] used the Functional Assessment of Cancer Therapy–Breast Cancer scale plus Arm Morbidity scale (FACT-B+4) to measure HRQOL. Utility scores were derived using a single–item linear analogue scale. Two studies [28, 31] measured HRQOL using the EQ-5D rated at three levels. QALYs for the above three studies were generated by multiplying one year of life by the mean utility score for that year. One study [32] used the 12-item Health Survey (SF-12) to measure the mental score at 12 months; however, they did not use the SF-12 to estimate QALYs.

Cost-effectiveness

Table 2 summarises the outcomes of the economic evaluations. All eight studies included in the review reported incremental cost-effectiveness ratios (ICER). None of the included studies applied a discount rate to the outcomes. Four of eight studies reported the ICER per QALY gained [27, 28, 30, 31]. Based on the QALY outcome, all of these studies [27, 28, 30, 31] reported that psychosocial interventions were cost-effective compared to usual care (Table 2).

Five studies calculated ICERs based on psychological outcomes such as distress, [25, 26] number of rehabilitated cases [27], mood, pain [29], fear of cancer progression, and mental

score [32] (Table 2). For distress, one study [25] reported that the psychosocial intervention (CBT) was cost-effective in reducing distress, while another [26] found their most intensive intervention arm, counselling + video + booklet, was higher in cost and less effective in reducing cancer-specific distress compared to the booklet alone and video alone arms. For the outcome of 'rehabilitated cases' described as the improvement in the FACT-B+4 score that reached minimal clinically meaningful difference (score increase of at least 3.5 points from 6 to 12 months post-diagnosis), the authors [27] found that the usual care arm was most efficient. Lemieux and colleagues [29] reported an incremental cost of $5,550 per clinical improvement in mood and an incremental cost of $4,309 per clinical improvement in pain, and the authors considered these costs acceptable compared to usual care [29]. One study [32] found that for both fear of cancer progression and mental score outcomes, the cognitive behavioural therapy-based intervention was cost-effective compared to usual care.

Table 3 presents the permutation matrix of the cost-effectiveness results, for both QALYs and psychological outcomes. Based on this matrix, six studies favoured psychosocial interventions [25, 27, 28, 30-32], one study favoured usual care [26], and for one study, additional incremental analysis would be needed to judge whether the added effect was worth the added cost or if the reduced effect was acceptable given reduced cost [29]. Of the six favoured psychosocial interventions, three were cognitive behavioural therapy interventions [25, 30, 32] one was a nurse-delivered telephone follow-up plus educational group program [31], one was a group based exercise and psychosocial intervention [27] and one was 10 individual (face-to-face or telephone) nurse-delivered support sessions [28] (see Table 3).

Quality appraisal

Figure 2 displays the quality score for each study using the CHEC-list. The overall quality score was combined with the percentage of criteria met. The included studies scored a maximum of 17 points out of the 19 on the CHEC-list, with most of the studies meeting more than 70% of the 19 criteria. The highest quality score achieved in this study was 89% by Kimman et al.{Kimman, 2011 #1046} and Mandelblatt et al{Mandelblatt, 2008 #330}.. Two studies, by Bares (42% of the criteria met) [25] and by Lemieux (53% of the criteria met) [29] lacked methodological rigour. In one study [25], the perspective chosen was not stated, not all costs and outcomes were properly identified and valued, and a sensitivity analysis was not conducted. In one study [29], the research question was not clearly defined and some relevant medical costs were not considered (e.g costs related to medical oncologists and GP visits). Of the six studies that identified a psychosocial intervention as cost-effective, five [27, 28, 30-32] were classified as good quality, with 74%, 89% and 84% of the criteria met, respectively; the sixth study [25] was classified as low quality (42% of the criteria met). The study that rejected the cost-effectiveness of the psychosocial intervention (counselling + educational booklets), was of good quality, with 89% of the criteria met [26].

All studies clearly described their study populations and competing alternatives. In four studies the research questions were not clearly stated [25, 28, 30, 31].
We judged the economic evaluation designs to be appropriate for all of the studies except for one study [29], who performed a cost minimisation analysis where we believed a cost-utility analysis would have been more appropriate. All but one study [25] undertook sensitivity analyses to assess the robustness of their findings [26-32], although at times the details of the factors tested were missing.

