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# INTERVENTIONS TO IMPROVE SCREENING AND APPROPRIATE REFERRAL OF CANCER PATIENTS FOR DISTRESS: SYSTEMATIC REVIEW

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## ABSTRACT

### Objectives

The primary aim of the review was to determine the effectiveness of strategies to improve clinician provision of distress screening and referral of patients with cancer.

### Design

Systematic review.

### Data sources

Electronic databases (Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, PsycINFO and CINAHL) were searched until July 2016.

### Inclusion criteria

Population: adult cancer patients and clinical staff members. Intervention: Any strategy that aimed to improve the rate of routine screening and referral for detected distress of cancer patients. Comparison: no intervention controls, 'usual' practice, or alternative interventions. Outcome: (primary) any measure of provision of screening and/or referral for distress, (secondary) psychosocial distress, unintended adverse effects. Design: trials with or without a temporal comparison group including randomised and non-randomised trials, and uncontrolled pre-post studies.

### Data extraction and analysis

Two review authors independently extracted data. Heterogeneity across studies precluded quantitative assessment via meta-analysis and so a narrative synthesis of the results is presented.

**Results**

Five studies met the inclusion criteria. All studies were set in oncology clinics or departments and used multiple implementation strategies. Using GRADE, the overall rating of the certainty of the body of evidence reported in this review was assessed as very low. Three studies received a methodological quality rating of weak and two studies received a rating of moderate. Only one of the five studies reported a significant improvement in referrals.

**Conclusions**

Current research provides inconsistent evidence from predominantly poor quality studies of the effectiveness of strategies to improve the routine implementation of distress screening and referral for cancer patients. The small number of trials to date combined with the low-quality evidence highlights the need for well-designed studies to identify effective support strategies to maximise the potential for successful implementation.

**Systematic review registration** PROSPERO registration number CRD4 2015017518.

**Strengths and limitations of this study**

- The first review to systematically synthesise evidence of the effectiveness of strategies to improve the rate of routine distress screening and referral for cancer patients
- The review performed a comprehensive search of the literature, included controlled trials of any design, and was inclusive of non-English literature
- Few studies met inclusion criteria, and heterogeneity of study design, primary and secondary outcomes precluded quantitative synthesis

## INTRODUCTION

### Rationale

Distress interferes with the ability to cope with cancer treatment, and can include problems that are disabling such as depression, anxiety, panic and feeling isolated or in a spiritual crisis [1]. Between 20% to 47% of cancer patients experience significant levels of distress [1]. Distress can arise in response to cancer related factors such as diagnosis and cancer progression, pain and adverse effects of treatment [2]. Distress in cancer patients may lead to non-adherence to treatment, poorer quality of life and may negatively impact survival [1 3] as well as increase treatment burden to the oncology team and health system [4]. Therefore, recognizing and treating distress in cancer populations is an important health priority.

Professional associations and clinical guidelines [5-9] including the National Comprehensive Cancer Network *Clinical Practice Guidelines in Oncology: Distress Management* [1] recommend that those responsible for the care of cancer patients routinely screen for distress and, as appropriate, refer for further assessment and support. These recommendations are based on systematic reviews and meta-analyses that have demonstrated screening improves the timely management of distress [3 10], improves adherence to treatment, reduces burden to the treatment team and can avoid progression to more severe anxiety or depression [1].

Despite evidence based guideline recommendations, screening and referral of cancer patients for distress is not routinely conducted by clinicians responsible for the clinical management of cancer [1 2 11]. Beginning in 2015, the American College of Surgeons Commission on Cancer (CoC) has required cancer centers to implement programs for distress screening as a criterion for accreditation (42). A recent cross-sectional survey of 20 National Comprehensive Network (NCCN) Institutions reported only 60% of services conducted outpatient distress screening, and even fewer services reported screening all patients (30%) as outlined in the

NCCN standards [12]. Systematic reviews of trials of strategies to improve depression or anxiety screening in primary care note that complex organisational interventions that incorporate multiple strategies are most effective in improving provision of care [13-15]. Such strategies include clinician education, opinion leaders, patient specific reminders, enhanced role of nurses, academic detailing, integrating screening into routine clinical reviews and a greater degree of coordination between services (for example between primary and secondary care) [13-15]. However, we are not aware of any previous systematic review of interventions to improve clinician routine provision of distress screening and appropriate referral of cancer patients per-se.

**Objectives**

The primary aims of the review were to determine the impact of trials of strategies to improve clinician rate of screening and referral of patients with cancer for distress. In particular, we assessed the impact of such interventions on:

i) improving screening of patients for psychosocial distress; and

ii) improving referral of patients with cancer who screen positive on a measure of distress for further assessment and/or psychosocial support

The secondary aims of the review were to:

i) Describe the effectiveness of such interventions on reducing psychosocial distress of patients with cancer;

ii) Describe any unintended adverse effects of such an intervention

**METHODS AND ANALYSIS**

The review methods were based on the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Statement [16]. The details of the methods have been reported elsewhere [17] and the protocol is registered with PROSPERO (registration number CRD42015017518).

**Eligibility criteria**

Study characteristics

*Types of studies*

Original studies including randomised controlled trials and non-randomised trials were included. Exclusion criteria were trials without parallel comparison or control groups. There were no restrictions based on length of follow-up, year of study publication or language. Studies could be published in peer review or grey literature.

*Participants*

Participants could include adult cancer patients and clinical staff members such as physicians and allied health professionals responsible for the care of cancer patients. Studies which examined screening for psychosocial distress and/or referral for carers of patients with cancer, or survivors of cancer, were excluded.

*Types of Interventions*

Interventions of strategies that aimed to improve the rate of screening procedures for distress and/or rate of referral for appropriate psychosocial support in health care settings were included. There are a range of potential strategies that could improve the likelihood of implementation of distress screening and referral in healthcare settings. For example, The Cochrane Effective Practice and Organisation of Care (EPOC) taxonomy is a framework for characterising educational, behavioural, financial, regulatory and organisational interventions

within the topic of 'implementation strategies' [18] and includes 22 sub-categories. Examples of strategies within the taxonomy include educational materials, performance monitoring, local consensus processes and educational outreach visits. Included interventions could be singular or multicomponent. Studies using clinical judgement of psychosocial distress alone, without use of a formal screening tool were excluded. Referral for psychosocial support was defined as any written or verbal offer or direction of a patient for further review, consultation, assessment or treatment with any health professional, including the primary oncology team or health service, offering psychosocial support such as psycho-oncology services. Studies were included if they implemented either distress screening only or distress screening and appropriate referral. Studies where research staff conduct screening or referral were excluded.

*Comparisons*

Studies with no intervention controls, 'usual' practice or alternative intervention comparison groups were included.

*Outcomes*

Primary outcomes:

i) Any measure of the provision of screening for distress (e.g. number or % of cancer patients screened).

ii) and/or any measure of the provision of referral for further assessment and/or psychosocial support (e.g. number or % of cancer patients referred) by a clinician responsible for the management of a cancer patient.

*Secondary outcomes:*

i) Any validated outcome measure of change in distress levels in the patients (e.g. distress outcome assessments such as the Kessler Psychological Distress Scale) [19].

ii) Any measure of adverse effects on patients, clinicians or health services; or barriers to performing screening such as clinician distress [20].

**Information sources**

Electronic databases

The following electronic databases were searched for potentially eligible studies published up until July 2016; the Cochrane Central Register of Controlled trials (CENTRAL) in the Cochrane Library, MEDLINE, EMBASE, PsycINFO and CINAHL. The Medline search strategy (supplementary file) was adapted for other databases and included filters used in other systematic reviews for population (cancer patients) [21], screening for distress [22] and referral [23] and psychosocial support [24].

Other sources

Studies were also obtained from the following sources:

- Reference lists of included studies
- Hand searching of 3 relevant journals in the field (published in the last 5 years); Journal of the National Comprehensive Cancer Network, Psychooncology and Supportive Care in Cancer
- Hand searching of conference abstracts published in the preceding 2 years from the International Psycho-Oncology Society and the Society of Behavioural Medicine
- A grey literature search using Google Scholar (published online in the last 5 years – the first 200 citations was examined)

**Study selection**

The titles and abstracts retrieved by electronic searches were exported to a reference management database (Endnote version X6) to remove duplicates. Two reviewers independently screened abstracts and titles using a standardised screening tool that was pilot tested with a sample of articles before use. The abstracts of papers that were in a language other than English were translated using Google Translate. If considered eligible or eligibility was unclear, professional translation of the full paper was undertaken.

The full texts of manuscripts were obtained for all potentially eligible trials for further examination and independently screened by two reviewers. For all manuscripts, the primary reason for exclusion was recorded and is documented in Figure 1. Discrepancies regarding study eligibility were resolved by discussion and consensus.

**Data extraction**

Two review authors (KM and EF) independently extracted data from the included trials using a pre-piloted data extraction form that was developed based on recommendations from the *Cochrane Handbook for Systematic Reviews of Interventions* [25]. Discrepancies regarding data extraction were resolved by discussion and consensus.

Data items

Data was sought for the following variables:

- Authors, year and journal
- Study eligibility, study design, health care provider type (e.g. nurses), country, health care setting (e.g. oncology clinic)
- Patient characteristics and demographics including cancer site, cancer stage, age, sex, cancer treatment type, treatment status (pre/undergoing/post)

- Characteristics of the intervention, including the duration, intervention strategies, screening instrument
- Trial primary and secondary outcomes, including sample size, the data collection method, validity of measures used, any measures of client uptake or use of psychosocial support services following referral, effect size, measures of change in distress
- Number of participants per experimental condition
- Information to allow assessment of risk of study bias

**Methodological quality assessment bias**

Two review authors (KM and EF) independently assessed the risk of bias of all included trials using the Effective Public Health Practice Project Quality Assessment Tool (EPHPP) for quantitative studies [26]. The use of the EPHPP tool was a post hoc change from protocol due to the study designs included in the review. This tool covers any quantitative study design and includes components of intervention integrity [25 27]. Any discrepancies were resolved through discussion. The EPHPP assesses six methodological dimensions: selection bias, study design, confounders, blinding, data collection methods, and withdrawals and dropouts. These domains are rated on a three-point scale (strong, moderate, weak) according to pre-defined criteria and procedures recommended for tool use, and then given an overall global rating. Those with no weak ratings were given an overall rating of strong, those with one weak rating were given an overall rating of moderate and those with two or more weak ratings across the six domains were given an overall weak rating. Two additional methodological dimensions provided by the tool are intervention integrity and analyses and these were also completed by the reviewers.

**Data analysis**

Summary measures

The small number of studies and differences in study design and primary and secondary outcomes reported in the included studies precluded the use of summary statistics to describe treatment effects. As such, the findings of included trials are described narratively.

Grading the strength of evidence

As recommended by the *Cochrane Handbook for Systematic Reviews of Interventions* [25], the overall quality of evidence on primary outcomes is presented using the GRADE (Grades of Recommendation, Assessment, Development and Evaluation) approach, which involves consideration of within-study risk of bias (methodological quality), directness of evidence, heterogeneity, precision of effect estimates and risk of publication bias. The overall quality of evidence was rated by two review authors (KM and EF) at four levels: high, moderate, low and very low.

**RESULTS**

A total of 18 542 citations were identified (after duplicates were removed) (Figure 1) for abstract and title screening. Just one study met the eligibility criteria (i.e. parallel control/comparison group). As such, and in an attempt to provide some evidence to guide researchers and practitioners regarding methods to improve patient distress screening and referral of cancer patients, we relaxed the design criteria and post-hoc rescreened all 18 542 citations and included studies with controlled trial designs without parallel control groups including uncontrolled pre post studies. The full text of 185 manuscripts were sought for further assessment against the review inclusion criteria (Figure 1). Of these, 178 were considered ineligible following the trial screening process. Seven publications describing 5 trials were included in the review.

**Included studies**

***Types of studies***

A description of the trial characteristics of included studies is provided in Table 1. One study was conducted in Japan [28], one in the Netherlands [29-31], one in Germany [32], one in Belgium [33] and one in Australia [34]. Studies were published between 2009 and 2014. There was considerable heterogeneity in the participants, interventions and outcomes (clinical heterogeneity) of included studies.

***Health providers***

All studies were set in oncology clinics or departments. In regards to the healthcare providers responsible for conducting the distress screening and/or referral, one study targeted nurses [34], one targeted radiation oncologists [29-31], one required pharmacists to perform the screening [28], one study involved both specialised breast care nurses and doctors [32] and one study utilised oncologists [33].

***Interventions***

All trials used multiple implementation strategies. The EPOC subcategories used to classify the implementation strategies employed by included studies in the review are provided in Table 2. Using EPOC taxonomy descriptors, all trials included educational materials and educational meetings, with two trials using only these strategies [33 34]. One trial utilised these strategies with the addition of educational outreach visits [29-31]. One study used a combination of educational materials, educational meetings, educational outreach visits and reminders [28]. One study tested an intervention consisting of organizational culture, continuous quality improvement, educational materials, educational meetings and reminders [32].

***Outcomes***

Implementation of distress screening and/or referral was primarily assessed using reviews of patient medical records [28-32 34], however one study did not report the data collection method [33]. None of the studies reported which staff completed the medical record reviews. All trials

reported the rates of referral for supports for those patients identified as distressed, however none of the studies examined the improvement in rates of distress screening. Change in distress levels were reported in one study [29-31]. No studies included a measure of potential adverse effects.

***Study design characteristics***

One of the included studies was a cluster randomised controlled trial [29-31], four were pre post studies [28 33 34] and one was a prospective consecutive study [32]. The cluster randomized controlled trial compared an intervention to a usual care control [29-31], three studies compared a screening program period to a usual care period [28 33 34] and one trial compared a screening program phase to a two-phase non-screening period [32].

**Methodological quality assessment**

Individual ratings for each study against the six methodological criteria from the EPHPP tool and the assigned global rating are reported in Table 6. Overall, three studies received a methodological quality rating of weak [32-34] and two studies received a rating of moderate [28-31]. For three of the four non-randomised studies [32 34 35], it was unclear whether confounders were adequately adjusted for and for the majority of studies, blinding of outcome assessors or study participants was not described. While most studies reported medical record reviews for the data collection method, no reference was made to their validity or reliability as an outcome measure, nor was a description of who conducted the audits provided, resulting in weak ratings for all studies. All studies were judged as using analyses as appropriate to study design.

**Effects of intervention on distress screening and/or referral**

None of the included trials reported on the effects of strategies to improve rates of distress screening provision. Only one of the five studies reported a significant improvement in rate of referrals [32]. Zemlin et al. [32] reported a significant positive trend for the number of patients that were informed/offered psycho-oncological interview ($t = 22.40$, $df = 2$, $p < 0.001$). The effects of interventions are presented according to the implementation strategies (classified using the EPOC taxonomy) employed by included studies.

***Educational materials and educational meetings***

Two studies examined the impact of educational materials and educational meetings on distress screening or referral [34 35]. Thewes et al. [34] conducted a pre post trial testing the feasibility and acceptability of introducing a routine psychological screening program using the Distress Thermometer (DT) to improve screening rates and timeliness of referral to psychosocial services in three rural outpatient oncology clinics in Australia. Nursing and psychosocial staff participated in a two-hour training session (educational meetings and educational materials) covering the rationale for screening, the screening instrument and the study procedure. The impact of the intervention on distress screening was not explicitly reported (i.e. the control period rates of screening). Five of eight cases (according to predefined PSYCH-6 cutoff criteria) and ten of 19 cases (according to DT cutoff) were referred to a social worker or psychologist in the control and intervention periods respectively. Due to the small number of cases, significance testing of differences between the pre-screening and screening phases was not conducted.

Bauwens et al. [33] conducted a pre post study to evaluate the impact of systematic screening with the Distress Barometer (DB) on detection rates of elevated distress and on rates of psychosocial referral at an oncology centre in Belgium. Oncologists were instructed in using the DB and given a written explanation (educational materials) on how to interpret the DB results in a collective 1 hour session (educational meetings). As this study did not aim to

improve rates of distress screening, but focused on oncologist detection of distress and subsequent referral, all patients were screened using the DB in both conditions. Consequently, the rates of distress screening prior to the study, conducted by oncologists or other professional staff, compared to the study period are unknown. Of those patients for whom referral was considered necessary, 40% in the usual care condition and 69% in the DB condition were actually referred to psychosocial care. The authors did not conduct an analysis to determine if there was a significant difference in these rates, however concluded that the implementation of screening using the DB led to increased numbers of referrals to psychosocial professionals.

***Educational materials, educational meetings and outreach visits***

Braeken et al. [29-31] conducted a cluster randomised controlled trial to study the effect of the implementation of the Screening Inventory Psychosocial Problems (SIPP) on the number and types of referrals of cancer patients to psychosocial caregivers in a radiation oncology department in the Netherlands. Radiation oncologists were randomised to a control or intervention group. Those in the intervention group were trained by a researcher and two social workers with experience in using and interpreting the SIPP during a 1 hour training session (educational meetings, educational materials and educational outreach visits). The study found no significant intervention effects were observed for the total number of patients referred to psychosocial care providers at any of the assessment time points (first three months, the last nine months and the total study period).

***Educational materials, educational meetings, educational outreach visits and reminders***

Ito and colleagues [28] conducted a pre post trial to examine the usefulness of a screening program (using the distress and impact thermometer; DIT) modified for cancer patients undergoing radiotherapy at an outpatient cancer treatment center in Japan. Prior to the

screening phase, all pharmacists attended a 2 hour lecture and (educational meetings) given by a trained psychiatrist (who also met with the pharmacists monthly; educational outreach visits) and underwent role play training to learn how to implement the DIT and referral for those patients scoring above the predetermined cutoff, (educational materials). When providing instructions to patients beginning chemotherapy and at the second visit, pharmacists invited patients to complete the DIT and a screening program sheet was completed by the pharmacists (reminders). The number of patients screened prior to the implementation of the screening program using the DIT or other measure was not assessed and 84.8% of patients were screened using the DIT in the intervention phase. The proportion of patients referred to the Psychiatric Service (and were subsequently confirmed to have major depression or adjustment disorder) during the screening program period compared to the usual care period was not significantly different between the two periods (2.7% during the program-period vs 1.0% during the usual care-period, $p = 0.46$).

***Educational materials, educational meetings, reminders, organizational culture, continuous quality improvement***

One study examined the effect of educational materials, educational meetings, reminders, organizational culture and continuous quality improvement on improvement in distress screening or referral. The trial by Zemlin et al. [32] was a prospective consecutive study that examined whether a screening and computer based psycho-oncological clinical pathway could improve the identification of breast cancer patients requiring psycho-oncological support at a gynaecology clinic in Germany. Prior to the introduction of the program, certified training courses were held for clinicians, gynaecologists and psychotherapists as well as other professional groups (educational meetings, educational materials, organizational culture) and every three to four months, cross-departmental meetings between psychology and gynaecology departments were held (continuous quality improvement). The authors

described the trial in three phases; in phase one, breast care nurses and doctors asked the patient about their interest in a psycho-oncological consultation where they felt necessary, and in phase two the nurses asked this of patients on the day of their admission. In phase three, the nurses conducted screening using the Hospital Anxiety and Depression Scale (HADS) with all patients and passed the HADS sheet to the physician (reminders). A predetermined cutoff indicated if referral was required. The proportion of patients screened with the HADS during phase three was 100%. The number of patients screened in phase one or two using the HADS or other measure was not assessed. The authors reported a significant positive trend for the number of patients offered referral for psycho-oncological care between phase one and three ($t = 22.40$, $df = 2$, $p < 0.001$).

**Secondary outcomes**

***Psychosocial distress***

Only one study compared patients' levels of distress at follow up using the distress screening measure implemented. Braeken et al. [29-31] found no significant intervention effects as measured by the HADS for patients' psychological distress at three months or 12 months after baseline, nor dichotomous distress outcomes (no distress or at least moderate distress) at three months, or 12 months after baseline.