Discussion

Incremental cost-effectiveness ratios (ICERs) from the studies included in this review

showed that psychosocial interventions can be a cost-effective approach in cancer care. Six

studies favoured psychosocial interventions compared to the next best alternative, one study

favoured usual care, and for one study, incremental analysis would be needed to judge if the

added effect was worth the added costs or if reduced effect was acceptable given the reduced

costs. The findings of this review provide us with important information about treatment

efficiency (i.e. cost-effectiveness) that can guide current policy and clinical practice. For

stronger evidence, however, future studies evaluating psychosocial interventions in cancer should include full economic evaluations.

Given the variability in the types of psychosocial interventions and alternatives evaluated, we could not provide a conclusive recommendation for the most cost-effective type of psychosocial intervention for psychological adjustment in cancer patients. Three of the six studies that favoured psychosocial interventions had adopted a cognitive behavioural therapy approach and two of those interventions were of good methodological quality; however, given the small number of available studies and limited selection of theoretical approaches captured by these studies, it is not possible to comment on the type of intervention that is most cost-effective in this context.

Guidelines have been published to guide the conduct, analysis and reporting of trial based economic evaluations [35]. Although the methodological quality of the economic evaluations in the eight studies in this review was good overall, there were some methodological flaws. First, there was a lack of clearly defined economic questions in most of the studies. A well-defined health economic question should state the perspective, the comparators, the time horizon, and also consider both costs and consequences. Second, only half the studies reported QALYs as an outcome. The QALY, which is a preference-based measure of health outcome that combines length of life and health-related quality of life, has been reported as the preferred outcome measure for many health system funders [35, 36]. The QALY has the advantage of enabling comparisons of cost-effectiveness between interventions in different health conditions, and for economists, the QALY offers the additional advantage of incorporating individual preferences for health states, thereby moving beyond the narrow biomedical model for evaluative research [35].

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Another important limitation of the studies was that the category costs were narrow in scope. Few studies adopted a societal perspective with the costs of lost productivity (i.e. indirect non-medical costs) reported by only three studies, despite being an important cost supported by the government social welfare. For example, Bradley et al. [37] estimated US cancer-related productivity losses of $142.4 billion in 2010. A limited focus on direct medical costs may result in underestimation of the total economic costs and lead to misleading conclusions. The adoption of societal perspective as a norm has been described as necessary in order for the economic evaluation to provide the correct incentives for decision makers to take into account, for both static and dynamic efficiency, when making decisions about allocation of resources for improvement of health {Jonsson, 2009 #3356}. However there is controversy around wheter the inclusion of productivity changes constitutes double counting and around the equity implications {Drummond MF, 2005 #3291}

This review has several strengths. First, we devised a broad search strategy to capture a range of psychological outcomes and psychosocial interventions from a comprehensive list of electronic databases. Second, to help clinicians and decision makers, we categorised the cost-effectiveness results in a permutation matrix to clearly indicate which interventions could be accepted or rejected on efficiency grounds. Third, we excluded cost consequence analyses, as these studies did not present aggregated results in the form of ICER or net benefit. From a clinical and policy-makers perspective, it is more helpful to present costs and effectiveness results as a single index (ICER), as this allows policy-makers to judge if the combined distribution of costs and effects for an intervention is cost-effective at a given willingness to pay threshold [36, 38].

A limitation of this review is that we did not conduct a search of the grey literature, particularly government reports, conference abstracts and unpublished theses, so publication bias could not be eliminated. Further, the studies included in this review were from different countries with different costs of healthcare and willingness to pay thresholds; therefore, we could not pool the results in a meta-analysis, or present all results on a single cost-effectiveness plane. In addition, In addition, the studies captured in this review varied widely in the format and design of interventions and the description of usual care. Lastly, most of the studies were conducted among breast cancer patients and this is likely to affect the generalisability of the results to other cancer populations and to men.

Conclusion

Despite the importance of cost-effectiveness studies for translating study findings into clinical practice and policy, there are relatively few cost-effectiveness studies of psychosocial interventions for cancer patients and survivors, in the literature. In this review, the emerging evidence suggests that offering information, emotional support, and psychological care to cancer patients and survivors can be cost-effective. Future studies should ideally evaluate a broader range of psychosocial interventions i.e. that use different theoretical approaches, to help decide which types of interventions are most cost-effective. Our review demonstrates that psychosocial interventions can be efficiently implemented and potentially integrated into the health care system as a complement to medical therapies.

The methodological quality of the available studies was relatively good but there is room for improvement. A stronger focus on transparency and consistency when reporting the methods

and findings of economic evaluations is needed to allow for greater comparisons across interventions, and to help clinicians, researchers and policy makers decide which are the most appropriate interventions. For better reporting, economic evaluations should clearly state the research question, include all costs (both direct and indirect) associated with cancer, and use a utility-based measure such as QALYs. Including these important factors in the design and reporting of future studies will assist in determining the cost-effectiveness of psychosocial interventions for improving health outcomes for people with cancer. Better evidence around the cost-effectiveness of psychosocial interventions in cancer will enable policy makers to consider economic value, along with clinical efficacy, when making resource allocation decisions.

References

[1]. Ell K, Quon B, Quinn DI, Dwight-Johnson M, Wells A, Lee PJ, Xie B: Improving treatment of depression among low-income patients with cancer: the design of the ADAPt-C study. *General Hospital Psychiatry* 2007, **29**(3):223-231.

[2]. Zabora J, BrintzenhofeSzoc K, Curbow B, Hooker C, Piantadosi S: The prevalence of psychological distress by cancer site. *Psycho-Oncology* 2001, **10**(1):19-28.

[3]. Jacobsen PB, Jim HS: Psychosocial interventions for anxiety and depression in adult cancer patients: achievements and challenges. *CA cancer journal for clinicians* 2008, **58**(4):214-230.

[4]. Fallowfield L, Ratcliffe D, Jenkins V, Saul J: Psychiatric morbidity and its recognition by doctors in patients with cancer. *British Journal of Cancer* 2001, **84**(8):1011-1015.

[5]. Institute of Medicine: Cancer care for the whole patient:Meeting psychologicla health needs. In*.* Washington DC: The National Academies Press; 2007.

[6]. Barsevick AM, Sweeney C, Haney E, Chung E: A systematic qualitative analysis of psychoeducational interventions for depression in patients with cancer. *Oncology Nursing Forum* 2002, **29**(1):73-84; quiz 85-77.

[7]. Meyer TJ, Mark MM: Effects of psychosocial interventions with adult cancer patients: a meta-analysis of randomized experiments. *Health Psychology* 1995, **14**(2):101-108.

[8]. Osborn RL, Demoncada AC, Feuerstein M: Psychosocial interventions for depression, anxiety, and quality of life in cancer survivors: meta-analyses. *International Journal of Psychiatry in Medicine* 2006, **36**(1):13-34.

[9]. Raingruber B: The effectiveness of psychosocial interventions with cancer patients: an integrative review of the literature (2006-2011). *ISRN Nursing* 2011, **2011**:638218.

[10]. Dieng M, Watts CG, Kasparian NA, Morton RL, Mann GJ, Cust AE: Improving subjective perception of personal cancer risk: systematic review and meta-analysis of educational interventions for people with cancer or at high risk of cancer. *Psycho-Oncology* 2014, **23**(6):613-625.

[11]. Carlson LE, Bultz BD: Efficacy and medical cost offset of psychosocial interventions in cancer care: making the case for economic analyses. *Psycho-Oncology* 2004, **13**(12):837-849; discussion 850-836.

[12]. Howard K: The cost-effectiveness of screening for anal cancer in men who have sex with men: a systematic review. *Sexual Health* 2012, **9**(6):610-619.

[13]. Owens DK: Analytic tools for public health decision making. *Medical Decision Making* 2002, **22**(5 Suppl):S3-10.

[14]. Henry DA, Hill SR, Harris A: Drug prices and value for money: the Australian Pharmaceutical Benefits Scheme. *JAMA* 2005, **294**(20):2630-2632.

[15]. Devlin N, Parkin D: Does NICE have a cost-effectiveness threshold and what other factors influence its decisions? A binary choice analysis. *Health Economics* 2004, **13**(5):437-452.

[16]. Gordon LG, Beesley VL, Scuffham PA: Evidence on the economic value of psychosocial interventions to alleviate anxiety and depression among cancer survivors: a systematic review. *Asia-Pacific Journal of Clinical Oncology* 2011, **7**(2):96-105.

[17]. Moher D, Liberati A, Tetzlaff J, Altman DG, Group P: Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *British Medical Journal* 2009, **339**:b2535.