***Reported adverse consequences***

No study explicitly assessed whether the intervention had adverse effects.

**Quality of the evidence**

Using GRADE, the overall rating of the certainty of the body of evidence reported in this review was assessed as very low. The primary outcomes examined were downgraded one level to reflect high risk of bias and further downgraded two levels due to clinical heterogeneity and inconsistency in reporting either rates of distress screening or referral

across both control and intervention periods. Since indirectness and imprecision also lowers the quality of the evidence, we downgraded two further levels on that basis. We found the quality of evidence to be of weak to moderate quality due to risk of bias using the EPHPP (Table 6), which identified a number of limitations, particularly among the pre post studies in regards to controlling for potential confounders.

## Discussion

This review sought to assess the impact of trials of strategies to improve clinician provision of:

screening of patients for distress; and referral for further assessment and/or psychosocial support where necessary. The review identified just one trial that met the prospectively registered inclusion criteria of having a parallel control trial design. When these criteria were relaxed to include those with a non-parallel control group a further four trials were included. None of the included trials reported on the effects of strategies to improve distress screening, and the intervention in just one trial was effective in improving the rates of referral for psycho-oncological support for distressed patients. Such findings highlight the sparse evidence base for this important element of cancer patient care, and leave health services and cancer professionals with little clear guidance of strategies to improve provision of these elements of care to their patients.

Our findings are consistent with previous systematic reviews of trials aiming to improve depression or anxiety screening in primary care that have found that improvement in care provision is more likely when complex organisational change strategies are used, such as coordination between departments, enhanced role of nurses and performance feedback, in addition to clinician education [13-15]. The trial by Zemlin et al. [32] was the only study included in the review to adopt a comprehensive implementation approach, and the only to report

significant improvement in referral of cancer patients for distress. Implementation strategies employed by other trials were primarily based on one off training and resource provision, suggesting that such support is insufficient. Comprehensive implementation strategies may be more likely to improve care given their greater capacity to address various barriers to screening and referral. Further research identifying they key barriers to such care, and the best strategies to address them in cancer services is therefore warranted.

Surprisingly, none of the included studies examined the impact of strategies to improve the rate of clinician provision of distress screening. Such a finding is of concern. Screening is a necessary pre-requisite to appropriate referral of cancer patients to psychological support. As screening for distress in cancer populations is low across jurisdictions [12], improving this form of care should represent a priority. Previous studies have used novel technologies to prompt screening by clinicians [36-38]. Such approaches should be examined in robust trial designs in cancer settings that allow for their impact on improving the rate of routine clinician provision of distress screening to be determined.

A number of methodological aspects of the study warrant highlighting and should be considered when interpreting the study findings. As far as the authors are aware, this is the first systematic review to examine the impact of interventions of strategies to improve the rate of clinician provision of distress screening and appropriate referral in cancer patients. The review was prospectively registered, followed a peer reviewed protocol and included a comprehensive search strategy examining over 18000 citations. There was substantial clinical and methodological heterogeneity in the included studies. Classification of EPOC taxonomy implementation strategies was also difficult due to the lack of detail reported on intervention components in the studies. Furthermore, all but one of the included studies were pre post trials. Such characteristics of the included studies precluded quantitative synthesis of the effects of these strategies.

**Conclusions**

The findings of this review suggest that there is considerable scope to improve implementation of distress screening and referral in cancer settings in order to establish a strong evidence base for future successful interventions. Implementation of distress screening and appropriate referral needs to be employed using a systematic method and assessed with appropriately controlled studies in order to determine the most effective approaches. Better reporting of outcomes and more detailed description of intervention components need to be prepared.

**Figure 1. PRISMA Flow Diagram**

## Table 1. Trial characteristics

| Study | Design | Study dates | Single-centre or multicentre | Setting | Country | Aim | Patient inclusion criteria | No. of patients | Mean age in years (SD) | Gender (male) | Tumour site/Tumour stage | Cancer treatment type/Stage of treatment |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Thewes et al. 2009 [34] | Pre post | NR. | Multicentre - 3 rural outpatient oncology clinics | Outpatient oncology clinics. | Australia | (i) Prospectively investigate the feasibility and acceptability of introducing a routine psychological screening program for rural oncology clinics; (ii) explore the impact of screening on rates and timeliness of referral to psychosocial services; and (iii) provide pilot data on the acceptability and utility of the DT as a screening tool within the rural Australian setting. | (i) Newly diagnosed with malignant disease; (ii) 18 years of age or older; (iii) able to give informed consent; and (iv) able to read English proficiently. | Unscreened cohort – 40. Screened cohort – 43. | 60.0 (10.5 SD). | 54.0% | Colorectal 22.9%, Breast 30.1%, Lung 14.5%, Other 13.2%, Haematological 9.6%, Skin 6.0%, Unknown primary 3.6%.<br><br>Localised/locally advanced 71.1%, Advanced or metastatic 28.9%. | Surgery 75.9%, chemotherapies 66.3%, RT 53%, endocrine therapies 32.5%.<br><br>Newly diagnosed patients. |
| Braeken et al. 2009 [29], 2013 [30] & 2013 [31] | Cluster randomised controlled trial | April 2008 – October 2010. | Single | Institute Verbeeten (BVI) - a radiation oncology department (Tilberg). | The Netherlands | To study the effect of the SIPP on the number and types of referrals of cancer patients with psychosocial problems to psychosocial caregivers. | i) Receiving RT; ii) most common cancer types such as lung, prostate, bladder, rectum, breast, cervix, endometrial, skin and Non-Hodgkin; iii) 18 years of age or older; and iv) no metastases. Exclusion criteria: i) receiving palliative treatment, ≤ 10 fractions of RT; ii) unable to read and speak Dutch; and iii) unable to complete questionnaires. | Control group – 300. Intervention group – 268. | Control group 62.4 (10.7 SD), intervention group 62.4 (10.8 SD). | Control group 47.0%, intervention group 31.7%. | Prostate/Bladder 24.1%, Lung 11.3%, Breast 50.0%, Cervix/Endometrial 1.6%, Rectum 9.0%, Non-Hodgkin Lymphoma 1.7%, Skin 2.3%. | 100% RT.<br><br>SIPP before the first consultation prior to RT and SIPP2 before the consultation at the end of RT. |
| Ito et al. 2011 [28] | Pre post | UP: April 1 - September 30, 2006. PP: April 1 | Single | Outpatient treatment center of the NCCH- | Japan | To examine the usefulness (rate of referral) of a screening program modified for outpatients | All consecutive cancer patients who began chemotherapy at the outpatient treatment | UP – 478. PP – 520. | UP 61.4 (10.8 SD), | UP 54.0%, PP | Lung 20.0%, Colon/rectum 18.2%, Breast 13.8%, Hematopoietic and | Chemotherapy.<br><br>Patients beginning chemotherapy at the outpatient |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | - September 30, 2007. | | E (Kashiwanoha, Kashiwa, Chiba). | | with cancer who are undergoing chemotherapy. | center of NCCH-E in Japan. | | PP 62.8 (10.9 SD). | 56.7%. | lymphatic tissue 12.8%, Stomach 7.9%, Pancreas 10.2%, Esophagus 5.5%, Liver, bile duct, gall bladder 4.6%, Head and Neck 2.8%, Other 4.0%.<br><br>Reported for PP only: Stage I 2.5%, Stage II 9.6%, Stage III 20.8%, Stage IV or recurrent 67.1%. | treatment center of the NCCH-E. |
| Zemlin et al. 2011[32] | Propsective consecutive study | NR. | Single | Clinic for Gynaecology of the University of Marburg Hospital (Marburg). | Germany | To examine whether a screening and computer-based psycho-oncological clinical pathway can improve the diagnosis of breast cancer patients requiring psycho-oncological support according to current guidelines. | Breast cancer patients who were in stationary treatment. | Phase 1 - 236, Phase II – 384, Phase III - 247. | 59.5 (12.2 SD). | 0.6% | Breast 100%.<br><br>Stage 0 (Ductal carcinoma in situ) 11.6%, Stage I 43.7%, Stage II 25.5%, Stage III 7.8%, Stage IV 11.2%. | Screening occurred on day of admission.<br><br>Stage of treatment NR. |
| Bauwens et al. 2014 [33] | Pre post | UP: May 2010. DB period June 2010. | Single | Oncology Centre of the University Hospital (UZ Brussel). | Belgium | To evaluate the impact of systematic screening with the DB on detection rates of patients with elevated distress and on rates of psychosocial referral compared to usual practice. | i) Ambulatory patients; ii) 18 years and older; iii) diagnosed with cancer; iv) sufficiently fluent in the languages of the study (Dutch or French); and iv) not affected by a cognitive disorder. | UP – 278, DB period – 304. | 58.92 (13.03 SD). | 32.0% | Breast 43.9%, Lung 10%, Colon 8.6%, Prostate 3.4%, Gynaecological 7.7%, Skin 9.5%, Brain 7.4%, Other 9.5%<br><br>Local disease 33%, Locoregional disease 38.6%, Advanced disease 28.4% | No treatment 24.3%, surgery 3.1%, RT 1.7%, chemotherapy 43.3%, medication 18.9%, RT + chemotherapy 2.1%, chemotherapy + medication 5.8%, RT + medication 0.7%<br><br>Diagnosis 2.1%, active treatment curative intent 22.7%, active treatment palliative intent 53.0%, cured 9.8%, remission (partial/complete) 3.3%, palliative care 0.3%, wait and see 5.0%, recent recurrence 3.8%. |

NR, not reported; DT, Distress Thermometer; UP, usual care period; PP, program period; DB, Distress Barometer; NCCH-E, National Cancer Center Hospital East; DT, Distress Thermometer, SIPP; Screening Inventory Psychosocial Problems; RT, Radiotherapy.

**Table 2. Definition of EPOC subcategories**

| EPOC subcategory | Definition |
|---|---|
| Educational materials | Distribution to individuals, or groups, of educational materials to support clinical care, i.e. any intervention in which knowledge is distributed. For example, this may be facilitated by the internet, learning critical appraisal skills; skills for electronic retrieval of information, diagnostic formulation; question formulation. |
| Educational meetings | Courses, workshops, conferences or other educational meetings. |
| Educational outreach visits or academic detailing | Personal visits by a trained person to health workers in their own settings, to provide information with the aim of changing practice. |
| Reminders | Manual or computerised interventions that prompt health workers to perform an action during a consultation with a patient, for example computer decision support systems. |
| Organisational culture | Strategies to change organisational culture. |
| Continuous quality improvement | An iterative process to review and improve care that includes involvement of healthcare teams, analysis of a process or system, a structured process improvement method or problem solving approach, and use of data analysis to assess changes. |

## Table 3. Intervention description

| Study | Healthcare providers | Distress screening tool | Referral criteria | Training | Intervention | Control/Comparison | Implementation Strategies |
|---|---|---|---|---|---|---|---|
| Thewes et al. 2009 [34] | Nurses | The DT - a single item screening measure that identifies level and causes of distress.<br><br>Respondents are asked to indicate their level of distress in the past week on an 11-point scale ranging from 0 ('None') to 10 ('Extreme'). | Screening cohort - for individuals who scored above the cut-off score (≥5), nursing staff were encouraged to assess problems and concerns and explore the patient's interest in receiving referral to psychosocial staff using the skills and strategies discussed in the initial training session. | Nursing and psychosocial staff participated in a 2 hour training session covering the screening procedure and suggestions for how to discuss the results of screening with patients who scored above cut-off. | Distress screening was completed immediately before an initial oncologist rural clinic appointment or chemotherapy education session. | All participants completed the SPHERE-Short at baseline; a 12-item questionnaire measuring common psychological and somatic distress developed and validated in Australia. The SPHERE- Short has 2 subscales: PSYCH-6 and somatic symptoms. A score of ≥2 on the PSYCH-6 subscale indicates a likely case of psychological disorder. | Educational materials, educational meetings. |
| Braeken et al. 2009 [29], 2013 [30] & 2013 [31] | Radiation oncologists | The SIPP - a short, valid and reliable 24-item self- reported questionnaire that systematically identifies psychosocial problems in Dutch cancer patients. Items are rated on a 3-point scale of 0 (no) to 2 (yes). Higher scores indicate poorer functioning. | Intervention: Potential referral to a psychosocial caregiver was based on the scores of the SIPP in combination with the radiation oncologist's judgement.<br><br>Control: According to the radiation oncologist's judgement about the presence or absence of psychosocial problems in patients. | Before the start of the study, the radiation oncologists in the experimental condition were trained in using and interpreting the SIPP during a 1 hour training session.<br><br>Training was given by the researcher and two social workers with experience in using and discussing the SIPP. | Patients received the SIPP just before the first and last consultation with the radiation oncologist. Psychosocial problems were discussed with the patient during the consultation and referral to a psychosocial caregiver occurred only with the permission of the patient.<br><br>The radiation oncologists were stratified according to general percentages of incoming patients they referred in 2006–2007 and then randomised to experimental or control condition. | Care as usual - no recent guidelines for the systematic assessment of psychosocial problems in cancer patients existed at the Institute Verbeeten. The radiation oncologist was able to refer patients to psychosocial caregivers (social workers) at the Institute Verbeeten based on their clinical judgement. | Educational materials, educational meetings, educational outreach visits. |
| Ito et al. 2011 [28] | Pharmacists | The DIT - a 2 item, self-administered rating scale.<br><br>Each 'distress' and 'impact' question is scored using an 11-point Likert scale, with scores ranging from 0 to 10 and a high score indicating an unfavourable status. | PP - if a patient scored equal to or more than each cut-off point (≥ 4 for distress and ≥ 3 for impact) the screening result was regarded as positive. | Before implementing the screening program, all the pharmacists attended a 2 hour lecture given by a trained psychiatrist regarding the epidemiology, impact, risk factors, under-recognition, and appropriate management of psychiatric disorders in cancer patients. Additionally, the pharmacists underwent role-play training to learn | Pharmacists providing instructions to patients beginning chemotherapy at their first and second visit also provided information regarding the Psychiatric Service using a brief pamphlet and invited the patients to complete the DIT. The pharmacist then completed the screening program sheet, which is a record of the patient's DIT scores.<br><br>The pharmacist recommended a consultation with the Psychiatric Service | UP was not described in detail. | Educational materials, educational meetings, educational outreach visits, reminders. |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | how to implement the DIT and to give recommendations for psychiatric referral. | to all the patients with a positive screening result and recorded the screening results on the medical chart. | | |
| Zemlin et al. 2011 [32] | BCN's and doctors | The HADS - scores of more than 13 indicate clinically suspected psychological distress. | Phase I – BCN's and doctors asked the patient about their interest in a psycho-oncological consultation where they felt necessary.<br><br>Phase II – BCN's asked all patients about their interest in a psycho-oncological consultation on day of admission.<br><br>Phase III – patients were referred to a psycho-oncological interview if i) they scored > 13 on the HADS; ii) the doctor had a clinical impression that the patient required referral; or iii) the patient desired referral. | Certified training courses for clinicians, gynaecologists and psychotherapists as well as other professional groups of the inpatient and outpatient network were carried out. | In Phase III, all patients completed the HADS questionnaire. The BCN evaluated the HADS and informed the patients about the possibility of a psycho-oncologic initial interview. The BCN passed the evaluated HADS sheet to the physician. For those patients with psycho-oncological need (threshold HADS score and/or clinically suspected treatment oriented psychological distress) the doctors recommended a psycho-oncological interview. Each patient with a desire for psycho-oncological care was logged and offered initial interview (regardless of HADS score). | In Phase I, BCN's and doctors asked the patient about their interest in a psycho-oncological consultation where they felt necessary. In addition, all patients received information on psychosocial support options. | Organizational culture, continuous quality improvement, educational materials, educational meetings, reminders. |
| Bauwens et al. 2014 [33] | Seven oncologists | The DB - comprises three parts:<br><br>1. The DT (described above). The VAS was slightly adapted by using a background colour effect with anchors labelled 'no distress' through 'moderate distress' and 'extreme distress'.<br><br>2. The CCS, which consists of 10 items that are rated on a coloured 5-point scale. Patients are required to rate how much each of a list of sources of distress has been troubling them lately.<br><br>3. Additional Wish-Needs Questions: 4 additional questions regarding complaints and needs for further medical information and/or support. | UP condition - oncologists used their own VAS assessment of distress to decide on an eventual referral. Whereas in the DB condition, the cut-off point for the DB (Distress Thermometer ≥4 and elevated CCS was used by the oncologists for this purpose. | In a collective 1 hour session held shortly before the DB condition, oncologists were instructed in using the DB and were given a written explanation on how to interpret DB results. | Two week period<br><br>DB condition - The DB was administered before the consultation with the oncologist.<br><br>Also in the DB condition, oncologists had a form with three other yes/no questions: (2) if they considered referral necessary, (3) if they actually gave an advice for referral and (4) if referral was accepted by patients. | 2 week period<br><br>UP condition - The DB was administered after the consultation with the oncologist.<br><br>Also in the UP condition, oncologists had a form with four other questions: (1) their rating of patients' distress on a VAS (0–10), (2) if they considered referral necessary, (3) if they actually gave advice for referral and (4) if referral was accepted by patients. | Educational materials, educational meetings. |

BCN, breast care nurse; DT, Distress Thermometer; DIT, Distress and Impact Thermometer; HADS, Hospital Anxiety and Depression Scale; DB, Distress Barometer; VAS, Visual Analogue Scale; CCS, Coloured Complaint Scale; PP, program period; UP, usual care period; SIPP; Screening Inventory Psychosocial Problems; SHPERE-Short, Somatic and Psychological Health Report Short form; PSYCH-6, psychological symptoms.