[18]. Hoch JS, Dewa CS: An introduction to economic evaluation: what's in a name? *Canadian Journal of Psychiatry Revue Canadienne de Psychiatrie* 2005, **50**(3):159-166.

[19]. Shiell A, Donaldson C, Mitton C, Currie G: Health economic evaluation. *Journal of Epidemiology and Community Health* 2002, **56**(2):85-88.

[20]. Drummond MF SM, Torrance GW, O'Brien BJ, Stoddart GL.: Methods for the economic evaluation of health care programmes. , 3rd edn: Oxford University Press; 2005.

[21]. Walker DG, Wilson RF, Sharma R, Bridges J, Niessen L, Bass EB, Frick K. In: *Best Practices for Conducting Economic Evaluations in Health Care: A Systematic Review of Quality Assessment Tools.* edn. Rockville (MD); 2012.

[22]. Shemilt I MM, Byford S, Drummond M, Eisenstein E, Knapp M, Mallender J, McDaid D, Vale L, Walker D: Chapter 15: Incorporating economics evidence. In Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0. In. Edited by Higgins JPT GS. Oxford, UK: The Cochrane Collaboration; 2011.

[23]. Nixon J, Khan KS, Kleijnen J: Summarising economic evaluations in systematic reviews: a new approach. *British Medical Journal* 2001, **322**(7302):1596-1598.

[24]. Evers S, Goossens M, de Vet H, van Tulder M, Ament A: Criteria list for assessment of methodological quality of economic evaluations: Consensus on Health Economic Criteria. *International Journal of Technology Assessment in Health Care* 2005, **21**(2):240-245.

[25]. Bares CB TP, Schwartz SM.: An exercise in cost-effectiveness analysis: treating emotional distress in melanoma patients *NHS Economic Evaluation Database* 2013(4).

[26]. Mandelblatt JS, Cullen J, Lawrence WF, Stanton AL, Yi B, Kwan L, Ganz PA: Economic evaluation alongside a clinical trial of psycho-educational interventions to improve adjustment to survivorship among patients with breast cancer. *Journal of Clinical Oncology* 2008, **26**(10):1684-1690.

[27]. Gordon LG, Scuffham P, Battistutta D, Graves N, Tweeddale M, Newman B: A cost-effectiveness analysis of two rehabilitation support services for women with breast cancer. *Breast Cancer Research and Treatment* 2005, **94**(2):123-133.

[28]. Strong V, Waters R, Hibberd C, Murray G, Wall L, Walker J, McHugh G, Walker A, Sharpe M: Management of depression for people with cancer (SMaRT oncology 1): a randomised trial. *Lancet* 2008, **372**(9632):40-48.

[29]. Lemieux J, Topp A, Chappell H, Ennis M, Goodwin PJ: Economic analysis of psychosocial group therapy in women with metastatic breast cancer. *Breast Cancer Research and Treatment* 2006, **100**(2):183-190.

[30]. Arving C, Brandberg Y, Feldman I, Johansson B, Glimelius B: Cost-utility analysis of individual psychosocial support interventions for breast cancer patients in a randomized controlled study. *Psycho-Oncology* 2013.

[31]. Kimman ML, Dirksen CD, Voogd AC, Falger P, Gijsen BCM, Thuring M, Lenssen A, F, Verkeyn J, Haekens C *et al*: Economic evaluation of four follow-up strategies after curative treatment for breast cancer: Results of an RCT. *European Journal of Cancer* 2011, **47**(8):1175-1185.

[32]. Sabariego C, Brach M, Herschbach P, Berg P, Stucki G: Cost-effectiveness of cognitive-behavioral group therapy for dysfunctional fear of progression in cancer patients. *European Journal of Health Economics* 2011, **12**(5):489-497.

[33]. Drummond M, Sculpher M: Common methodological flaws in economic evaluations. *Medical Care* 2005, **43**(7 Suppl):5-14.

[34]. McKenzie L, van der Pol M: Mapping the EORTC QLQ C-30 onto the EQ-5D instrument: the potential to estimate QALYs without generic preference data. *Value in Health* 2009, **12**(1):167-171.

[35]. Petrou S, Gray A: Economic evaluation alongside randomised controlled trials: design, conduct, analysis, and reporting. *British Medical Journal* 2011, **342**:d1548.

[36]. Drummond MF, Jefferson TO: Guidelines for authors and peer reviewers of economic submissions to the BMJ. The BMJ Economic Evaluation Working Party. *British Medical Journal* 1996, **313**(7052):275-283.

[37]. Bradley CJ, Yabroff KR, Dahman B, Feuer EJ, Mariotto A, Brown ML: Productivity costs of cancer mortality in the United States: 2000-2020. *Journal of the National Cancer Institute* 2008, **100**(24):1763-1770.

[38]. Gold MSJ, Russell, LB. Weinstein, MC.: Cost-effectiveness in Health and Medicine: Report of the Panel on Cost-effectiveness in Health Medicine. In: *Oxford university press.* New York; 1996: 283-285.

<u>Title and legends of figures</u>

Figure 1. Flow chart of study selection

Incremental effectiveness

	+	0	-
+	No studies **A**	No studies **B**	• *(Mandelblatt et al.):* Psycho-educational intervention comprising of a peer-modelled video support + information booklet + 2 individual counselling sessions by a trained cancer educator **versus** information booklet + peer-modelled video support **versus** information booklet alone. **C**
0	No studies **D**	*(Lemieux et al.):* Weekly professionally led supportive-expressive psychosocial group (6 to 10 participants) therapy + usual care **versus** usual care alone. **E**	No studies **F**
-	*Cognitive-behavioural therapy based interventions* • *(Arving et al.):* Cognitive-behavioural therapy based individual nurse support **versus** CBT based individual psychologist support **versus** usual care alone • *(Bares et al.):* Individual cognitive-behavioural therapy plus usual care **versus** usual care alone. *Psycho-educational interventions* • *(Kimman et al.):* Nurse-led telephone follow-up comprising a mammography combined with an outpatient visit and telephone interviews **versus** Short educational group program + Nurse-led telephone follow-up **versus** Short educational group program +Hospital follow up **versus** Hospital follow up as usual • *(Kimman et al.):* Nurse-led telephone follow-up comprising a mammography combined with an outpatient visit and telephone interviews **versus** Short educational group program + Nurse-led telephone follow-up **versus** Short educational group program +Hospital follow up **versus** Hospital follow up as usual • **(Strong et al.)**: 10 nurse-delivered individual support sessions comprising education about depression, problem-solving and communication with doctors + usual care versus usual care alone. *Psychosocial interventions* • *(Gordon et al.):* Home-based individual physiotherapy intervention **versus** group-based exercise and psychosocial intervention **versus** no intervention **G**	*(Sabariego et al.)* Directive group psycho-therapy: 4 cognitive-behavioural group therapy oriented sessions + 3-week inpatient rehabilitation program **versus** Non-directive group psychotherapy: 4 supportive experimental group therapy sessions + 3-week inpatient rehabilitation program. **H**	No studies **J**

Incremental costs

Figure 2. Guidance for decision makers based on cost-effectiveness results, presented as a permutation matrix

The dark orange colour ▮ indicates that the decision is strongly favoured either accepted (box G) or rejected (box C). The light orange colour ▮ indicates a situation in which a decision is less favoured either accepted (D and H) or rejected (B and F). The boxes A and J indicates cases in which there is no obvious decision—that is, some form of financial or clinical trade off is required or no differences are observed (box E).

Figure 3. Summary appraisal of the methodological quality of the included studies based on the 19-item Consensus Health Economic Criteria (CHEC)-list criteria -list criteria.

Table 1. Characteristics of included studies

First author	Year	Country	Type of cancer	Population	Intervention	Comparator	Mean age in years /proportion of men and women
Arving C. [30]	2013	Sweden	Breast cancer	Consecutive breast cancer patients starting adjuvant therapy (*N*=168)	Individual (face to face or telephone) cognitive-behavioural therapy based psychosocial support to breast cancer patients provided by: (1) oncology nurses or (2) psychologists. Participants received between 0 and 23 support sessions depending on needs.	Usual care included contacts with medical staf, referrals to psychiatrist or social worker for discussion.	55 (for all groups) 100% women
Bares C. [25]	2002	USA	Melanoma	Melanoma patients at the multidisciplinary melanoma clinic at the University of Michigan Comprehensive Cancer centre. (n=38)	Usual care plus individual cognitive-behavioural therapy consisted of: (1) sessions intended to provide instruction in skills acquisition (2) workbook containing sections on relaxation training, challenging of negative thoughts and problem-solving	Usual care included regular contact with the patient's oncologist and medical staff. Mental health services were also available as needed.	Not reported
Gordon L. [27]	2005	Australia	Breast cancer	Breast cancer survivors (N=275)	(1) Home-based physiotherapy intervention (DAART) (2) 8 sessions Group-based exercise and psychosocial support group (STRETCH)	Non- intervention sample	59 (group 1) 54 (group 2) 55 (Non-intervention) 100% women
Kimman M. [31]	2011	The Netherlands	Breast cancer	Women who have recently (less than 6 weeks) completed breast cancer treatment (N=299)	(1)Nurse-led telephone follow-up comprising a mammography combined with an outpatient visit and telephone interviews (2)Short educational group program + Nurse-led telephone follow-up (3)Short educational group program +Hospital follow up	Hospital follow up as usual: five outpatient clinic visits including one mammography	56 100% women