## Table 4. Primary outcomes

| Study | Distress screening | | Referral | |
|---|---|---|---|---|
| | Measure; data collection method | Results | Measure; data collection method | Results |
| Thewes et al. 2009 [34] | Proportion of patients screened.<br><br>NR. | Pre-screening phase – proportion of patients screened (using any distress screening tool) was not reported.<br><br>Screening phase – all patients were screened using the DT. | Proportion of patients referred in the pre-screening phase compared to the screening phase.<br><br>Review of referral records and databases. | Pre-screening phase - Of the 8 PSYCH-6 cases in the pre-screening phase, 6 were referred to a CCC and 5 to a social worker/psychologist.<br><br>Screening phase – 10/19 (53%) patients that met the DT cutoff were referred to a social worker or psychologist (11 of 14 PSYCH-6 cases were referred to the CCC and 8 to a social worker/psychologist). |
| Braeken et al. 2009 [29], 2013 [30] & 2013 [31] | Proportion of patients screened.<br><br>NR. | Control group – proportion of patients screened (using any distress screening tool) was not reported.<br><br>Intervention group – 263/268 (98%) were screened using the SIPP before the first consultation. 250/268 (96%) were screened using the SIPP before end of radiotherapy consultation. | The number of referrals of patients with psychosocial problems to psychosocial workers at the Institute Verbeeten and/or to external health care providers (e.g. psychologists, psychiatrists). Three dichotomous outcome variables (yes/no) during the first 3 months, the last 9 months, and the total study period.<br><br>Measured at 3 and 12 months after baseline assessment with a self-developed questionnaire by the patient and from registration records of the psychosocial caregivers at the Institute Verbeeten. | First 3 months - Control group 29/300 (9.7%) vs intervention group 34/268 (12.7%) patients referred (NS).<br><br>Last 9 months – Control group 24/300 (8%) vs intervention group 19/268 (7.1%) patients referred (NS).<br><br>Group differences in these outcomes were analysed using Generalized Estimating Equations with patients at level 1 and radiation oncologists at level 2. All models were adjusted for baseline differences with respect to gender and cancer diagnosis. Analyses were taken on an intention-to-treat principle.<br><br>Numbers of referrals did not differ significantly between the intervention and control group at 3 months (β =1.41(SE±.81), 9 months (β =-1.41(SE±1.21) or overall months (β =-.67(SE±.78). |
| Ito et al. 2011 [28] | Proportion of patients screened.<br><br>NR. | UP – proportion of patients screened (using any distress screening tool) was not reported.<br><br>PP – 441/520 (84.8%). | Proportion of patients referred to the Psychiatric Service and treated for MDD or AD among all the outpatients who had begun a new chemotherapy regimen within 3 months of their visit to the outpatient clinic.<br><br>Data extracted from patients' medical charts and the computerized database of the electronic medical record at NCCH-E. | Retrospective cohort analysis (Chi-squared test comparing patients treated during the pp with historical control data gathered during the UP).<br><br>UP – 5/478 (1.0%) vs PP – 15/520 (2.7%) patients referred to the Psychiatric Service with subsequent confirmed and treated for MDD or ADs ($p$ = .46). |
| Zemlin et al. 2011 [32] | Proportion of patients screened.<br><br>NR. | Proportion of patients screened in Phase I or II screened (using any distress screening tool) was not reported.<br><br>All patients in Phase III were screened using the HADS. | Proportion of patients offered referral for psycho-oncological interview.<br><br>Medical records. | Univariate data analysis.<br><br>Cochran-Armitage test.<br><br>Phase I – 194/236 (82.2%) vs Phase II 344/384 (89.6%) vs Phase III 236/247 (95.5%) were informed/offered the psycho-oncological interview. There was a significant positive trend for the number of |

| | | | | |
|---|---|---|---|---|
| | | | | patients informed about the psycho-oncological care available (t = 22.40, df = 2, $p$ <0.001). |
| Bauwens et al. 2014 [33] | Proportion of patients screened.<br><br>NR. | UP condition – all patients were screened with the DB after consult with oncologist (therefore not used as part of the referral decision).<br><br>DB condition – all patients were screened with the DB prior to consult with the oncologist. | Necessary referrals (UP condition: referrals necessary as per oncologists' VAS ratings, DB condition: referrals necessary for all patients with distress according to the DB).<br><br>Self-assessment. | UP condition – 13.8% of patients with elevated distress (or 5.4% of all patients), DB condition - 100% of patients with distress (or 41.6% of all patients). |
| | | | Referrals made (UP condition: proportion of patients for whom referral was considered necessary by the oncologists and were actually referred to psychosocial care, DB condition: proportion of patients with elevated distress that were referred).<br><br>Self-assessment. | UP condition – 6/15 patients, DB condition - 85/123 patients. |

NR, not reported; DT, Distress Thermometer; UP, usual care period; SIPP; Screening Inventory Psychosocial Problems; DB, Distress Barometer; MDD, Major Depressive Disorder; AD, Adjustment Disorder; NCCH-E, National Cancer Center Hospital East; VAS, visual analogue scale; CCC, cancer care coordinator; NS, not significant.

## Table 5. Secondary outcomes

| Study | Measure; data collection method | Results |
|---|---|---|
| Braeken et al. 2009 [29], 2013 [30] & 2013 [31] | Extent of psychological symptoms at 3 months and 12 months after baseline.<br><br>Measured with the HADS and the GHQ-12 (assesses with 12 items whether the patient considers him- or herself better, the same, worse or much worse over the previous four weeks than he/she "usually" is. Total scores range from 0 to 12). Patients complete these self- reported questionnaires at baseline and at 3 and 12 months after the baseline period. | Mixed effects' modelling.<br><br>No significant intervention effects were observed for patients' extent of psychological distress. (3 months after baseline mean psychological distress score control group 2.85 vs intervention group 2.74, $p = 0.19$; 12 months after baseline mean psychological distress score control group 2.14 vs intervention group 1.96, $p = 0.12$). |
| | Group differences in the proportion of dichotomous distress outcome (no or at least moderate distress) at 3 months and 12 months after baseline.<br><br>Measured with HADS and GHQ-12. | Generalised estimating equations.<br><br>No significant intervention effects were observed for proportion of patients with distress (3 months after baseline control group 39% vs experimental group 38.4%, $p = .036$; 12 months after baseline control group 24.7% vs intervention group 24.3%, $p = 0.39$). |

HADS, Hospital Anxiety and Depression Scale; GHQ-12, Goldberg's General Health Questionnaire-12 item version.

**Table 6. Ratings of methodological quality: strong (S), moderate (M) and weak (W)**

| **Study** | *Selection bias* | *Study design* | *Confounders* | *Blinding* | *Data collection* | *Withdrawals* | *Global rating* |
|---|---|---|---|---|---|---|---|
| Thewes et al. 2009 [34] | Moderate | Moderate | Weak | Moderate | Weak | Moderate | Weak |
| Braeken et al. 2009 [29], 2013 [30] & 2013 [31]. | Moderate | Strong | Strong | Moderate | Weak | Strong | Moderate |
| Ito et al. 2011 [28] | Moderate | Moderate | Strong | Moderate | Weak | Moderate | Moderate |
| Zemlin et al. 2011 [32] | Moderate | Moderate | Weak | Moderate | Weak | Moderate | Weak |
| Bauwens et al. 2014 [33] | Moderate | Moderate | Weak | Weak | Weak | Weak | Weak |

## AUTHORS' CONTRIBUTIONS

KM and LW conceptualised the review with input from BB, AB, SAH, AKB, GC, CW, JB, DB, EF. KM and EF conducted screening, data extraction and methodological quality analysis. KM and LW drafted the manuscript. All authors contributed to subsequent drafts and have approved the final version of the manuscript.

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## COMPETING INTERESTS

The authors declare that they have no competing interests.

## DATA SHARING STATEMENT

No additional data available.

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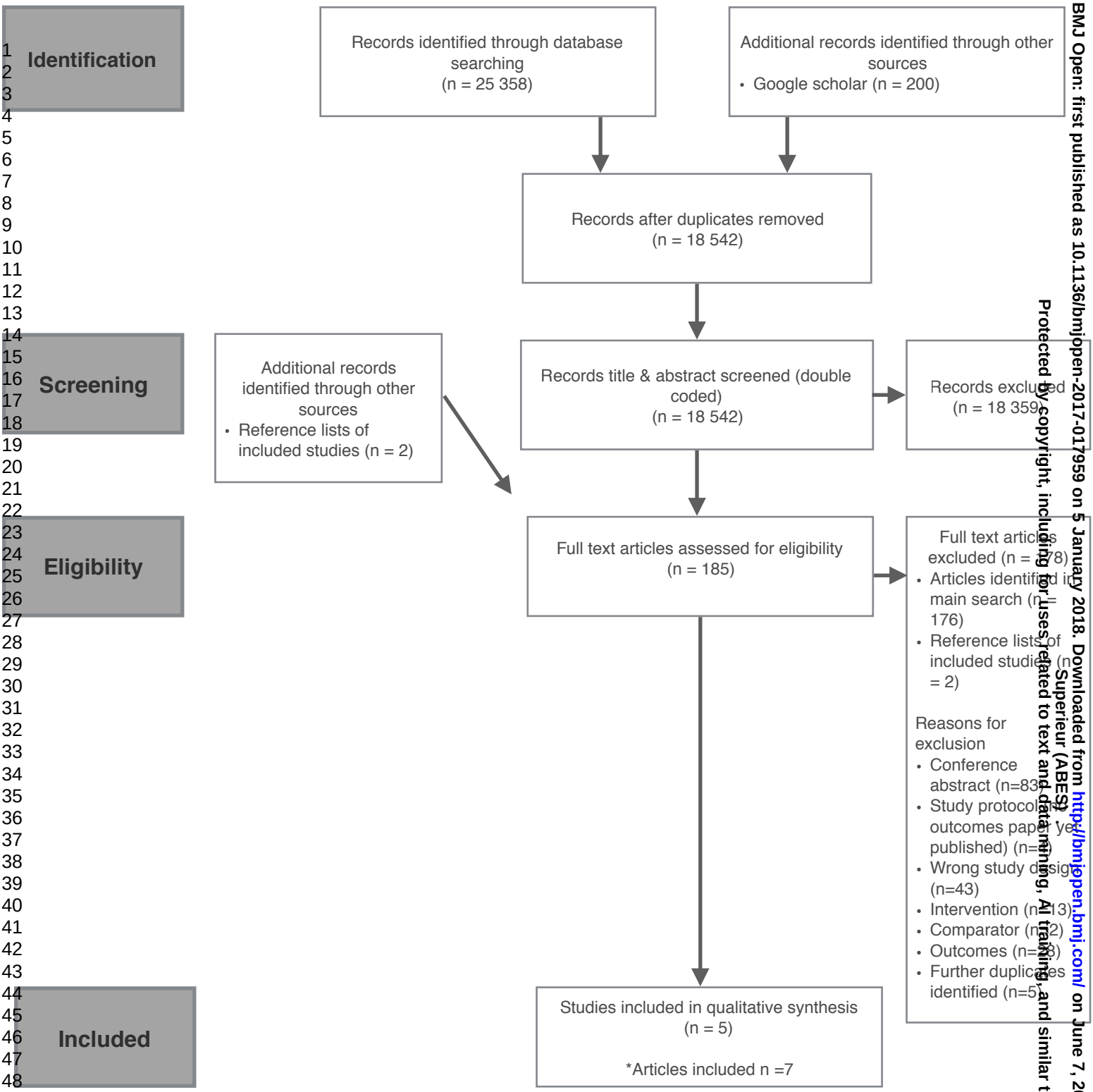

## MEDLINE SEARCH STRATEGY

1. cancer*.mp.
2. exp Neoplasms/
3. tumo?r*.mp.
4. malignan*.mp.
5. exp Adenocarcinoma/
6. exp Leukemia/
7. leukaemia*.mp.
8. metastat*.mp.
9. exp Carcinoma/
10. exp Medical Oncology/
11. exp Sarcoma/
12. choriocarcinoma*.mp.
13. lymphoma*.mp.
14. teratoma*.mp.
15. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14
16. screen*.mp.
17. measure*.mp.
18. assess*.mp.
19. Questionnaires/
20. Diagnosis/
21. instrument.mp.
22. validat*.mp.
23. 16 or 17 or 18 or 19 or 20 or 21 or 22
24. distress*.mp.

25. Stress, Psychological/

26. Anxiety/ or exp Anxiety Disorders/

27. Depression/

28. depress*.mp.

29. exp Depressive Disorder/

30. Dysthymic Disorder/

31. Adjustment Disorders/

32. "Quality of Life"/

33. psychosocial.mp.

34. Depressive Disorder, Major/

35. 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34

36. (psychosocial adj3 (care* or support* or service*)).mp.

37. Counseling/

38. (psychological adj3 (support* or care* or service* or therap* or intervention*)).mp.

39. exp Psychotherapy/

40. Mental Health Services/

41. (psycho oncology or psychooncology).mp.

42. Supportive care.mp.

43. Support service*.mp.

44. Social Support/

45. 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44

46. Intervention Studies/

47. implement*.mp.

48. disseminat*.mp.

49. adopt*.mp.

50. practice*.mp.

51. organi?ational change*.mp.

52. diffusion.mp.

53. system* change*.mp.

54. quality improvement*.mp.

55. transform*.mp.

56. translat*.mp.

57. transfer*.mp.

58. uptake*.mp.

59. sustainab*.mp.

60. institutionali*.mp.

61. routin*.mp.

62. maintenance.mp.

63. capacity.mp.

64. incorporat*.mp.

65. adher*.mp.

66. program*.mp.

67. integrat*.mp.

68. scal*.mp.

69. Randomized Controlled Trial/

70. Non randomized controlled trial*.mp.

71. Random Allocation/

72. Evaluation Studies/

73. Pilot study.mp. or Pilot Projects/

74. Evaluation Studies as Topic/

75. Cohort Studies/

76. Controlled Before-After Studies/

77. Historically Controlled Study/

78. Cross-Sectional Studies/

79. (intervention$ adj5 stud$).mp.

80. feasibility pilot*.mp.

81. sequential cohort.mp.

82. Interrupted-time-series stud*.mp.

83. case series.mp.

84. program*.mp.

85. intervention*.mp.

86. Random*.ab.

87. exp clinical trial/

88. trial.ab.

89. double blind.ab.

90. single blind.ab.

91. experiment*.mp.

92. (pretest or pre test).mp.

93. (posttest or post test).mp.

94. (pre post or prepost).mp.

95. Before after.mp.

96. (Quasi-randomised or quasi-randomized or quasi-randomized or quazi-randomised).mp.

97. stepped wedge.mp.

98. Comprehensive cohort.mp.

99. Natural experiment.mp.

100. (Quasi experiment or quazi experiments).mp.

101. (Randomised encouragement trial or randomized encouragement trial).mp.

102. (Staggered enrolment trial or staggered enrollment trial).mp.

103. (Nonrandomised or non randomised or nonrandomized or non randomized).mp.

104. Interrupted time series.mp.

105. (Time series and trial).mp.

106. Multiple baseline.mp.

107. 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 6 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or 90 or 91 or 92 or 93 or 94 or 95 or 96 or 97 or 98 or 99 or 100 or 101 or 102 or 103 or 104 or 105 or 106

108. 15 and 23 and 35 and 45 and 107

109. psychology.mp. or Psychology/

110. social work*.mp.

111. 45 or 109 or 110

112. 15 and 23 and 35 and 107 and 111

# PRISMA 2009 Checklist

| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| **TITLE** | | | |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | 1 |
| **ABSTRACT** | | | |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | 2-3 |
| **INTRODUCTION** | | | |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | 4-5 |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | 5-6 |
| **METHODS** | | | |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | 6 |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | 6-8 |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | 8-9 |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | 8, S1 |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | 9 |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | 9-10 |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | 9-10 |
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | 10-11 |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | 11 |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$) for each meta-analysis. | 11 |

# PRISMA 2009 Checklist



| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| Risk of bias across studies | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). | 10-11 |
| Additional analyses | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | N/A |
| **RESULTS** | | | |
| Study selection | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | 11- 12, F1 |
| Study characteristics | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | 12-13 |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | 13, 17-18 |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | 14-17 |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | N/A |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | 10-11, 17-18 |
| Additional analysis | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | N/A |
| **DISCUSSION** | | | |
| Summary of evidence | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | 18-19 |
| Limitations | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | 19-20 |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | 20 |
| **FUNDING** | | | |
| Funding | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | 31 |

*From:* Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

BMJ Open

# INTERVENTIONS TO IMPROVE SCREENING AND APPROPRIATE REFERRAL OF CANCER PATIENTS FOR PSYCHOSOCIAL DISTRESS: SYSTEMATIC REVIEW



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| | |

# INTERVENTIONS TO IMPROVE SCREENING AND APPROPRIATE REFERRAL OF CANCER PATIENTS FOR PSYCHOSOCIAL DISTRESS: SYSTEMATIC REVIEW

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**Keywords:** distress; screening; referral; cancer; review

**Word count:** 4464

## ABSTRACT

### Objectives

The primary aim of the review was to determine the effectiveness of strategies to improve clinician provision of psychosocial distress screening and referral of patients with cancer.

### Design

Systematic review.

### Data sources

Electronic databases (Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, PsycINFO and CINAHL) were searched until July 2016.

### Inclusion criteria

Population: adult cancer patients and clinical staff members. Intervention: Any strategy that aimed to improve the rate of routine screening and referral for detected distress of cancer patients. Comparison: no intervention controls, 'usual' practice, or alternative interventions. Outcome: (primary) any measure of provision of screening and/or referral for distress, (secondary) psychosocial distress, unintended adverse effects. Design: trials with or without a temporal comparison group including randomised and non-randomised trials, and uncontrolled pre-post studies.

### Data extraction and analysis

Two review authors independently extracted data. Heterogeneity across studies precluded quantitative assessment via meta-analysis and so a narrative synthesis of the results is presented.

**Results**

Five studies met the inclusion criteria. All studies were set in oncology clinics or departments and used multiple implementation strategies. Using GRADE, the overall rating of the certainty of the body of evidence reported in this review was assessed as very low. Three studies received a methodological quality rating of weak and two studies received a rating of moderate. Only one of the five studies reported a significant improvement in referrals.

**Conclusions**

The review identified five studies of predominantly poor quality examining the effectiveness of strategies to improve the routine implementation of distress screening and referral for cancer patients. Future research using robust research designs, including randomised assignment are needed to identify effective support strategies to maximise the potential for successful implementation of distress screening and referral for patients with cancer.

**Systematic review registration** PROSPERO registration number CRD4 2015017518.

**Strengths and limitations of this study**

- The first review to systematically synthesise evidence of the effectiveness of strategies to improve the rate of routine distress screening and referral for cancer patients

- The review performed a comprehensive search of the literature, included controlled trials of any design, and was inclusive of non-English literature
- Few studies met inclusion criteria, and heterogeneity of study design, primary and secondary outcomes precluded quantitative synthesis

## INTRODUCTION

### Rationale

Psychosocial distress can be defined as an unpleasant experience of an emotional or psychological nature including depression, anxiety and other/mood/adjustment disorders[1]. Estimates of the prevalence of psychosocial distress vary due to the type and stage of cancer, patient age, gender and race, as well as the definition of distress used. However overall, surveys have found between 20% to 47% of cancer patients experience significant levels of distress[1]. Psychosocial distress can arise in response to cancer related factors such as diagnosis and cancer progression, pain and adverse effects of treatment. Psychosocial distress in cancer patients may lead to non-adherence to treatment, poorer quality of life and may negatively impact survival, as well as increase treatment burden to the oncology team and health system[1-4]. Therefore, recognizing and treating distress in cancer populations is an important health priority.

Professional associations and clinical guidelines including the National Comprehensive Cancer Network *Clinical Practice Guidelines in Oncology: Distress Management*[1] recommend that those responsible for the care of cancer patients routinely screen for distress and, as appropriate, refer for further assessment and support. Clinical practice guideline recommendations are based on evidence that screening improves the timely management of distress[3,5], and systematic reviews and meta-analyses that have demonstrated psychosocial intervention reduces distress (such as depression and anxiety[6,7], particularly when participants are prescreened[8].

Despite clinical practice guideline recommendations, screening and referral of cancer patients for psychosocial distress is not routinely conducted by clinicians responsible for the clinical management of cancer [1,2,9]. Beginning in 2015, the American College of Surgeons

Commission on Cancer (CoC) has required cancer centers to implement programs for distress screening as a criterion for accreditation[10]. A recent cross-sectional survey of 20 National Comprehensive Network (NCCN) Institutions reported only 60% of services conducted outpatient distress screening, and even fewer services reported screening all patients (30%) as outlined in the NCCN standards[9]. Systematic reviews of trials of strategies to improve depression or anxiety screening in primary care note that complex organisational interventions that incorporate multiple strategies are most effective in improving provision of care[11-13]. Such strategies include clinician education, opinion leaders, patient specific reminders, enhanced role of nurses, academic detailing, integrating screening into routine clinical reviews and a greater degree of coordination between services (for example between primary and secondary care) [11-13]. However, we are not aware of any previous systematic review of interventions to improve clinician routine provision of distress screening and appropriate referral of cancer patients per-se.

**Objectives**

The primary aim of this review was to assess for cancer patients the impact of trials of strategies to improve clinician delivery of psychosocial distress care compared to usual care on rates of psychosocial distress screening and referral for further assessment and/or psychosocial support.

The secondary aims of the review were to:

i) Describe the effectiveness of such interventions on reducing psychosocial distress of patients with cancer;

ii) Describe any unintended adverse effects of such an intervention

**METHODS AND ANALYSIS**

The review will be reported consistent with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Statement[14]. The details of the methods have been reported elsewhere[15] and the protocol is registered with PROSPERO (registration number CRD42015017518).