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Author	Year	Country	Cancer type	Population	Intervention	Control	Sample characteristics
Lemieux J. [29]	2006	Canada	Breast cancer	Women with metastatic breast cancer (N=125)	Weekly supportive-expressive psychosocial group (6 to 10 participants) therapy and professionally led + usual care	Usual care alone including access to necessary medical, surgical, or psychosocial care. Every four to six months, educational materials about breast cancer and its treatment, as well as about relaxation and nutrition were provided.	49 (intervention) 52 (control) 100% women
Mandelblatt J. [26]	2008	USA	Breast cancer	Women completing breast cancer treatment (N=389)	(1) Psycho-educational intervention comprising of a video support + booklet + 2 individual counselling session (one face to face and 1 telephone) (2) Booklet + video support	Booklet alone	58 100% women
Sabariego C. [32]	2011	Germany	Mixed cancers	Cancer patients receiving inpatient rehabilitation. Breast 59%, colorectal 8%, bladder/prostate 8%, gynaecologic 8% other cancer 16% (N = 174)	Directive group psychotherapy : 4 cognitive-behavioural group therapy oriented sessions + 3-week inpatient rehabilitation program	Non- directive group psychotherapy : 4 supportive experimental group therapy sessions + 3-week inpatient rehabilitation program	54 (Group 1) 54 (Group 2) Group 1: 86% females and 14% males. Control:86% females and 15% males.
Strong V. [28]	2008	UK	Mixed cancers	Breast 44%, gynaecologic 15%,	Up to 10 (face to face or telephone) nurse delivered sessions comprising education	Usual care including free	57 (same in both groups) Intervention: 69% females

colon 6%, other cancer patients 34% (N = 200)	about depression, problem-solving and communication with doctors + usual care	access to treatment to depression.	and 31% males. Control:72% females and 28% males

Table 2. Summary of economic evaluation methods and results

First author Year	Type of Economic Evaluation	Perspective	Time horizon	Reference year for costs	Currency	Categories of costs included	Utility/ health outcomes	Psychological outcomes	Incremental cost effectiveness ratio (ICER) or incremental net benefit (INB) results	Sensitivity analyses/factors
Arving, C. [30] 2013	Cost-utility analysis	Health care system	2 years	2006	Euro €	Direct medical costs Intervention costs	Quality adjusted life years EORTC-QLC-C30		Both INS IPS dominated the Usual care Cost: INS=€18670, IPS=€20419, Usual care =€25800 QALYs: INS=1.52QALY, IPS=1.59QALY and Usual care =1.43QALY.	Several one-way sensitivity analyses/ QALY calculations, tumor size, lymph node metastases, number of support sessions
Bares, C. [25] 2002	Cost-effectiveness analysis	Health care system	1 year	Not specified	USD $	Direct medical costs Intervention costs	-	Distress, coping style, anxiety and health functioning Global Severity Index of the BSI was used.	ICER for Usual care =$402.37 for 1 point decrease of the GSI score, ICER for Usual care +cognitive behavioural therapy=$7.66 for 1 point decrease of the GSI score	Not reported
Gordon, L. [27] 2005	Cost-effectiveness analysis	Societal	1 year	2004	AUD $	Direct medical costs, Direct non-medical costs, Indirect non-medical costs	Quality adjusted life years FACT-B+4	Rehabilitated cases=clinical improvement based on FACT_B+4 scores	DAART: ICER= $2217 per rehabilitated case; STRETCH: ICER =$31367 per rehabilitated case; ICER for the non intervention group was negative. The non intervention group dominated. The ICER for DAART was AU$1344 per QALY gained and AU$14478 per QALY gained for the STRETCH. The non intervention group dominated.	Several one-way sensitivity analyses and a probabilistic sensitivity analysis/cost, utility scores, probability of rehabilitated cases.