**Eligibility criteria**

Study characteristics

*Types of studies*

Original studies including randomised controlled trials and non-randomised trials were included. Exclusion criteria were trials without parallel comparison or control groups. Due to the limited number of studies (explained further in the results section) we later included studies without parallel control groups including uncontrolled pre post studies. There were no restrictions based on length of follow-up, year of study publication or language. Studies could be published in peer review or grey literature.

*Participants*

Participants could include adult cancer patients and clinical staff members such as physicians and allied health professionals responsible for the care of cancer patients. Studies which examined screening for psychosocial distress and/or referral for carers of patients with cancer, or survivors of cancer, were excluded.

*Types of Interventions*

Interventions of strategies that aimed to improve the rate of screening procedures for psychosocial distress and/or rate of referral for appropriate psychosocial support in health care settings were included. There are a range of potential strategies that could improve the

likelihood of implementation of distress screening and referral in healthcare settings. For example, The Cochrane Effective Practice and Organisation of Care (EPOC) taxonomy is a framework for characterising educational, behavioural, financial, regulatory and organisational interventions within the topic of 'implementation strategies'[16] and includes 22 sub-categories. Examples of strategies within the taxonomy include educational materials, performance monitoring, local consensus processes and educational outreach visits. Included interventions could be singular or multicomponent. Studies using clinical judgement of psychosocial distress alone, without use of a formal screening tool were excluded. Referral for psychosocial support was defined as any written or verbal offer or direction of a patient for further review, consultation, assessment or treatment with any health professional, including the primary oncology team or health service, offering psychosocial support such as psycho-oncology services. Studies were included if they implemented either distress screening only or distress screening and appropriate referral. Studies where research staff conduct screening or referral were excluded.

*Comparisons*

Studies with no intervention controls, 'usual' practice periods or alternative intervention comparison groups were included.

*Outcomes*

Primary outcomes:

i) Any measure of the provision of screening for psychosocial distress (e.g. number or % of cancer patients screened).

ii) and/or any measure of the provision of referral for further assessment and/or psychosocial support (e.g. number or % of cancer patients referred) by a clinician responsible for the management of a cancer patient.

*Secondary outcomes:*

i) Any validated outcome measure of change in psychosocial distress levels in the patients (e.g. distress outcome assessments such as the Kessler Psychological Distress Scale).

ii) Any measure of adverse effects on patients, clinicians or health services; or barriers to performing screening such as displacement of other clinical priorities.

**Information sources**

Electronic databases

The following electronic databases were searched for potentially eligible studies published up until July 2016; the Cochrane Central Register of Controlled trials (CENTRAL) in the Cochrane Library, MEDLINE, EMBASE, PsycINFO and CINAHL. The Medline search strategy (supplementary file) was adapted for other databases and included filters used in other systematic reviews for population (cancer patients)[17], screening for distress[18] and referral[19] and psychosocial support[20].

Other sources

Studies were also obtained from the following sources:

- Reference lists of included studies

- Hand searching of 3 relevant journals in the field (published in the last 5 years); Journal of the National Comprehensive Cancer Network, Psychooncology and Supportive Care in Cancer
- Hand searching of conference abstracts published in the preceding 2 years from the International Psycho-Oncology Society and the Society of Behavioural Medicine
- A grey literature search using Google Scholar (published online in the last 5 years – the first 200 citations was examined)

**Study selection**

The titles and abstracts retrieved by electronic searches were exported to a reference management database (Endnote version X6) to remove duplicates. Two reviewers independently screened abstracts and titles using a standardised screening tool that was pilot tested with a sample of articles before use. The abstracts of papers that were in a language other than English were translated using Google Translate. If considered eligible or eligibility was unclear, professional translation of the full paper was undertaken.

The full texts of manuscripts were obtained for all potentially eligible trials for further examination and independently screened by two reviewers. For all manuscripts, the primary reason for exclusion was recorded and is documented in Figure 1. Discrepancies regarding study eligibility were resolved by discussion and consensus.

**Data extraction**

Two review authors (KM and EF) independently extracted data from the included trials using a pre-piloted data extraction form that was developed based on recommendations from the *Cochrane Handbook for Systematic Reviews of Interventions*[21]. Discrepancies regarding data extraction were resolved by discussion and consensus.

Data items

Data was sought for the following variables:

- Authors, year and journal
- Study eligibility, study design, health care provider type (e.g. nurses), country, health care setting (e.g. oncology clinic)
- Patient characteristics and demographics including cancer site, cancer stage, age, sex, cancer treatment type, treatment status (pre/undergoing/post)
- Characteristics of the intervention, including the duration, intervention strategies, screening instrument
- Trial primary and secondary outcomes, including sample size, the data collection method, validity of measures used, any measures of client uptake or use of psychosocial support services following referral, effect size, measures of change in distress
- Number of participants per experimental condition
- Information to allow assessment of risk of study bias

**Methodological quality assessment bias**

Two review authors (KM and EF) independently assessed the risk of bias of all included trials using the Effective Public Health Practice Project Quality Assessment Tool (EPHPP) for quantitative studies[22]. The use of the EPHPP tool was a post hoc change from protocol due to the study designs included in the review. This tool covers any quantitative study design and includes components of intervention integrity. Any discrepancies were resolved through discussion. The EPHPP assesses six methodological dimensions: selection bias, study design, confounders, blinding, data collection methods, and withdrawals and dropouts. These domains are rated on a three-point scale (strong, moderate, weak) according to pre-

defined criteria and procedures recommended for tool use, and then given an overall global rating. Those with no weak ratings were given an overall rating of strong, those with one weak rating were given an overall rating of moderate and those with two or more weak ratings across the six domains were given an overall weak rating. Two additional methodological dimensions provided by the tool are intervention integrity and analyses and these were also completed by the reviewers.

**Data analysis**

Summary measures

The small number of studies and differences in study design and primary and secondary outcomes reported in the included studies precluded the use of summary statistics to describe treatment effects. As such, the findings of included trials are described narratively.

Grading the strength of evidence

As recommended by the *Cochrane Handbook for Systematic Reviews of Interventions*[21], the overall quality of evidence on primary outcomes is presented using the GRADE (Grades of Recommendation, Assessment, Development and Evaluation) approach, which involves consideration of within-study risk of bias (methodological quality), directness of evidence, heterogeneity, precision of effect estimates and risk of publication bias. The overall quality of evidence was rated by two review authors (KM and EF) at four levels: high, moderate, low and very low.

**RESULTS**

A total of 18 542 citations were identified (after duplicates were removed) (Figure 1) for abstract and title screening. Just one study met the eligibility criteria (i.e. parallel control/comparison group). As such, and in an attempt to provide some evidence to guide researchers and practitioners regarding methods to improve patient distress screening and

referral of cancer patients, we relaxed the design criteria and post-hoc rescreened all 18 542 citations and included studies with controlled trial designs without parallel control groups including uncontrolled pre post studies. The full text of 185 manuscripts were sought for further assessment against the review inclusion criteria (Figure 1). Of these, 178 were considered ineligible following the trial screening process. Seven publications describing 5 trials were included in the review.

## Included studies

### *Types of studies*

A description of the trial characteristics of included studies is provided in Table 1. One study was conducted in Japan[23], one in the Netherlands[24-26], one in Germany[27], one in Belgium[28] and one in Australia[29]. Studies were published between 2009 and 2014. There was considerable heterogeneity in the participants, interventions and outcomes (clinical heterogeneity) of included studies.

### *Health providers*

All studies were set in oncology clinics or departments. In regards to the healthcare providers responsible for conducting the distress screening and/or referral, one study targeted nurses[29], one targeted radiation oncologists[24-26], one required pharmacists to perform the screening[23], one study involved both specialised breast care nurses and doctors[27] and one study utilised oncologists[28].

### *Interventions*

All trials used multiple implementation strategies. The EPOC subcategories used to classify the implementation strategies employed by included studies in the review are provided in Table 2. The interventions employed in the included studies, as well as the specific EPOC subcategories identified in each study are presented in Table 3. Using EPOC taxonomy

descriptors, all trials included educational materials and educational meetings, with two trials using only these strategies[28-29]. One trial utilised these strategies with the addition of educational outreach visits[24-26]. One study used a combination of educational materials, educational meetings, educational outreach visits and reminders[23]. One study tested an intervention consisting of organizational culture, continuous quality improvement, educational materials, educational meetings and reminders[27].

***Outcomes***

The primary and secondary outcomes are presented in Tables 4 and 5. Implementation of distress screening and/or referral was primarily assessed using reviews of patient medical records[23-27,29], however one study did not report the data collection method[28]. None of the studies reported which staff completed the medical record reviews. All trials reported the rates of referral for supports for those patients identified as distressed, however none of the studies examined the improvement in rates of distress screening. Change in distress levels were reported in one study[24-26]. No studies included a measure of potential adverse effects.

***Study design characteristics***

One of the included studies was a cluster randomised controlled trial[24-26], three were pre post studies[23,28,29] and one was a prospective consecutive study[27]. The cluster randomized controlled trial compared an intervention to a usual care control[24-26], three studies compared a screening program period to a usual care period[23,28,29], and one trial compared a screening program phase to a two-phase non-screening period[27].

**Methodological quality assessment**

Individual ratings for each study against the six methodological criteria from the EPHPP tool and the assigned global rating are reported in Table 6. Overall, three studies received a methodological quality rating of weak[27-29] and two studies received a rating of moderate[23-26].

For three of the four non-randomised studies[27-29], it was unclear whether confounders were adequately adjusted for and for the majority of studies, blinding of outcome assessors or study participants was not described. While most studies reported medical record reviews for the data collection method, no reference was made to their validity or reliability as an outcome measure, nor was a description of who conducted the audits provided, resulting in weak ratings for all studies. All studies were judged as using analyses as appropriate to study design.

**Effects of intervention on distress screening and/or referral**

None of the included trials reported on the effects of strategies to improve rates of distress screening provision. Only one of the five studies reported a significant improvement in rate of referrals[27]. Zemlin et al.[27] reported a significant positive trend for the proportion of patients that were informed/offered psycho-oncological interview ($t = 22.40$, $df = 2$, $p < 0.001$). The effects of interventions are presented according to the implementation strategies (classified using the EPOC taxonomy) employed by included studies.

***Educational materials and educational meetings***

Two studies examined the impact of educational materials and educational meetings only on distress screening or referral[28,29]. Thewes et al. [29] conducted a pre post trial testing the feasibility and acceptability of introducing a routine psychological screening program using the Distress Thermometer (DT) to improve screening rates and timeliness of referral to psychosocial services in three rural outpatient oncology clinics in Australia. Nursing and psychosocial staff participated in a two-hour training session (educational meetings and educational materials) covering the rationale for screening, the screening instrument and the study procedure. The impact of the intervention on distress screening was not explicitly reported (i.e. the control period rates of screening). Five of eight cases (according to

predefined PSYCH-6 cutoff criteria) and ten of 19 cases (according to DT cutoff) were referred to a social worker or psychologist in the control and intervention periods respectively. Due to the small number of cases, significance testing of differences between the pre-screening and screening phases was not conducted.

Bauwens et al.[28] conducted a pre post study to evaluate the impact of systematic screening with the Distress Barometer (DB) on detection rates of elevated distress and on rates of psychosocial referral at an oncology centre in Belgium. Oncologists were instructed in using the DB and given a written explanation (educational materials) on how to interpret the DB results in a collective 1 hour session (educational meetings). As this study did not aim to improve rates of distress screening, but focused on oncologist detection of distress and subsequent referral, all patients were screened using the DB in both conditions. Consequently, the rates of distress screening prior to the study, conducted by oncologists or other professional staff, compared to the study period are unknown. In the usual care period, using oncologists' judgement, referral was considered necessary for 5.4% of all patients. In the DB condition, referral was considered necessary for 41.6% of all patients. Of those patients for whom referral was considered necessary, 40% (6/15) in the usual care period and 69% (85/123) in the DB condition were actually referred to psychosocial care. The authors did not conduct an analysis to determine if there was a significant difference in these rates, however concluded that the implementation of screening using the DB led to increased numbers of referrals to psychosocial professionals.

***Educational materials, educational meetings and outreach visits***

Braeken et al.[24-26] conducted a cluster randomised controlled trial to study the effect of the implementation of the Screening Inventory Psychosocial Problems (SIPP) on the number and types of referrals of cancer patients to psychosocial caregivers in a radiation oncology department in the Netherlands. Radiation oncologists were randomised to a control or

intervention group. Those in the intervention group were trained by a researcher and two social workers with experience in using and interpreting the SIPP during a 1 hour training session (educational meetings, educational materials and educational outreach visits). The study found no significant intervention effects were observed for the total number of patients referred to psychosocial care providers at any of the assessment time points (first three months, the last nine months and the total study period).

***Educational materials, educational meetings, educational outreach visits and reminders***

Ito and colleagues[23] conducted a pre post trial to examine the usefulness of a screening program (using the distress and impact thermometer; DIT) modified for cancer patients undergoing radiotherapy at an outpatient cancer treatment center in Japan. Prior to the screening phase, all pharmacists attended a 2 hour lecture and (educational meetings) given by a trained psychiatrist (who also met with the pharmacists monthly; educational outreach visits) and underwent role play training to learn how to implement the DIT and referral for those patients scoring above the predetermined cutoff, (educational materials). When providing instructions to patients beginning chemotherapy and at the second visit, pharmacists invited patients to complete the DIT and a screening program sheet was completed by the pharmacists (reminders). The proportion of patients screened prior to the implementation of the screening program using the DIT or other measure was not assessed and 84.8% of patients were screened using the DIT in the intervention phase. The proportion of patients referred to the Psychiatric Service (and were subsequently confirmed to have major depression or adjustment disorder) during the screening program period compared to the usual care period was not significantly different between the two periods (2.7% during the program-period vs 1.0% during the usual care-period, $p = 0.46$).

***Educational materials, educational meetings, reminders, organizational culture, continuous quality improvement***

One study examined the effect of educational materials, educational meetings, reminders, organizational culture and continuous quality improvement on improvement in distress screening or referral. The trial by Zemlin et al.[27] was a prospective consecutive study that aimed to integrate psycho-oncological early detection and diagnostics as an integral part of everyday practice routines of acute inpatient care within the multidisciplinary diagnosis and care chain of breast cancer patients at a gynaecology clinic in Germany. Prior to the introduction of the program, certified training courses were held for clinicians, gynaecologists and psychotherapists as well as other professional groups (educational meetings, educational materials, organizational culture) and every three to four months, cross-departmental meetings between psychology and gynaecology departments were held (continuous quality improvement). The authors described the trial in three phases; in phase one, breast care nurses and doctors asked the patient about their interest in a psycho-oncological consultation where they felt necessary, and in phase two the nurses asked this of patients on the day of their admission. In phase three, the nurses conducted screening using the Hospital Anxiety and Depression Scale (HADS) with all patients and passed the HADS sheet to the physician (reminders). A predetermined cutoff indicated if referral was required. The proportion of patients screened with the HADS during phase three was 100%. The proportion of patients screened in phase one or two using the HADS or other measure was not assessed. The authors reported a significant positive trend for the proportion of patients offered referral for psycho-oncological care between phase one and three ($t = 22.40$, $df = 2$, $p < 0.001$).

**Secondary outcomes**

***Psychosocial distress***

Only one study compared patients' levels of distress at follow up using the distress screening measure implemented. Braeken et al.[24-26] found no significant intervention effects as

measured by the HADS for patients' psychological distress at three months or 12 months after baseline, nor dichotomous distress outcomes (no distress or at least moderate distress) at three months, or 12 months after baseline.

***Reported adverse consequences***

No study explicitly assessed whether the intervention had adverse effects.

**Quality of the evidence**

Using GRADE, the overall rating of the certainty of the body of evidence reported in this review was assessed as very low. The primary outcomes examined were downgraded one level to reflect high risk of bias and further downgraded two levels due to clinical heterogeneity and inconsistency in reporting either rates of distress screening or referral across both control and intervention periods. Since indirectness and imprecision also lowers the quality of the evidence, we downgraded two further levels on that basis. We found the quality of evidence to be of weak to moderate quality due to risk of bias using the EPHPP (Table 6), which identified a number of limitations, particularly among the pre post studies in regards to controlling for potential confounders.

**Discussion**

This review sought to assess the impact of trials of strategies to improve clinician provision of: screening of cancer patients for psychosocial distress; and referral for further assessment and/or psychosocial support where necessary. The review identified just one trial that met the prospectively registered inclusion criteria of having a parallel control trial design. When these criteria were relaxed to include those with a non-parallel control group a further four trials were included. None of the included trials reported on the effects of strategies to improve distress screening, and the intervention in just one trial was effective in improving the rates of referral for psycho-oncological support for distressed patients. None of the included studies

examined the improvement in rates of distress screening. This was likely due to the study designs (i.e. mostly pre-post) and consequently, conclusions regarding the effectiveness of the screening procedures introduced, and the implications for improvements in referral are limited. Such findings highlight the sparse evidence base for this important element of cancer patient care, and leave health services and cancer professionals with little clear guidance of strategies to improve provision of these elements of care to their patients.

Our findings are consistent with previous systematic reviews of trials aiming to improve depression or anxiety screening in primary care that have found that improvement in care provision is more likely when complex organisational change strategies are used, such as coordination between departments, enhanced role of nurses and performance feedback, in addition to clinician education[11-13]. The findings of the review highlight that the implementation of routine psychosocial screening and referral in cancer is complex and more rigorous research is needed. The trial by Zemlin et al.[27] was the only study included in the review to adopt a comprehensive implementation approach, and the only to report significant improvement in offer of referral of cancer patients for distress. Implementation strategies employed by other trials were primarily based on one off training and resource provision, suggesting that such support is insufficient. Comprehensive implementation strategies may be more likely to improve care given their greater capacity to address various barriers to screening and referral. Interestingly, Zemlin et al[27] was the only study to describe strategies employed to change the organisational culture of the healthcare setting, specifically, defining responsibilities and tasks between the specialist disciplines and the medical and nursing staff involved in the treatment team, training certificates, as well as regular meetings to facilitate communication. It may be that simpler interventions are less effective in implementing routine provision of this care because they fail to address the organisational culture of the setting. Strengthening team communication[23] and making clinicians more aware of their role

and responsibilities in distress screening and referral for cancer patients [25] may improve the rates of this care delivery. Further research identifying they key barriers to such care, and the best strategies to address them in cancer services is therefore warranted.

Surprisingly, none of the included studies examined the impact of strategies to improve the rate of clinician provision of psychosocial distress screening. Such a finding is of concern. Screening is a necessary pre-requisite to appropriate referral of cancer patients to psychological support. As screening for psychosocial distress in cancer populations is low across jurisdictions[30], improving this form of care should represent a priority. Previous studies have used novel technologies to prompt screening by clinicians[31-33]. Such approaches should be examined in robust trial designs in cancer settings that allow for their impact on improving the rate of routine clinician provision of distress screening to be determined.

A number of methodological aspects of the study warrant highlighting and should be considered when interpreting the study findings. As far as the authors are aware, this is the first systematic review to examine the impact of interventions of strategies to improve the rate of clinician provision of distress screening and appropriate referral in cancer patients. The review was prospectively registered, followed a peer reviewed protocol and included a comprehensive search strategy examining over 18000 citations. There was substantial clinical and methodological heterogeneity in the included studies. Classification of EPOC taxonomy implementation strategies was also difficult due to the lack of detail reported on intervention components in the studies. Furthermore, only one of the studies was a randomised controlled trial. Such characteristics of the included studies precluded quantitative synthesis of the effects of these strategies.

**Conclusions**

The findings of this review suggest that there is considerable scope to improve implementation of psychosocial distress screening and referral in cancer settings in order to

establish a strong evidence base for future successful interventions. Implementation of psychosocial distress screening and appropriate referral needs to be employed using a systematic method and assessed with appropriately controlled studies in order to determine the most effective approaches. Better reporting of outcomes and more detailed description of intervention components need to be prepared.

**Figure 1. PRISMA Flow Diagram**

## Table 1. Trial characteristics

| Study | Design | Study dates | Single-centre or multicentre | Setting | Country | Aim | Patient inclusion criteria | No. of patients | Mean age in years (SD) | Gender (male) | Tumour site/Tumour stage | Cancer treatment type/Stage of treatment |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Thewes et al. 2009[29] | Pre post | NR. | Multicentre - 3 rural outpatient oncology clinics | Outpatient oncology clinics. | Australia | (i) Prospectively investigate the feasibility and acceptability of introducing a routine psychological screening program for rural oncology clinics; (ii) explore the impact of screening on rates and timeliness of referral to psychosocial services; and (iii) provide pilot data on the acceptability and utility of the DT as a screening tool within the rural Australian setting. | (i) Newly diagnosed with malignant disease; (ii) 18 years of age or older; (iii) able to give informed consent; and (iv) able to read English proficiently. | Unscreened cohort – 40. Screened cohort – 43. | 60.0 (10.5 SD). | 54.0% | Colorectal 22.9%, Breast 30.1%, Lung 14.5%, Other 13.2%, Haematological 9.6%, Skin 6.0%, Unknown primary 3.6%.<br><br>Localised/locally advanced 71.1%, Advanced or metastatic 28.9%. | Surgery 75.9%, chemotherapies 66.3%, RT 53%, endocrine therapies 32.5%.<br><br>Newly diagnosed patients. |
| Braeken et al. 2009[24], 2013[25] & 2013[26] | Cluster randomised controlled trial | April 2008 – October 2010. | Single | Institute Verbeeten (BVI) - a radiation oncology department (Tilberg). | The Netherlands | To study the effect of the SIPP on the number and types of referrals of cancer patients with psychosocial problems to psychosocial caregivers. | i) Receiving RT; ii) most common cancer types such as lung, prostate, bladder, rectum, breast, cervix, endometrial, skin and Non-Hodgkin; iii) 18 years of age or older; and iv) no metastases. Exclusion criteria: i) receiving palliative treatment, ≤ 10 fractions of RT; ii) unable to read and speak Dutch; and iii) unable to complete questionnaires. | Control group – 300. Intervention group – 268. | Control group 62.4 (10.7 SD), intervention group 62.4 (10.8 SD). | Control group 47.0%, intervention group 31.7%. | Prostate/Bladder 24.1%, Lung 11.3%, Breast 50.0%, Cervix/Endometrial 1.6%, Rectum 9.0%, Non-Hodgkin Lymphoma 1.7%, Skin 2.3%. | 100% RT.<br><br>SIPP before the first consultation prior to RT and SIPP2 before the consultation at the end of RT. |
| Ito et al. 2011[23] | Pre post | UP: April 1 - September 30, 2006. PP: April 1 | Single | Outpatient treatment center of the NCCH- | Japan | To examine the usefulness (rate of referral) of a screening program modified for outpatients | All consecutive cancer patients who began chemotherapy at the outpatient treatment | UP – 478. PP – 520. | UP 61.4 (10.8 SD), | UP 54.0%, PP | Lung 20.0%, Colon/rectum 18.2%, Breast 13.8%, Hematopoietic and | Chemotherapy.<br><br>Patients beginning chemotherapy at the outpatient |

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| | | - September 30, 2007. | | E (Kashiwanoha, Kashiwa, Chiba). | | with cancer who are undergoing chemotherapy. | center of NCCH-E in Japan. | | PP 62.8 (10.9 SD). | 56.7%. | lymphatic tissue 12.8%, Stomach 7.9%, Pancreas 10.2%, Esophagus 5.5%, Liver, bile duct, gall bladder 4.6%, Head and Neck 2.8%, Other 4.0%.<br><br>Reported for PP only: Stage I 2.5%, Stage II 9.6%, Stage III 20.8%, Stage IV or recurrent 67.1%. | treatment center of the NCCH-E. |
| Zemlin et al. 2011[27] | Propsective consecutive study | NR. | Single | Clinic for Gynaecology of the University of Marburg Hospital (Marburg). | Germany | To examine whether a screening and computer-based psycho-oncological clinical pathway can improve the diagnosis of breast cancer patients requiring psycho-oncological support according to current guidelines. | Breast cancer patients who were in stationary treatment. | Phase 1 - 236, Phase II – 384, Phase III - 247. | 59.5 (12.2 SD). | 0.6% | Breast 100%.<br><br>Stage 0 (Ductal carcinoma in situ) 11.6%, Stage I 43.7%, Stage II 25.5%, Stage III 7.8%, Stage IV 11.2%. | Screening occurred on day of admission.<br><br>Stage of treatment NR. |
| Bauwens et al. 2014[28] | Pre post | UP: May 2010. DB period June 2010. | Single | Oncology Centre of the University Hospital (UZ Brussel). | Belgium | To evaluate the impact of systematic screening with the DB on detection rates of patients with elevated distress and on rates of psychosocial referral compared to usual practice. | i) Ambulatory patients; ii) 18 years and older; iii) diagnosed with cancer; iv) sufficiently fluent in the languages of the study (Dutch or French); and iv) not affected by a cognitive disorder. | UP – 278, DB period – 304. | 58.92 (13.03 SD). | 32.0% | Breast 43.9%, Lung 10%, Colon 8.6%, Prostate 3.4%, Gynaecological 7.7%, Skin 9.5%, Brain 7.4%, Other 9.5%<br><br>Local disease 33%, Locoregional disease 38.6%, Advanced disease 28.4% | No treatment 24.3%, surgery 3.1%, RT 1.7%, chemotherapy 43.3%, medication 18.9%, RT + chemotherapy 2.1%, chemotherapy + medication 5.8%, RT + medication 0.7%<br><br>Diagnosis 2.1%, active treatment curative intent 22.7%, active treatment palliative intent 53.0%, cured 9.8%, remission (partial/complete) 3.3%, palliative care 0.3%, wait and see 5.0%, recent recurrence 3.8%. |

NR, not reported; DT, Distress Thermometer; UP, usual care period; PP, program period; DB, Distress Barometer; NCCH-E, National Cancer Center Hospital East; DT, Distress Thermometer, SIPP; Screening Inventory Psychosocial Problems; RT, Radiotherapy.

**Table 2. Definition of EPOC subcategories**

| EPOC subcategory | Definition |
|---|---|
| Educational materials | Distribution to individuals, or groups, of educational materials to support clinical care, i.e. any intervention in which knowledge is distributed. For example, this may be facilitated by the internet, learning critical appraisal skills; skills for electronic retrieval of information, diagnostic formulation; question formulation. |
| Educational meetings | Courses, workshops, conferences or other educational meetings. |
| Educational outreach visits or academic detailing | Personal visits by a trained person to health workers in their own settings, to provide information with the aim of changing practice. |
| Reminders | Manual or computerised interventions that prompt health workers to perform an action during a consultation with a patient, for example computer decision support systems. |
| Organisational culture | Strategies to change organisational culture. |
| Continuous quality improvement | An iterative process to review and improve care that includes involvement of healthcare teams, analysis of a process or system, a structured process improvement method or problem solving approach, and use of data analysis to assess changes. |

## Table 3. Intervention description

| Study | Healthcare providers | Distress screening tool | Referral criteria | Training | Intervention | Control/Comparison | EPOC subcategories |
|---|---|---|---|---|---|---|---|
| Thewes et al. 2009[29] | Nurses | The DT - a single item screening measure that identifies level and causes of distress.<br><br>Respondents are asked to indicate their level of distress in the past week on an 11-point scale ranging from 0 ('None') to 10 ('Extreme'). | Screening cohort - for individuals who scored above the cut-off score (≥5), nursing staff were encouraged to assess problems and concerns and explore the patient's interest in receiving referral to psychosocial staff using the skills and strategies discussed in the initial training session. | Nursing and psychosocial staff participated in a 2 hour training session covering the screening procedure and suggestions for how to discuss the results of screening with patients who scored above cut-off. | Distress screening was completed immediately before an initial oncologist rural clinic appointment or chemotherapy education session. | All participants completed the SPHERE-Short at baseline; a 12-item questionnaire measuring common psychological and somatic distress developed and validated in Australia. The SPHERE- Short has 2 subscales: PSYCH-6 and somatic symptoms. A score of ≥2 on the PSYCH-6 subscale indicates a likely case of psychological disorder. | Educational materials, educational meetings. |
| Braeken et al. 2009[24], 2013[25] & 2013[26] | Radiation oncologists | The SIPP - a short, valid and reliable 24-item self- reported questionnaire that systematically identifies psychosocial problems in Dutch cancer patients. Items are rated on a 3-point scale of 0 (no) to 2 (yes). Higher scores indicate poorer functioning. | Intervention: Potential referral to a psychosocial caregiver was based on the scores of the SIPP in combination with the radiation oncologist's judgement.<br><br>Control: According to the radiation oncologist's judgement about the presence or absence of psychosocial problems in patients. | Before the start of the study, the radiation oncologists in the experimental condition were trained in using and interpreting the SIPP during a 1 hour training session.<br><br>Training was given by the researcher and two social workers with experience in using and discussing the SIPP. | Patients received the SIPP just before the first and last consultation with the radiation oncologist. Psychosocial problems were discussed with the patient during the consultation and referral to a psychosocial caregiver occurred only with the permission of the patient.<br><br>The radiation oncologists were stratified according to general percentages of incoming patients they referred in 2006–2007 and then randomised to experimental or control condition. | Care as usual - no recent guidelines for the systematic assessment of psychosocial problems in cancer patients existed at the Institute Verbeeten. The radiation oncologist was able to refer patients to psychosocial caregivers (social workers) at the Institute Verbeeten based on their clinical judgement. | Educational materials, educational meetings, educational outreach visits. |
| Ito et al. 2011[23] | Pharmacists | The DIT - a 2 item, self-administered rating scale.<br><br>Each 'distress' and 'impact' question is scored using an 11-point Likert scale, with scores ranging from 0 to 10 and a high score indicating an unfavourable status. | PP - if a patient scored equal to or more than each cut-off point (≥ 4 for distress and ≥ 3 for impact) the screening result was regarded as positive. | Before implementing the screening program, all the pharmacists attended a 2 hour lecture given by a trained psychiatrist regarding the epidemiology, impact, risk factors, under-recognition, and appropriate management of psychiatric disorders in cancer patients. Additionally, the pharmacists underwent role-play training to learn | Pharmacists providing instructions to patients beginning chemotherapy at their first and second visit also provided information regarding the Psychiatric Service using a brief pamphlet and invited the patients to complete the DIT. The pharmacist then completed the screening program sheet, which is a record of the patient's DIT scores.<br><br>The pharmacist recommended a consultation with the Psychiatric Service | UP was not described in detail. | Educational materials, educational meetings, educational outreach visits, reminders. |

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| | | | | how to implement the DIT and to give recommendations for psychiatric referral. | to all the patients with a positive screening result and recorded the screening results on the medical chart. | | |
| Zemlin et al. 2011[27] | BCN's and doctors | The HADS - scores of more than 13 indicate clinically suspected psychological distress. | Phase I – BCN's and doctors asked the patient about their interest in a psycho-oncological consultation where they felt necessary.<br><br>Phase II – BCN's asked all patients about their interest in a psycho-oncological consultation on day of admission.<br><br>Phase III – patients were referred to a psycho-oncological interview if i) they scored > 13 on the HADS; ii) the doctor had a clinical impression that the patient required referral; or iii) the patient desired referral. | Certified training courses for clinicians, gynaecologists and psychotherapists as well as other professional groups of the inpatient and outpatient network were carried out. | In Phase III, all patients completed the HADS questionnaire. The BCN evaluated the HADS and informed the patients about the possibility of a psycho-oncologic initial interview. The BCN passed the evaluated HADS sheet to the physician. For those patients with psycho-oncological need (threshold HADS score and/or clinically suspected treatment oriented psychological distress) the doctors recommended a psycho-oncological interview. Each patient with a desire for psycho-oncological care was logged and offered initial interview (regardless of HADS score). | In Phase I, BCN's and doctors asked the patient about their interest in a psycho-oncological consultation where they felt necessary. In addition, all patients received information on psychosocial support options. | Organizational culture, continuous quality improvement, educational materials, educational meetings, reminders. |
| Bauwens et al. 2014[28] | Seven oncologists | The DB - comprises three parts:<br><br>1. The DT (described above). The VAS was slightly adapted by using a background colour effect with anchors labelled 'no distress' through 'moderate distress' and 'extreme distress'.<br><br>2. The CCS, which consists of 10 items that are rated on a coloured 5-point scale. Patients are required to rate how much each of a list of sources of distress has been troubling them lately.<br><br>3. Additional Wish-Needs Questions: 4 additional questions regarding complaints and needs for further medical information and/or support. | UP condition - oncologists used their own VAS assessment of distress to decide on an eventual referral. Whereas in the DB condition, the cut-off point for the DB (Distress Thermometer ≥4 and elevated CCS was used by the oncologists for this purpose. | In a collective 1 hour session held shortly before the DB condition, oncologists were instructed in using the DB and were given a written explanation on how to interpret DB results. | Two week period<br><br>DB condition - The DB was administered before the consultation with the oncologist.<br><br>Also in the DB condition, oncologists had a form with three other yes/no questions: (2) if they considered referral necessary, (3) if they actually gave an advice for referral and (4) if referral was accepted by patients. | 2 week period<br><br>UP condition - The DB was administered after the consultation with the oncologist.<br><br>Also in the UP condition, oncologists had a form with four other questions: (1) their rating of patients' distress on a VAS (0–10), (2) if they considered referral necessary, (3) if they actually gave advice for referral and (4) if referral was accepted by patients. | Educational materials, educational meetings. |

BCN, breast care nurse; DT, Distress Thermometer; DIT, Distress and Impact Thermometer; HADS, Hospital Anxiety and Depression Scale; DB, Distress Barometer; VAS, Visual Analogue Scale; CCS, Coloured Complaint Scale; PP, program period; UP, usual care period; SIPP; Screening Inventory Psychosocial Problems; SHPERE-Short, Somatic and Psychological Health Report Short form; PSYCH-6, psychological symptoms.

## Table 4. Primary outcomes

| Study | Distress screening | | Referral | |
|---|---|---|---|---|
| | Measure; data collection method | Results | Measure; data collection method | Results |
| Thewes et al. 2009[29] | Proportion of patients screened.<br><br>NR. | Pre-screening phase – proportion of patients screened (using any distress screening tool) was not reported.<br><br>Screening phase – all patients were screened using the DT. | Proportion of patients referred in the pre-screening phase compared to the screening phase.<br><br>Review of referral records and databases. | Pre-screening phase - Of the 8 PSYCH-6 cases in the pre-screening phase, 6 were referred to a CCC and 5 to a social worker/psychologist.<br><br>Screening phase – 10/19 (53%) patients that met the DT cutoff were referred to a social worker or psychologist (11 of 14 PSYCH-6 cases were referred to the CCC and 8 to a social worker/psychologist). |
| Braeken et al. 2009[24], 2013[25] & 2013[26] | Proportion of patients screened.<br><br>NR. | Control group – proportion of patients screened (using any distress screening tool) was not reported.<br><br>Intervention group – 263/268 (98%) were screened using the SIPP before the first consultation. 250/268 (96%) were screened using the SIPP before end of radiotherapy consultation. | The number of referrals of patients with psychosocial problems to psychosocial workers at the Institute Verbeeten and/or to external health care providers (e.g. psychologists, psychiatrists). Three dichotomous outcome variables (yes/no) during the first 3 months, the last 9 months, and the total study period.<br><br>Measured at 3 and 12 months after baseline assessment with a self-developed questionnaire by the patient and from registration records of the psychosocial caregivers at the Institute Verbeeten. | First 3 months - Control group 29/300 (9.7%) vs intervention group 34/268 (12.7%) patients referred (NS).<br><br>Last 9 months – Control group 24/300 (8%) vs intervention group 19/268 (7.1%) patients referred (NS).<br><br>Group differences in these outcomes were analysed using Generalized Estimating Equations with patients at level 1 and radiation oncologists at level 2. All models were adjusted for baseline differences with respect to gender and cancer diagnosis. Analyses were taken on an intention-to-treat principle.<br><br>Generalised Estimating Equations found that numbers of referrals did not differ significantly between the intervention and control group at 3 months (β =1.41(SE±.81), 9 months (β =-1.41(SE±1.21) or overall months (β =-.67(SE±.78). |
| Ito et al. 2011[23] | Proportion of patients screened.<br><br>NR. | UP – proportion of patients screened (using any distress screening tool) was not reported.<br><br>PP – 441/520 (84.8%). | Proportion of patients referred to the Psychiatric Service and treated for MDD or AD among all the outpatients who had begun a new chemotherapy regimen within 3 months of their visit to the outpatient clinic.<br><br>Data extracted from patients' medical charts and the computerized database of the electronic medical record at NCCH-E. | Retrospective cohort analysis (Chi-squared test comparing patients treated during the PP with historical control data gathered during the UP).<br><br>UP – 5/478 (1.0%) vs PP – 15/520 (2.7%) patients referred to the Psychiatric Service with subsequent confirmed and treated for MDD or ADs ($p$ = .46). |
| Zemlin et al. 2011[27] | Proportion of patients screened.<br><br>NR. | Proportion of patients screened in Phase I or II screened (using any distress screening tool) was not reported.<br><br>All patients in Phase III were screened using the HADS. | Proportion of patients offered referral for psycho-oncological interview.<br><br>Medical records. | Univariate data analysis.<br><br>Cochran-Armitage test.<br><br>Phase I – 194/236 (82.2%) vs Phase II 344/384 (89.6%) vs Phase III 236/247 (95.5%) were informed/offered the psycho-oncological |

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| | | | | interview. There was a significant positive trend for the proportion of patients informed about the psycho-oncological care available (t = 22.40, df = 2, $p$ <0.001). |
| Bauwens et al. 2014[28] | Proportion of patients screened.<br><br>NR. | UP condition – all patients were screened with the DB after consult with oncologist (therefore not used as part of the referral decision).<br><br>DB condition – all patients were screened with the DB prior to consult with the oncologist. | Necessary referrals (UP condition: referrals necessary as per oncologists' VAS ratings, DB condition: referrals necessary for all patients with distress according to the DB).<br><br>Self-assessment. | UP condition – 13.8% of patients with elevated distress (or 5.4% of all patients), DB condition - 100% of patients with distress (or 41.6% of all patients). |
| | | | Referrals made (UP condition: proportion of patients for whom referral was considered necessary by the oncologists and were actually referred to psychosocial care, DB condition: proportion of patients with elevated distress that were referred).<br><br>Self-assessment. | UP condition – 6/15 patients, DB condition - 85/123 patients. |

NR, not reported; DT, Distress Thermometer; UP, usual care period; SIPP; Screening Inventory Psychosocial Problems; PP, program period; DB, Distress Barometer; MDD, Major Depressive Disorder; AD, Adjustment Disorder; NCCH-E, National Cancer Center Hospital East; VAS, visual analogue scale; CCC, cancer care coordinator; NS, not significant.

## Table 5. Secondary outcomes

| Study | Measure; data collection method | Results |
|---|---|---|
| Braeken et al. 2009[24], 2013[25] & 2013[26] | Extent of psychological symptoms at 3 months and 12 months after baseline.<br><br>Measured with the HADS and the GHQ-12 (assesses with 12 items whether the patient considers him- or herself better, the same, worse or much worse over the previous four weeks than he/she "usually" is. Total scores range from 0 to 12). Patients complete these self- reported questionnaires at baseline and at 3 and 12 months after the baseline period. | Mixed effects' modelling.<br><br>No significant intervention effects were observed for patients' extent of psychological distress. (3 months after baseline mean psychological distress score control group 2.85 vs intervention group 2.74, $p = 0.19$; 12 months after baseline mean psychological distress score control group 2.14 vs intervention group 1.96, $p = 0.12$). |
| | Group differences in the proportion of dichotomous distress outcome (no or at least moderate distress) at 3 months and 12 months after baseline.<br><br>Measured with HADS and GHQ-12. | Generalised estimating equations.<br><br>No significant intervention effects were observed for proportion of patients with distress (3 months after baseline control group 39% vs experimental group 38.4%, $p = .036$; 12 months after baseline control group 24.7% vs intervention group 24.3%, $p = 0.39$). |

HADS, Hospital Anxiety and Depression Scale; GHQ-12, Goldberg's General Health Questionnaire-12 item version.