Study	Analysis type	Perspective	Time horizon	Price year	Currency	Costs	Outcomes	Instruments	Results	Sensitivity analysis
Kimman, M. [31] 2011	Cost-effectiveness analysis	Societal	1 year	2008	Euro €	Direct medical costs, Direct non-medical costs, Indirect non-medical costs	Quality adjusted life years EQ-5D (level 3)		Hospital follow up +educational group program yielded an ICER of € 235 per QALY gained and was dominated by the Telephone follow up +educational group program	Several one-way sensitivity analyses/unit prices of telephone contacts and hospital visits; the highest reported duration of telephone call and the generic cost price for a hospital visit; the use of Dutch EQ-5D tariff for utility scores.
Lemieux, J. [29] 2006	Cost-minimisation analysis and Cost-effectiveness analysis	Health care system	1 year	2002/2003	CAN $	Direct medical costs Intervention costs	Survival, mood, pain POMS	Mood and pain POMS	Incremental cost of $5550 for an effect of 0.5 for mood and an incremental cost of $4309 for an effect size of 0.5 for pain.	One-way and two-way sensitivity analysis/ total cost; hospitalisation costs calculations methods; total cost estimates for a range of ±20%; benefit of mood and pain using different effects (small, medium, large).
Mandelblatt, J. [26] 2008	Cost-effectiveness analysis	Societal	1 year	2002	USD $	Direct medical costs (excluding medications	-	Distress and vitality IES-R, MOS	The most intensive intervention, counselling+video+booklet	one-way sensitivity analysis/cost and effect of

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						costs) Intervention costs		SF-36	was higher in cost and lower in change in distress. Video + NCI booklet dominated the other with an ICER of $7275 per change in cancer specific distress for all women. For women with high preparedness counselling + video + booklet ICER of $1066 per change in cancer specific distress.	counselling.
Sabriego, C. [32] 2011	Cost-effectiveness analysis	Societal	1 year	2004	Euro €	Direct medical costs, Direct non-medical costs, Indirect non-medical costs	Mental score (SF-12)	Fear of progression (Fear of Progression Questionnaire), mental component score (SF-12)	Cognitive behavioural therapy was the dominant strategy with an ICER of minus €78741 for an additional reduction of fear of progression; ICER of minus €16975 for an additional improved mental score.	Presented confidence intervals from bootstrap and acceptability curves from the ICERs
Strong, V. [28] 2008	Cost-utility analysis	Health care system	1 year	2006	Pounds £	Direct medical costs (excluding cancer treatment costs) Intervention costs	Quality adjusted life years EORTC-QLC-C30, EQ-5D (level 3).	Depression (SCL-20, DSM-IV), anxiety (SCL-90)	The ICER for the intervention was £5278 per QALY gained. The intervention dominated.	Simple one-way sensitivity analysis/confidence interval of the costs and effects.

DAART = Domiciliary allied and acute care rehabilitation team, STRETCH = Strength through recreation exercise togetherness care health, EORTC-QLC-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire, EQ-5D = Euro Quality of Life -5-Dimensional Classification, INS = individual nurse support, IPS = individual psychologist support, DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, SCL-20 = Symptom Checklist Depression Scale - 20-item, IES-R = Revised Impact of Events Scale, MOS = Medical Outcomes Study, SF-36 = Short Form, POMS = Profile of Mood States, NCI = National Cancer Institute, FACT-B+4 = Functional Assessment of Cancer Therapy –Breast Cancer plus arm morbidity scale. BSI = Brief Symptom Inventory, GSI = Global Severity Index.

Table 3: Summary appraisal of the methodological quality of the included studies based on the 19-item Consensus Health Economic Criteria (CHEC)-list criteria -list criteria.

Study	Number of criteria met N (%)
Kimman et al. 2011	17 (89%)
Mandelblatt et al. 2008	17 (89%)
Sabariego et al. 2011	16 (84%)
Arving et al. 2013	14 (74%)
Gordon et al. 2005	14 (74%)
Strong et al. 2008	14 (74%)
Lemieux et al. 2006	10 (53%)
Bares et al. 2002	8 (42%)