**Table 6. Ratings of methodological quality: strong (S), moderate (M) and weak (W)**

| **Study** | *Selection bias* | *Study design* | *Confounders* | *Blinding* | *Data collection* | *Withdrawals* | *Global rating* |
|---|---|---|---|---|---|---|---|
| Thewes et al. 2009[29] | Moderate | Moderate | Weak | Moderate | Weak | Moderate | Weak |
| Braeken et al. 2009[24], 2013[25] & 2013[26] | Moderate | Strong | Strong | Moderate | Weak | Strong | Moderate |
| Ito et al. 2011[23] | Moderate | Moderate | Strong | Moderate | Weak | Moderate | Moderate |
| Zemlin et al. 2011[27] | Moderate | Moderate | Weak | Moderate | Weak | Moderate | Weak |
| Bauwens et al. 2014[28] | Moderate | Moderate | Weak | Weak | Weak | Weak | Weak |

## AUTHORS' CONTRIBUTIONS

KM and LW conceptualised the review with input from BB, AB, SAH, AKB, GC, CW, JB, DB, EF. KM and EF conducted screening, data extraction and methodological quality analysis. KM and LW drafted the manuscript. All authors contributed to subsequent drafts and have approved the final version of the manuscript.

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## COMPETING INTERESTS

The authors declare that they have no competing interests.

## DATA SHARING STATEMENT

No additional data available.

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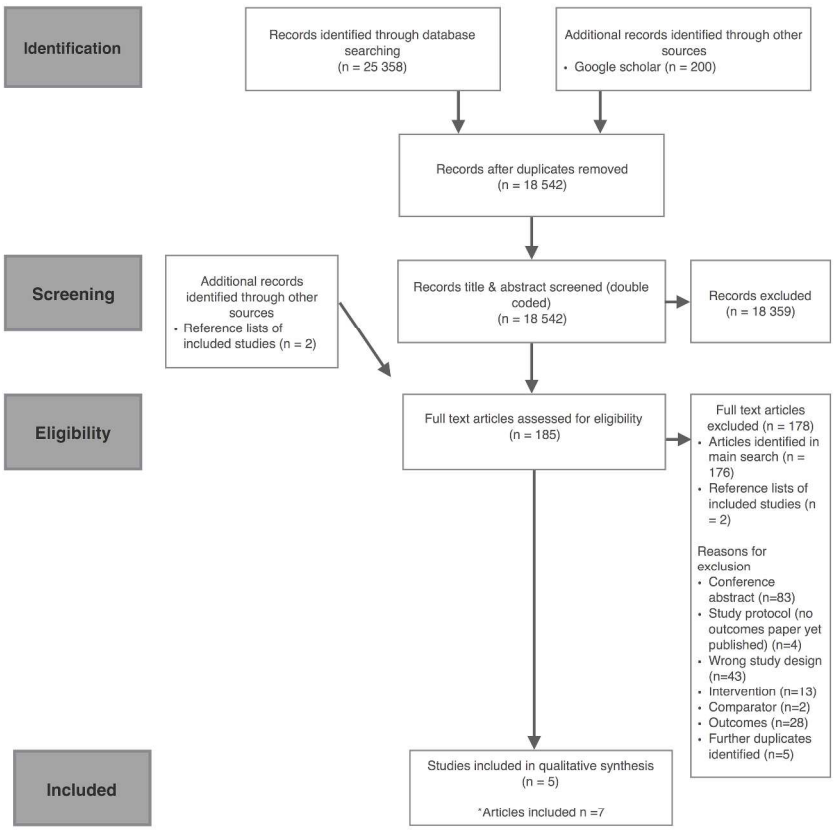


Figure 1. PRISMA Flow Diagram

296x420mm (300 x 300 DPI)

## MEDLINE SEARCH STRATEGY

1. cancer*.mp.
2. exp Neoplasms/
3. tumo?r*.mp.
4. malignan*.mp.
5. exp Adenocarcinoma/
6. exp Leukemia/
7. leukaemia*.mp.
8. metastat*.mp.
9. exp Carcinoma/
10. exp Medical Oncology/
11. exp Sarcoma/
12. choriocarcinoma*.mp.
13. lymphoma*.mp.
14. teratoma*.mp.
15. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14
16. screen*.mp.
17. measure*.mp.
18. assess*.mp.
19. Questionnaires/
20. Diagnosis/
21. instrument.mp.
22. validat*.mp.
23. 16 or 17 or 18 or 19 or 20 or 21 or 22
24. distress*.mp.

25. Stress, Psychological/

26. Anxiety/ or exp Anxiety Disorders/

27. Depression/

28. depress*.mp.

29. exp Depressive Disorder/

30. Dysthymic Disorder/

31. Adjustment Disorders/

32. "Quality of Life"/

33. psychosocial.mp.

34. Depressive Disorder, Major/

35. 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34

36. (psychosocial adj3 (care* or support* or service*)).mp.

37. Counseling/

38. (psychological adj3 (support* or care* or service* or therap* or intervention*)).mp.

39. exp Psychotherapy/

40. Mental Health Services/

41. (psycho oncology or psychooncology).mp.

42. Supportive care.mp.

43. Support service*.mp.

44. Social Support/

45. 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44

46. Intervention Studies/

47. implement*.mp.

48. disseminat*.mp.

49. adopt*.mp.

50. practice*.mp.

51. organi?ational change*.mp.

52. diffusion.mp.

53. system* change*.mp.

54. quality improvement*.mp.

55. transform*.mp.

56. translat*.mp.

57. transfer*.mp.

58. uptake*.mp.

59. sustainab*.mp.

60. institutionali*.mp.

61. routin*.mp.

62. maintenance.mp.

63. capacity.mp.

64. incorporat*.mp.

65. adher*.mp.

66. program*.mp.

67. integrat*.mp.

68. scal*.mp.

69. Randomized Controlled Trial/

70. Non randomized controlled trial*.mp.

71. Random Allocation/

72. Evaluation Studies/

73. Pilot study.mp. or Pilot Projects/

74. Evaluation Studies as Topic/

75. Cohort Studies/

76. Controlled Before-After Studies/

77. Historically Controlled Study/

78. Cross-Sectional Studies/

79. (intervention$ adj5 stud$).mp.

80. feasibility pilot*.mp.

81. sequential cohort.mp.

82. Interrupted-time-series stud*.mp.

83. case series.mp.

84. program*.mp.

85. intervention*.mp.

86. Random*.ab.

87. exp clinical trial/

88. trial.ab.

89. double blind.ab.

90. single blind.ab.

91. experiment*.mp.

92. (pretest or pre test).mp.

93. (posttest or post test).mp.

94. (pre post or prepost).mp.

95. Before after.mp.

96. (Quasi-randomised or quasi-randomized or quasi-randomized or quazi-randomised).mp.

97. stepped wedge.mp.

98. Comprehensive cohort.mp.

99. Natural experiment.mp.

100. (Quasi experiment or quazi experiments).mp.

101. (Randomised encouragement trial or randomized encouragement trial).mp.

102. (Staggered enrolment trial or staggered enrollment trial).mp.

103. (Nonrandomised or non randomised or nonrandomized or non randomized).mp.

104. Interrupted time series.mp.

105. (Time series and trial).mp.

106. Multiple baseline.mp.

107. 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 6 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or 90 or 91 or 92 or 93 or 94 or 95 or 96 or 97 or 98 or 99 or 100 or 101 or 102 or 103 or 104 or 105 or 106

108. 15 and 23 and 35 and 45 and 107

109. psychology.mp. or Psychology/

110. social work*.mp.

111. 45 or 109 or 110

112. 15 and 23 and 35 and 107 and 111

# PRISMA 2009 Checklist

| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| **TITLE** | | | |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | 1 |
| **ABSTRACT** | | | |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | 2-3 |
| **INTRODUCTION** | | | |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | 5-6 |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | 6 |
| **METHODS** | | | |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | 7 |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | 7-9 |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | 9-10 |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | 9 |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | 10 |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | 10-11 |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | 11 |
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | 11-12 |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | 12 |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$) for each meta-analysis. | 12-13 |

# PRISMA 2009 Checklist



| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| Risk of bias across studies | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). | 14-15 |
| Additional analyses | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | N/A |
| **RESULTS** | | | |
| Study selection | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | 12-13, F1 |
| Study characteristics | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | 13-14 Tables 1, 3, 4, 5 |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | Table 6 |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | 14-15 |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | 15-18 |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | 19 |
| Additional analysis | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | N/A |
| **DISCUSSION** | | | |
| Summary of evidence | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | 19-21 |
| Limitations | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | 19-21 |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | 21-22 |
| **FUNDING** | | | |
| Funding | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | 33 |

*From:* Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

BMJ Open

# INTERVENTIONS TO IMPROVE SCREENING AND APPROPRIATE REFERRAL OF CANCER PATIENTS FOR PSYCHOSOCIAL DISTRESS: SYSTEMATIC REVIEW



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| | |

# INTERVENTIONS TO IMPROVE SCREENING AND APPROPRIATE REFERRAL OF CANCER PATIENTS FOR PSYCHOSOCIAL DISTRESS: SYSTEMATIC REVIEW

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**Keywords:** distress; screening; referral; cancer; review

**Word count:** 4644

## ABSTRACT

### Objectives

The primary aim of the review was to determine the effectiveness of strategies to improve clinician provision of psychosocial distress screening and referral of patients with cancer.

### Design

Systematic review.

### Data sources

Electronic databases (Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, PsycINFO and CINAHL) were searched until July 2016.

### Inclusion criteria

Population: adult cancer patients and clinical staff members. Intervention: Any strategy that aimed to improve the rate of routine screening and referral for detected distress of cancer patients. Comparison: no intervention controls, 'usual' practice, or alternative interventions. Outcome: (primary) any measure of provision of screening and/or referral for distress, (secondary) psychosocial distress, unintended adverse effects. Design: trials with or without a temporal comparison group including randomised and non-randomised trials, and uncontrolled pre-post studies.

### Data extraction and analysis

Two review authors independently extracted data. Heterogeneity across studies precluded quantitative assessment via meta-analysis and so a narrative synthesis of the results is presented.

**Results**

Five studies met the inclusion criteria. All studies were set in oncology clinics or departments and used multiple implementation strategies. Using GRADE, the overall rating of the certainty of the body of evidence reported in this review was assessed as very low. Three studies received a methodological quality rating of weak and two studies received a rating of moderate. Only one of the five studies reported a significant improvement in referrals.

**Conclusions**

The review identified five studies of predominantly poor quality examining the effectiveness of strategies to improve the routine implementation of distress screening and referral for cancer patients. Future research using robust research designs, including randomised assignment are needed to identify effective support strategies to maximise the potential for successful implementation of distress screening and referral for patients with cancer.

**Systematic review registration** PROSPERO registration number CRD4 2015017518.

**Strengths and limitations of this study**

- The first review to systematically synthesise evidence of the effectiveness of strategies to improve the rate of routine distress screening and referral for cancer patients

- The review performed a comprehensive search of the literature, included controlled trials of any design, and was inclusive of non-English literature
- Few studies met inclusion criteria, and heterogeneity of study design, primary and secondary outcomes precluded quantitative synthesis

## INTRODUCTION

### Rationale

Psychosocial distress can be defined as an unpleasant experience of an emotional or psychological nature including depression, anxiety and other/mood/adjustment disorders[1]. Estimates of the prevalence of psychosocial distress vary due to the type and stage of cancer, patient age, gender and race, as well as the definition of distress used. Psychosocial distress can arise in response to cancer related factors such as diagnosis and cancer progression, pain and adverse effects of treatment. Psychosocial distress in cancer patients may lead to non-adherence to treatment, poorer quality of life and may negatively impact survival, as well as increase treatment burden to the oncology team and health system[1-4]. Therefore, recognizing and treating distress in cancer populations is an important health priority.

Professional associations and clinical guidelines including the National Comprehensive Cancer Network *Clinical Practice Guidelines in Oncology: Distress Management*[1] recommend that those responsible for the care of cancer patients routinely screen for distress and, as appropriate, refer for further assessment and support. Clinical practice guideline recommendations are based on evidence that screening improves the timely management of distress[3,5], and systematic reviews and meta-analyses that have demonstrated psychosocial intervention reduces distress (such as depression and anxiety[6,7], particularly when participants are prescreened[8].

The efficacy of distress screening for improving patient outcomes has been challenged in the literature. A recent systematic review failed to find evidence that distress screening improved distress outcomes among cancer patients[9]. Another systematic review that examined screening for distress in cancer settings found that those studies reporting a lack of benefit to distress screening in patients with cancer lacked appropriate follow-up care of distressed

patients, while trials that linked screening with mandatory referral or intervention showed improvement in patient outcomes [10]. Whilst screening itself may not be sufficient to improve patient outcomes, it is a necessary pre requisite to identify those patients who could benefit from evidence based treatment and guides clinical decision making[1]. Consequently, clinical guidelines recommend screening *and* referral protocols in cancer settings. It is clear that well-designed trials are needed to further evaluate the effectiveness of screening and referral on patient outcomes. However, in the absence of strong evidence from robust trials that suggest distress screening and referral should not be conducted, clinicians should be guided by clinical practice guidelines.

Despite clinical practice guideline recommendations, screening and referral of cancer patients for psychosocial distress is not routinely conducted by clinicians responsible for the clinical management of cancer [1,2,11]. Beginning in 2015, the American College of Surgeons Commission on Cancer (CoC) has required cancer centers to implement programs for distress screening as a criterion for accreditation[12]. A recent cross-sectional survey of 20 National Comprehensive Network (NCCN) Institutions reported only 60% of services conducted outpatient distress screening, and even fewer services reported screening all patients (30%) as outlined in the NCCN standards[11]. Systematic reviews of trials of strategies to improve depression or anxiety screening in primary care note that complex organisational interventions that incorporate multiple strategies are most effective in improving provision of care[13-15]. Such strategies include clinician education, opinion leaders, patient specific reminders, enhanced role of nurses, academic detailing, integrating screening into routine clinical reviews and a greater degree of coordination between services (for example between primary and secondary care) [13-15]. However, we are not aware of any previous systematic review of interventions to improve clinician routine provision of distress screening and

appropriate referral of cancer patients per-se. It is the discrepancy between these guideline recommendations and current practice that this review aims to address.

**Objectives**

The primary aim of this review was to assess for cancer patients the impact of trials of strategies to improve clinician delivery of psychosocial distress care compared to usual care on rates of psychosocial distress screening and referral for further assessment and/or psychosocial support.

The secondary aims of the review were to:

i) Describe the effectiveness of such interventions on reducing psychosocial distress of patients with cancer;

ii) Describe any unintended adverse effects of such an intervention

**METHODS AND ANALYSIS**

The review will be reported consistent with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Statement[16]. The details of the methods have been reported elsewhere[17] and the protocol is registered with PROSPERO (registration number CRD42015017518).

**Eligibility criteria**

Study characteristics

*Types of studies*

Original studies including randomised controlled trials and non-randomised trials were included. Exclusion criteria were trials without parallel comparison or control groups. Due to the limited number of studies (explained further in the results section) we later included

studies without parallel control groups including uncontrolled pre post studies. There were no restrictions based on length of follow-up, year of study publication or language. Studies could be published in peer review or grey literature.

*Participants*

Participants could include adult cancer patients and clinical staff members such as physicians and allied health professionals responsible for the care of cancer patients. Studies which examined screening for psychosocial distress and/or referral for carers of patients with cancer, or survivors of cancer, were excluded.

*Types of Interventions*

Interventions of strategies that aimed to improve the rate of screening procedures for psychosocial distress and/or rate of referral for appropriate psychosocial support in health care settings were included. There are a range of potential strategies that could improve the likelihood of implementation of distress screening and referral in healthcare settings. For example, The Cochrane Effective Practice and Organisation of Care (EPOC) taxonomy is a framework for characterising educational, behavioural, financial, regulatory and organisational interventions within the topic of 'implementation strategies'[18] and includes 22 sub-categories. Examples of strategies within the taxonomy include educational materials, performance monitoring, local consensus processes and educational outreach visits. Included interventions could be singular or multicomponent. Studies using clinical judgement of psychosocial distress alone, without use of a formal screening tool were excluded. Referral for psychosocial support was defined as any written or verbal offer or direction of a patient for further review, consultation, assessment or treatment with any health professional, including the primary oncology team or health service, offering psychosocial support such as psycho-oncology services. Studies were included if they implemented either distress

screening only or distress screening and appropriate referral. Studies where research staff conduct screening or referral were excluded.

*Comparisons*

Studies with no intervention controls, 'usual' practice periods or alternative intervention comparison groups were included.

*Outcomes*

Primary outcomes:

i) Any measure of the provision of screening for psychosocial distress (e.g. number or % of cancer patients screened).

ii) and/or any measure of the provision of referral for further assessment and/or psychosocial support (e.g. number or % of cancer patients referred) by a clinician responsible for the management of a cancer patient.

*Secondary outcomes:*

i) Any validated outcome measure of change in psychosocial distress levels in the patients (e.g. distress outcome assessments such as the Kessler Psychological Distress Scale).

ii) Any measure of adverse effects on patients, clinicians or health services; or barriers to performing screening such as displacement of other clinical priorities.

**Information sources**

Electronic databases

The following electronic databases were searched for potentially eligible studies published up until July 2016; the Cochrane Central Register of Controlled trials (CENTRAL) in the

Cochrane Library, MEDLINE, EMBASE, PsycINFO and CINAHL. The Medline search strategy (supplementary file) was adapted for other databases and included filters used in other systematic reviews for population (cancer patients)[19], screening for distress[20] and referral[21] and psychosocial support[22].

Other sources

Studies were also obtained from the following sources:

- Reference lists of included studies
- Hand searching of 3 relevant journals in the field (published in the last 5 years); Journal of the National Comprehensive Cancer Network, Psychooncology and Supportive Care in Cancer
- Hand searching of conference abstracts published in the preceding 2 years from the International Psycho-Oncology Society and the Society of Behavioural Medicine
- A grey literature search using Google Scholar (published online in the last 5 years – the first 200 citations was examined)

**Study selection**

The titles and abstracts retrieved by electronic searches were exported to a reference management database (Endnote version X6) to remove duplicates. Two reviewers independently screened abstracts and titles using a standardised screening tool that was pilot tested with a sample of articles before use. The abstracts of papers that were in a language other than English were translated using Google Translate. If considered eligible or eligibility was unclear, professional translation of the full paper was undertaken.

The full texts of manuscripts were obtained for all potentially eligible trials for further examination and independently screened by two reviewers. For all manuscripts, the primary

reason for exclusion was recorded and is documented in Figure 1. Discrepancies regarding study eligibility were resolved by discussion and consensus.

**Data extraction**

Two review authors (KM and EF) independently extracted data from the included trials using a pre-piloted data extraction form that was developed based on recommendations from the *Cochrane Handbook for Systematic Reviews of Interventions*[23]. Discrepancies regarding data extraction were resolved by discussion and consensus.

Data items

Data was sought for the following variables:

- Authors, year and journal
- Study eligibility, study design, health care provider type (e.g. nurses), country, health care setting (e.g. oncology clinic)
- Patient characteristics and demographics including cancer site, cancer stage, age, sex, cancer treatment type, treatment status (pre/undergoing/post)
- Characteristics of the intervention, including the duration, intervention strategies, screening instrument
- Trial primary and secondary outcomes, including sample size, the data collection method, validity of measures used, any measures of client uptake or use of psychosocial support services following referral, effect size, measures of change in distress
- Number of participants per experimental condition
- Information to allow assessment of risk of study bias

**Methodological quality assessment bias**

Two review authors (KM and EF) independently assessed the risk of bias of all included trials using the Effective Public Health Practice Project Quality Assessment Tool (EPHPP) for quantitative studies[24]. The use of the EPHPP tool was a post hoc change from protocol due to the study designs included in the review. This tool covers any quantitative study design and includes components of intervention integrity. Any discrepancies were resolved through discussion. The EPHPP assesses six methodological dimensions: selection bias, study design, confounders, blinding, data collection methods, and withdrawals and dropouts. These domains are rated on a three-point scale (strong, moderate, weak) according to pre-defined criteria and procedures recommended for tool use, and then given an overall global rating. Those with no weak ratings were given an overall rating of strong, those with one weak rating were given an overall rating of moderate and those with two or more weak ratings across the six domains were given an overall weak rating. Two additional methodological dimensions provided by the tool are intervention integrity and analyses and these were also completed by the reviewers.

**Data analysis**

Summary measures

The small number of studies and differences in study design and primary and secondary outcomes reported in the included studies precluded the use of summary statistics to describe treatment effects. As such, the findings of included trials are described narratively.

Grading the strength of evidence

As recommended by the *Cochrane Handbook for Systematic Reviews of Interventions*[23], the overall quality of evidence on primary outcomes is presented using the GRADE (Grades of Recommendation, Assessment, Development and Evaluation) approach, which involves consideration of within-study risk of bias (methodological quality), directness of evidence,

heterogeneity, precision of effect estimates and risk of publication bias. The overall quality of evidence was rated by two review authors (KM and EF) at four levels: high, moderate, low and very low.

## RESULTS

A total of 18 542 citations were identified (after duplicates were removed) (Figure 1) for abstract and title screening. Just one study met the eligibility criteria (i.e. parallel control/comparison group). As such, and in an attempt to provide some evidence to guide researchers and practitioners regarding methods to improve patient distress screening and referral of cancer patients, we relaxed the design criteria and post-hoc rescreened all 18 542 citations and included studies with controlled trial designs without parallel control groups including uncontrolled pre post studies. The full text of 185 manuscripts were sought for further assessment against the review inclusion criteria (Figure 1). Of these, 178 were considered ineligible following the trial screening process. Seven publications describing 5 trials were included in the review.

### Included studies

#### *Types of studies*

A description of the trial characteristics of included studies is provided in Table 1. One study was conducted in Japan[25], one in the Netherlands[26-28], one in Germany[29], one in Belgium[30] and one in Australia[31]. Studies were published between 2009 and 2014. There was considerable heterogeneity in the participants, interventions and outcomes (clinical heterogeneity) of included studies.

#### *Health providers*

All studies were set in oncology clinics or departments. In regards to the healthcare providers responsible for conducting the distress screening and/or referral, one study targeted nurses[31],

one targeted radiation oncologists[26-28], one required pharmacists to perform the screening[25], one study involved both specialised breast care nurses and doctors[29] and one study utilised oncologists[30].

***Interventions***

All trials used multiple implementation strategies. The EPOC subcategories used to classify the implementation strategies employed by included studies in the review are provided in Table 2. The interventions employed in the included studies, as well as the specific EPOC subcategories identified in each study are presented in Table 3. Using EPOC taxonomy descriptors, all trials included educational materials and educational meetings, with two trials using only these strategies[30-31]. One trial utilised these strategies with the addition of educational outreach visits[26-28]. One study used a combination of educational materials, educational meetings, educational outreach visits and reminders[25]. One study tested an intervention consisting of organizational culture, continuous quality improvement, educational materials, educational meetings and reminders[29].

***Outcomes***

The primary and secondary outcomes are presented in Tables 4 and 5. Implementation of distress screening and/or referral was primarily assessed using reviews of patient medical records[25-29,31], however one study did not report the data collection method[28]. None of the studies reported which staff completed the medical record reviews. All trials reported the rates of referral for supports for those patients identified as distressed, however none of the studies examined the improvement in rates of distress screening. Change in distress levels were reported in one study[26-28]. No studies included a measure of potential adverse effects.

***Study design characteristics***

One of the included studies was a cluster randomised controlled trial[26-28], three were pre post studies[25,30,31] and one was a prospective consecutive study[29]. The cluster randomized

controlled trial compared an intervention to a usual care control[26-28], three studies compared a screening program period to a usual care period[25,30,31], and one trial compared a screening program phase to a two-phase non-screening period[29].

**Methodological quality assessment**

Individual ratings for each study against the six methodological criteria from the EPHPP tool and the assigned global rating are reported in Table 6. Overall, three studies received a methodological quality rating of weak[29-31] and two studies received a rating of moderate[25-28]. For three of the four non-randomised studies[29-31], it was unclear whether confounders were adequately adjusted for and for the majority of studies, blinding of outcome assessors or study participants was not described. While most studies reported medical record reviews for the data collection method, no reference was made to their validity or reliability as an outcome measure, nor was a description of who conducted the audits provided, resulting in weak ratings for all studies. All studies were judged as using analyses as appropriate to study design.

**Effects of intervention on distress screening and/or referral**

None of the included trials reported on the effects of strategies to improve rates of distress screening provision. Only one of the five studies reported a significant improvement in rate of referrals[27]. Zemlin et al.[29] reported a significant positive trend for the proportion of patients that were informed/offered psycho-oncological interview ($t = 22.40$, $df = 2$, $p < 0.001$). The effects of interventions are presented according to the implementation strategies (classified using the EPOC taxonomy) employed by included studies.

***Educational materials and educational meetings***

Two studies examined the impact of educational materials and educational meetings only on distress screening or referral[30,31]. Thewes et al. [231]conducted a pre post trial testing the feasibility and acceptability of introducing a routine psychological screening program using the Distress Thermometer (DT) to improve screening rates and timeliness of referral to psychosocial services in three rural outpatient oncology clinics in Australia. Nursing and psychosocial staff participated in a two-hour training session (educational meetings and educational materials) covering the rationale for screening, the screening instrument and the study procedure. The impact of the intervention on distress screening was not explicitly reported (i.e. the control period rates of screening). Five of eight cases (according to predefined PSYCH-6 cutoff criteria) and ten of 19 cases (according to DT cutoff) were referred to a social worker or psychologist in the control and intervention periods respectively. Due to the small number of cases, significance testing of differences between the pre-screening and screening phases was not conducted.

Bauwens et al.[30] conducted a pre post study to evaluate the impact of systematic screening with the Distress Barometer (DB) on detection rates of elevated distress and on rates of psychosocial referral at an oncology centre in Belgium. Oncologists were instructed in using the DB and given a written explanation (educational materials) on how to interpret the DB results in a collective 1 hour session (educational meetings). As this study did not aim to improve rates of distress screening, but focused on oncologist detection of distress and subsequent referral, all patients were screened using the DB in both conditions. Consequently, the rates of distress screening prior to the study, conducted by oncologists or other professional staff, compared to the study period are unknown. In the usual care period, using oncologists' judgement, referral was considered necessary for 5.4% of all patients. In the DB condition, referral was considered necessary for 41.6% of all patients. Of those patients for whom referral was considered necessary, 40% (6/15) in the usual care period and

69% (85/123) in the DB condition were actually referred to psychosocial care. The authors did not conduct an analysis to determine if there was a significant difference in these rates, however concluded that the implementation of screening using the DB led to increased numbers of referrals to psychosocial professionals.

***Educational materials, educational meetings and outreach visits***

Braeken et al.[26-28] conducted a cluster randomised controlled trial to study the effect of the implementation of the Screening Inventory Psychosocial Problems (SIPP) on the number and types of referrals of cancer patients to psychosocial caregivers in a radiation oncology department in the Netherlands. Radiation oncologists were randomised to a control or intervention group. Those in the intervention group were trained by a researcher and two social workers with experience in using and interpreting the SIPP during a 1 hour training session (educational meetings, educational materials and educational outreach visits). The study found no significant intervention effects were observed for the total number of patients referred to psychosocial care providers at any of the assessment time points (first three months, the last nine months and the total study period).

***Educational materials, educational meetings, educational outreach visits and reminders***

Ito and colleagues[25] conducted a pre post trial to examine the usefulness of a screening program (using the distress and impact thermometer; DIT) modified for cancer patients undergoing radiotherapy at an outpatient cancer treatment center in Japan. Prior to the screening phase, all pharmacists attended a 2 hour lecture and (educational meetings) given by a trained psychiatrist (who also met with the pharmacists monthly; educational outreach visits) and underwent role play training to learn how to implement the DIT and referral for those patients scoring above the predetermined cutoff, (educational materials). When providing instructions to patients beginning chemotherapy and at the second visit, pharmacists invited patients to complete the DIT and a screening program sheet was

completed by the pharmacists (reminders). The proportion of patients screened prior to the implementation of the screening program using the DIT or other measure was not assessed and 84.8% of patients were screened using the DIT in the intervention phase. The proportion of patients referred to the Psychiatric Service (and were subsequently confirmed to have major depression or adjustment disorder) during the screening program period compared to the usual care period was not significantly different between the two periods (2.7% during the program-period vs 1.0% during the usual care-period, $p = 0.46$).

***Educational materials, educational meetings, reminders, organizational culture, continuous quality improvement***

One study examined the effect of educational materials, educational meetings, reminders, organizational culture and continuous quality improvement on improvement in distress screening or referral. The trial by Zemlin et al.[29] was a prospective consecutive study that aimed to integrate psycho-oncological early detection and diagnostics as an integral part of everyday practice routines of acute inpatient care within the multidisciplinary diagnosis and care chain of breast cancer patients at a gynaecology clinic in Germany. Prior to the introduction of the program, certified training courses were held for clinicians, gynaecologists and psychotherapists as well as other professional groups (educational meetings, educational materials, organizational culture) and every three to four months, cross-departmental meetings between psychology and gynaecology departments were held (continuous quality improvement). The authors described the trial in three phases; in phase one, breast care nurses and doctors asked the patient about their interest in a psycho-oncological consultation where they felt necessary, and in phase two the nurses asked this of patients on the day of their admission. In phase three, the nurses conducted screening using the Hospital Anxiety and Depression Scale (HADS) with all patients and passed the HADS sheet to the physician (reminders). A predetermined cutoff indicated if referral was required.

The proportion of patients screened with the HADS during phase three was 100%. The proportion of patients screened in phase one or two using the HADS or other measure was not assessed. The authors reported a significant positive trend for the proportion of patients offered referral for psycho-oncological care between phase one and three ($t = 22.40$, $df = 2$, $p < 0.001$).

**Secondary outcomes**

***Psychosocial distress***

Only one study compared patients' levels of distress at follow up using the distress screening measure implemented. Braeken et al.[26-28] found no significant intervention effects as measured by the HADS for patients' psychological distress at three months or 12 months after baseline, nor dichotomous distress outcomes (no distress or at least moderate distress) at three months, or 12 months after baseline.

***Reported adverse consequences***

No study explicitly assessed whether the intervention had adverse effects.

**Quality of the evidence**

Using GRADE, the overall rating of the certainty of the body of evidence reported in this review was assessed as very low. The primary outcomes examined were downgraded one level to reflect high risk of bias and further downgraded two levels due to clinical heterogeneity and inconsistency in reporting either rates of distress screening or referral across both control and intervention periods. Since indirectness and imprecision also lowers the quality of the evidence, we downgraded two further levels on that basis. We found the quality of evidence to be of weak to moderate quality due to risk of bias using the EPHPP (Table 6), which identified a number of limitations, particularly among the pre post studies in regards to controlling for potential confounders.

## Discussion

This review sought to assess the impact of trials of strategies to improve clinician provision of: screening of cancer patients for psychosocial distress; and referral for further assessment and/or psychosocial support where necessary. The review identified just one trial that met the prospectively registered inclusion criteria of having a parallel control trial design. When these criteria were relaxed to include those with a non-parallel control group a further four trials were included. Largely due to study designs (i.e. mostly pre-post), none of the included studies were able to provide quality evidence for the effectiveness of screening procedures in improving in rates of distress screening. The intervention in just one trial was effective in significantly improving the rates of referral for psycho-oncological support for distressed patients. Such findings highlight the sparse evidence base for this important element of cancer patient care, and leave health services and cancer professionals with little clear guidance of strategies to improve provision of these elements of care to their patients.

Our findings are consistent with previous systematic reviews of trials aiming to improve depression or anxiety screening in primary care that have found that improvement in care provision is more likely when complex organisational change strategies are used, such as coordination between departments, enhanced role of nurses and performance feedback, in addition to clinician education[13-15]. The findings of the review highlight that the implementation of routine psychosocial screening and referral in cancer is complex and more rigorous research is needed. The trial by Zemlin et al.[29] was the only study included in the review to adopt a comprehensive implementation approach, and the only to report significant improvement in offer of referral of cancer patients for distress. Implementation strategies employed by other trials were primarily based on one off training and resource provision, suggesting that such support is insufficient. Comprehensive implementation strategies may be more likely to improve care given their greater capacity to address various barriers to

screening and referral. Interestingly, Zemlin et al[29] was the only study to describe strategies employed to change the organisational culture of the healthcare setting, specifically, defining responsibilities and tasks between the specialist disciplines and the medical and nursing staff involved in the treatment team, training certificates, as well as regular meetings to facilitate communication. It may be that simpler interventions are less effective in implementing routine provision of this care because they fail to address the organisational culture of the setting. Strengthening team communication[25] and making clinicians more aware of their role and responsibilities in distress screening and referral for cancer patients [27] may improve the rates of this care delivery. Further research identifying they key barriers to such care, and the best strategies to address them in cancer services is therefore warranted.

Surprisingly, none of the included studies examined the impact of strategies employed (e.g. training) to improve the rate of clinician provision of psychosocial distress screening. Due to the majority of study designs not employing a parallel comparison group, the review does not provide quality evidence regarding the effectiveness of implementation strategies to improve screening or referral. Such a finding is of concern. Screening is a necessary pre-requisite to appropriate referral of cancer patients to psychological support. As screening for psychosocial distress in cancer populations is low across jurisdictions[32], improving this form of care should represent a priority. Previous studies have used novel technologies to prompt screening by clinicians[33-35]. Such approaches should be examined in robust trial designs in cancer settings that allow for their impact on improving the rate of routine clinician provision of distress screening to be determined.

A number of methodological aspects of the study warrant highlighting and should be considered when interpreting the study findings. As far as the authors are aware, this is the first systematic review to examine the impact of interventions of strategies to improve the rate of clinician provision of distress screening and appropriate referral in cancer patients.

The review was prospectively registered, followed a peer reviewed protocol and included a comprehensive search strategy examining over 18000 citations. There was substantial clinical and methodological heterogeneity in the included studies. Classification of EPOC taxonomy implementation strategies was also difficult due to the lack of detail reported on intervention components in the studies. Furthermore, only one of the studies was a randomised controlled trial. Such characteristics of the included studies precluded quantitative synthesis of the effects of these strategies.

**Conclusions**

The findings of this review suggest that there is considerable scope to improve implementation of psychosocial distress screening and referral in cancer settings in order to establish a strong evidence base for future successful interventions. Implementation of psychosocial distress screening and appropriate referral needs to be employed using a systematic method and assessed with appropriately controlled studies in order to determine the most effective approaches. Better reporting of outcomes and more detailed description of intervention components need to be prepared.

**Figure 1. PRISMA Flow Diagram**

## Table 1. Trial characteristics

| Study | Design | Study dates | Single-centre or multicentre | Setting | Country | Aim | Patient inclusion criteria | No. of patients | Mean age in years (SD) | Gender (male) | Tumour site/Tumour stage | Cancer treatment type/Stage of treatment |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Thewes et al. 2009[31] | Pre post | NR. | Multicentre - 3 rural outpatient oncology clinics | Outpatient oncology clinics. | Australia | (i) Prospectively investigate the feasibility and acceptability of introducing a routine psychological screening program for rural oncology clinics; (ii) explore the impact of screening on rates and timeliness of referral to psychosocial services; and (iii) provide pilot data on the acceptability and utility of the DT as a screening tool within the rural Australian setting. | (i) Newly diagnosed with malignant disease; (ii) 18 years of age or older; (iii) able to give informed consent; and (iv) able to read English proficiently. | Unscreened cohort – 40. Screened cohort – 43. | 60.0 (10.5 SD). | 54.0% | Colorectal 22.9%, Breast 30.1%, Lung 14.5%, Other 13.2%, Haematological 9.6%, Skin 6.0%, Unknown primary 3.6%.<br><br>Localised/locally advanced 71.1%, Advanced or metastatic 28.9%. | Surgery 75.9%, chemotherapies 66.3%, RT 53%, endocrine therapies 32.5%.<br><br>Newly diagnosed patients. |
| Braeken et al. 2009[26], 2013[27] & 2013[28] | Cluster randomised controlled trial | April 2008 – October 2010. | Single | Institute Verbeeten (BVI) - a radiation oncology department (Tilberg). | The Netherlands | To study the effect of the SIPP on the number and types of referrals of cancer patients with psychosocial problems to psychosocial caregivers. | i) Receiving RT; ii) most common cancer types such as lung, prostate, bladder, rectum, breast, cervix, endometrial, skin and Non-Hodgkin; iii) 18 years of age or older; and iv) no metastases. Exclusion criteria: i) receiving palliative treatment, ≤ 10 fractions of RT; ii) unable to read and speak Dutch; and iii) unable to complete questionnaires. | Control group – 300. Intervention group – 268. | Control group 62.4 (10.7 SD), intervention group 62.4 (10.8 SD). | Control group 47.0%, intervention group 31.7%. | Prostate/Bladder 24.1%, Lung 11.3%, Breast 50.0%, Cervix/Endometrial 1.6%, Rectum 9.0%, Non-Hodgkin Lymphoma 1.7%, Skin 2.3%. | 100% RT.<br><br>SIPP before the first consultation prior to RT and SIPP2 before the consultation at the end of RT. |
| Ito et al. 2011[25] | Pre post | UP: April 1 - September 30, 2006. PP: April 1 | Single | Outpatient treatment center of the NCCH- | Japan | To examine the usefulness (rate of referral) of a screening program modified for outpatients | All consecutive cancer patients who began chemotherapy at the outpatient treatment | UP – 478. PP – 520. | UP 61.4 (10.8 SD), | UP 54.0%, PP | Lung 20.0%, Colon/rectum 18.2%, Breast 13.8%, Hematopoietic and | Chemotherapy.<br><br>Patients beginning chemotherapy at the outpatient |

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| | | - September 30, 2007. | | E (Kashiwanoha, Kashiwa, Chiba). | | with cancer who are undergoing chemotherapy. | center of NCCH-E in Japan. | | PP 62.8 (10.9 SD). | 56.7%. | lymphatic tissue 12.8%, Stomach 7.9%, Pancreas 10.2%, Esophagus 5.5%, Liver, bile duct, gall bladder 4.6%, Head and Neck 2.8%, Other 4.0%.<br><br>Reported for PP only: Stage I 2.5%, Stage II 9.6%, Stage III 20.8%, Stage IV or recurrent 67.1%. | treatment center of the NCCH-E. |
| Zemlin et al. 2011[29] | Propsective consecutive study | NR. | Single | Clinic for Gynaecology of the University of Marburg Hospital (Marburg). | Germany | To examine whether a screening and computer-based psycho-oncological clinical pathway can improve the diagnosis of breast cancer patients requiring psycho-oncological support according to current guidelines. | Breast cancer patients who were in stationary treatment. | Phase 1 - 236, Phase II – 384, Phase III - 247. | 59.5 (12.2 SD). | 0.6% | Breast 100%.<br><br>Stage 0 (Ductal carcinoma in situ) 11.6%, Stage I 43.7%, Stage II 25.5%, Stage III 7.8%, Stage IV 11.2%. | Screening occurred on day of admission.<br><br>Stage of treatment NR. |
| Bauwens et al. 2014[30] | Pre post | UP: May 2010. DB period June 2010. | Single | Oncology Centre of the University Hospital (UZ Brussel). | Belgium | To evaluate the impact of systematic screening with the DB on detection rates of patients with elevated distress and on rates of psychosocial referral compared to usual practice. | i) Ambulatory patients; ii) 18 years and older; iii) diagnosed with cancer; iv) sufficiently fluent in the languages of the study (Dutch or French); and iv) not affected by a cognitive disorder. | UP – 278, DB period – 304. | 58.92 (13.03 SD). | 32.0% | Breast 43.9%, Lung 10%, Colon 8.6%, Prostate 3.4%, Gynaecological 7.7%, Skin 9.5%, Brain 7.4%, Other 9.5%<br><br>Local disease 33%, Locoregional disease 38.6%, Advanced disease 28.4% | No treatment 24.3%, surgery 3.1%, RT 1.7%, chemotherapy 43.3%, medication 18.9%, RT + chemotherapy 2.1%, chemotherapy + medication 5.8%, RT + medication 0.7%<br><br>Diagnosis 2.1%, active treatment curative intent 22.7%, active treatment palliative intent 53.0%, cured 9.8%, remission (partial/complete) 3.3%, palliative care 0.3%, wait and see 5.0%, recent recurrence 3.8%. |

NR, not reported; DT, Distress Thermometer; UP, usual care period; PP, program period; DB, Distress Barometer; NCCH-E, National Cancer Center Hospital East; DT, Distress Thermometer, SIPP; Screening Inventory Psychosocial Problems; RT, Radiotherapy.

**Table 2. Definition of EPOC subcategories**

| EPOC subcategory | Definition |
|---|---|
| Educational materials | Distribution to individuals, or groups, of educational materials to support clinical care, i.e. any intervention in which knowledge is distributed. For example, this may be facilitated by the internet, learning critical appraisal skills; skills for electronic retrieval of information, diagnostic formulation; question formulation. |
| Educational meetings | Courses, workshops, conferences or other educational meetings. |
| Educational outreach visits or academic detailing | Personal visits by a trained person to health workers in their own settings, to provide information with the aim of changing practice. |
| Reminders | Manual or computerised interventions that prompt health workers to perform an action during a consultation with a patient, for example computer decision support systems. |
| Organisational culture | Strategies to change organisational culture. |
| Continuous quality improvement | An iterative process to review and improve care that includes involvement of healthcare teams, analysis of a process or system, a structured process improvement method or problem solving approach, and use of data analysis to assess changes. |

## Table 3. Intervention description

| Study | Healthcare providers | Distress screening tool | Referral criteria | Training | Intervention | Control/Comparison | EPOC subcategories |
|---|---|---|---|---|---|---|---|
| Thewes et al. 2009[31] | Nurses | The DT - a single item screening measure that identifies level and causes of distress.<br><br>Respondents are asked to indicate their level of distress in the past week on an 11-point scale ranging from 0 ('None') to 10 ('Extreme'). | Screening cohort - for individuals who scored above the cut-off score (≥5), nursing staff were encouraged to assess problems and concerns and explore the patient's interest in receiving referral to psychosocial staff using the skills and strategies discussed in the initial training session. | Nursing and psychosocial staff participated in a 2 hour training session covering the screening procedure and suggestions for how to discuss the results of screening with patients who scored above cut-off. | Distress screening was completed immediately before an initial oncologist rural clinic appointment or chemotherapy education session. | All participants completed the SPHERE-Short at baseline; a 12-item questionnaire measuring common psychological and somatic distress developed and validated in Australia. The SPHERE- Short has 2 subscales: PSYCH-6 and somatic symptoms. A score of ≥2 on the PSYCH-6 subscale indicates a likely case of psychological disorder. | Educational materials, educational meetings. |
| Braeken et al. 2009[26], 2013[27] & 2013[28] | Radiation oncologists | The SIPP - a short, valid and reliable 24-item self- reported questionnaire that systematically identifies psychosocial problems in Dutch cancer patients. Items are rated on a 3-point scale of 0 (no) to 2 (yes). Higher scores indicate poorer functioning. | Intervention: Potential referral to a psychosocial caregiver was based on the scores of the SIPP in combination with the radiation oncologist's judgement.<br><br>Control: According to the radiation oncologist's judgement about the presence or absence of psychosocial problems in patients. | Before the start of the study, the radiation oncologists in the experimental condition were trained in using and interpreting the SIPP during a 1 hour training session.<br><br>Training was given by the researcher and two social workers with experience in using and discussing the SIPP. | Patients received the SIPP just before the first and last consultation with the radiation oncologist. Psychosocial problems were discussed with the patient during the consultation and referral to a psychosocial caregiver occurred only with the permission of the patient.<br><br>The radiation oncologists were stratified according to general percentages of incoming patients they referred in 2006–2007 and then randomised to experimental or control condition. | Care as usual - no recent guidelines for the systematic assessment of psychosocial problems in cancer patients existed at the Institute Verbeeten. The radiation oncologist was able to refer patients to psychosocial caregivers (social workers) at the Institute Verbeeten based on their clinical judgement. | Educational materials, educational meetings, educational outreach visits. |
| Ito et al. 2011[25] | Pharmacists | The DIT - a 2 item, self-administered rating scale.<br><br>Each 'distress' and 'impact' question is scored using an 11-point Likert scale, with scores ranging from 0 to 10 and a high score indicating an unfavourable status. | PP - if a patient scored equal to or more than each cut-off point (≥ 4 for distress and ≥ 3 for impact) the screening result was regarded as positive. | Before implementing the screening program, all the pharmacists attended a 2 hour lecture given by a trained psychiatrist regarding the epidemiology, impact, risk factors, under-recognition, and appropriate management of psychiatric disorders in cancer patients. Additionally, the pharmacists underwent role-play training to learn | Pharmacists providing instructions to patients beginning chemotherapy at their first and second visit also provided information regarding the Psychiatric Service using a brief pamphlet and invited the patients to complete the DIT. The pharmacist then completed the screening program sheet, which is a record of the patient's DIT scores.<br><br>The pharmacist recommended a consultation with the Psychiatric Service | UP was not described in detail. | Educational materials, educational meetings, educational outreach visits, reminders. |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | how to implement the DIT and to give recommendations for psychiatric referral. | to all the patients with a positive screening result and recorded the screening results on the medical chart. | | |
| Zemlin et al. 2011[29] | BCN's and doctors | The HADS - scores of more than 13 indicate clinically suspected psychological distress. | Phase I – BCN's and doctors asked the patient about their interest in a psycho-oncological consultation where they felt necessary.<br><br>Phase II – BCN's asked all patients about their interest in a psycho-oncological consultation on day of admission.<br><br>Phase III – patients were referred to a psycho-oncological interview if i) they scored > 13 on the HADS; ii) the doctor had a clinical impression that the patient required referral; or iii) the patient desired referral. | Certified training courses for clinicians, gynaecologists and psychotherapists as well as other professional groups of the inpatient and outpatient network were carried out. | In Phase III, all patients completed the HADS questionnaire. The BCN evaluated the HADS and informed the patients about the possibility of a psycho-oncologic initial interview. The BCN passed the evaluated HADS sheet to the physician. For those patients with psycho-oncological need (threshold HADS score and/or clinically suspected treatment oriented psychological distress) the doctors recommended a psycho-oncological interview. Each patient with a desire for psycho-oncological care was logged and offered initial interview (regardless of HADS score). | In Phase I, BCN's and doctors asked the patient about their interest in a psycho-oncological consultation where they felt necessary. In addition, all patients received information on psychosocial support options. | Organizational culture, continuous quality improvement, educational materials, educational meetings, reminders. |
| Bauwens et al. 2014[30] | Seven oncologists | The DB - comprises three parts:<br><br>1. The DT (described above). The VAS was slightly adapted by using a background colour effect with anchors labelled 'no distress' through 'moderate distress' and 'extreme distress'.<br><br>2. The CCS, which consists of 10 items that are rated on a coloured 5-point scale. Patients are required to rate how much each of a list of sources of distress has been troubling them lately.<br><br>3. Additional Wish-Needs Questions: 4 additional questions regarding complaints and needs for further medical information and/or support. | UP condition - oncologists used their own VAS assessment of distress to decide on an eventual referral. Whereas in the DB condition, the cut-off point for the DB (Distress Thermometer ≥4 and elevated CCS was used by the oncologists for this purpose. | In a collective 1 hour session held shortly before the DB condition, oncologists were instructed in using the DB and were given a written explanation on how to interpret DB results. | Two week period<br><br>DB condition - The DB was administered before the consultation with the oncologist.<br><br>Also in the DB condition, oncologists had a form with three other yes/no questions: (2) if they considered referral necessary, (3) if they actually gave an advice for referral and (4) if referral was accepted by patients. | 2 week period<br><br>UP condition - The DB was administered after the consultation with the oncologist.<br><br>Also in the UP condition, oncologists had a form with four other questions: (1) their rating of patients' distress on a VAS (0–10), (2) if they considered referral necessary, (3) if they actually gave advice for referral and (4) if referral was accepted by patients. | Educational materials, educational meetings. |

BCN, breast care nurse; DT, Distress Thermometer; DIT, Distress and Impact Thermometer; HADS, Hospital Anxiety and Depression Scale; DB, Distress Barometer; VAS, Visual Analogue Scale; CCS, Coloured Complaint Scale; PP, program period; UP, usual care period; SIPP; Screening Inventory Psychosocial Problems; SHPERE-Short, Somatic and Psychological Health Report Short form; PSYCH-6, psychological symptoms.

## Table 4. Primary outcomes

| Study | Distress screening | | Referral | |
|---|---|---|---|---|
| | Measure; data collection method | Results | Measure; data collection method | Results |
| Thewes et al. 2009[31] | Proportion of patients screened.<br><br>NR. | Pre-screening phase – proportion of patients screened (using any distress screening tool) was not reported.<br><br>Screening phase – all patients were screened using the DT. | Proportion of patients referred in the pre-screening phase compared to the screening phase.<br><br>Review of referral records and databases. | Pre-screening phase - Of the 8 PSYCH-6 cases in the pre-screening phase, 6 were referred to a CCC and 5 to a social worker/psychologist.<br><br>Screening phase – 10/19 (53%) patients that met the DT cutoff were referred to a social worker or psychologist (11 of 14 PSYCH-6 cases were referred to the CCC and 8 to a social worker/psychologist). |
| Braeken et al. 2009[26], 2013[27] & 2013[28] | Proportion of patients screened.<br><br>NR. | Control group – proportion of patients screened (using any distress screening tool) was not reported.<br><br>Intervention group – 263/268 (98%) were screened using the SIPP before the first consultation. 250/268 (96%) were screened using the SIPP before end of radiotherapy consultation. | The number of referrals of patients with psychosocial problems to psychosocial workers at the Institute Verbeeten and/or to external health care providers (e.g. psychologists, psychiatrists). Three dichotomous outcome variables (yes/no) during the first 3 months, the last 9 months, and the total study period.<br><br>Measured at 3 and 12 months after baseline assessment with a self-developed questionnaire by the patient and from registration records of the psychosocial caregivers at the Institute Verbeeten. | First 3 months - Control group 29/300 (9.7%) vs intervention group 34/268 (12.7%) patients referred (NS).<br><br>Last 9 months – Control group 24/300 (8%) vs intervention group 19/268 (7.1%) patients referred (NS).<br><br>Group differences in these outcomes were analysed using Generalized Estimating Equations with patients at level 1 and radiation oncologists at level 2. All models were adjusted for baseline differences with respect to gender and cancer diagnosis. Analyses were taken on an intention-to-treat principle.<br><br>Generalised Estimating Equations found that numbers of referrals did not differ significantly between the intervention and control group at 3 months (β =-0.16, SE±0.34, p=0.32), 9 months (β =0.22, SE±0.28, p = 0.22) or overall months (β =-0.04, SE±0.28, p = 0.44). |
| Ito et al. 2011[25] | Proportion of patients screened.<br><br>NR. | UP – proportion of patients screened (using any distress screening tool) was not reported.<br><br>PP – 441/520 (84.8%). | Proportion of patients referred to the Psychiatric Service and treated for MDD or AD among all the outpatients who had begun a new chemotherapy regimen within 3 months of their visit to the outpatient clinic.<br><br>Data extracted from patients' medical charts and the computerized database of the electronic medical record at NCCH-E. | Retrospective cohort analysis (Chi-squared test comparing patients treated during the PP with historical control data gathered during the UP).<br><br>UP – 5/478 (1.0%) vs PP – 15/520 (2.7%) patients referred to the Psychiatric Service with subsequent confirmed and treated for MDD or ADs ($p$ = .46). |
| Zemlin et al. 2011[29] | Proportion of patients screened.<br><br>NR. | Proportion of patients screened in Phase I or II screened (using any distress screening tool) was not reported.<br><br>All patients in Phase III were screened using the HADS. | Proportion of patients offered referral for psycho-oncological interview.<br><br>Medical records. | Univariate data analysis.<br><br>Cochran-Armitage test.<br><br>Phase I – 194/236 (82.2%) vs Phase II 344/384 (89.6%) vs Phase |

| | | | | |
|---|---|---|---|---|
| | | | | III 236/247 (95.5%) were informed/offered the psycho-oncological interview. There was a significant positive trend for the proportion of patients informed about the psycho-oncological care available (t = 22.40, df = 2, $p$ <0.001). |
| Bauwens et al. 2014[30] | Proportion of patients screened.<br><br>NR. | UP condition – all patients were screened with the DB after consult with oncologist (therefore not used as part of the referral decision).<br><br>DB condition – all patients were screened with the DB prior to consult with the oncologist. | Necessary referrals (UP condition: referrals necessary as per oncologists' VAS ratings, DB condition: referrals necessary for all patients with distress according to the DB).<br><br>Self-assessment. | UP condition – 13.8% of patients with elevated distress (or 5.4% of all patients), DB condition - 100% of patients with distress (or 41.6% of all patients). |
| | | | Referrals made (UP condition: proportion of patients for whom referral was considered necessary by the oncologists and were actually referred to psychosocial care, DB condition: proportion of patients with elevated distress that were referred).<br><br>Self-assessment. | UP condition – 6/15 patients, DB condition - 85/123 patients. |

NR, not reported; DT, Distress Thermometer; UP, usual care period; SIPP; Screening Inventory Psychosocial Problems; PP, program period; DB, Distress Barometer; MDD, Major Depressive Disorder; AD, Adjustment Disorder; NCCH-E, National Cancer Center Hospital East; VAS, visual analogue scale; CCC, cancer care coordinator; NS, not significant.

## Table 5. Secondary outcomes

| Study | Measure; data collection method | Results |
|---|---|---|
| Braeken et al. 2009[26], 2013[27] & 2013[28] | Extent of psychological symptoms at 3 months and 12 months after baseline.<br><br>Measured with the HADS and the GHQ-12 (assesses with 12 items whether the patient considers him- or herself better, the same, worse or much worse over the previous four weeks than he/she "usually" is. Total scores range from 0 to 12). Patients complete these self- reported questionnaires at baseline and at 3 and 12 months after the baseline period. | Mixed effects' modelling.<br><br>No significant intervention effects were observed for patients' extent of psychological distress. (3 months after baseline mean psychological distress score control group 2.85 vs intervention group 2.74, $p = 0.19$; 12 months after baseline mean psychological distress score control group 2.14 vs intervention group 1.96, $p = 0.12$). |
| | Group differences in the proportion of dichotomous distress outcome (no or at least moderate distress) at 3 months and 12 months after baseline.<br><br>Measured with HADS and GHQ-12. | Generalised estimating equations.<br><br>No significant intervention effects were observed for proportion of patients with distress (3 months after baseline control group 39% vs experimental group 38.4%, $p = .036$; 12 months after baseline control group 24.7% vs intervention group 24.3%, $p = 0.39$). |

HADS, Hospital Anxiety and Depression Scale; GHQ-12, Goldberg's General Health Questionnaire-12 item version.

**Table 6. Ratings of methodological quality: strong (S), moderate (M) and weak (W)**

| **Study** | *Selection bias* | *Study design* | *Confounders* | *Blinding* | *Data collection* | *Withdrawals* | *Global rating* |
|---|---|---|---|---|---|---|---|
| Thewes et al. 2009[31] | Moderate | Moderate | Weak | Moderate | Weak | Moderate | Weak |
| Braeken et al. 2009[26], 2013[27] & 2013[28] | Moderate | Strong | Strong | Moderate | Weak | Strong | Moderate |
| Ito et al. 2011[25] | Moderate | Moderate | Strong | Moderate | Weak | Moderate | Moderate |
| Zemlin et al. 2011[29] | Moderate | Moderate | Weak | Moderate | Weak | Moderate | Weak |
| Bauwens et al. 2014[30] | Moderate | Moderate | Weak | Weak | Weak | Weak | Weak |

## AUTHORS' CONTRIBUTIONS

KM and LW conceptualised the review with input from BB, AB, SAH, AKB, GC, CW, JB, DB, EF. KM and EF conducted screening, data extraction and methodological quality analysis. KM and LW drafted the manuscript. All authors contributed to subsequent drafts and have approved the final version of the manuscript.

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## COMPETING INTERESTS

The authors declare that they have no competing interests.

## DATA SHARING STATEMENT

No additional data available.

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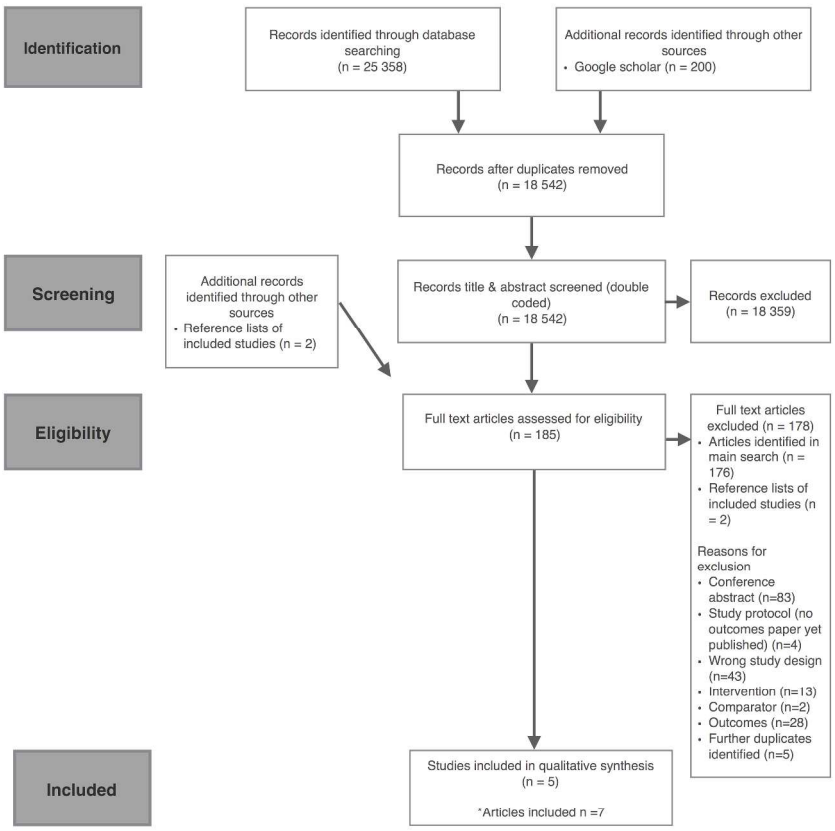


Figure 1. PRISMA Flow Diagram

296x420mm (300 x 300 DPI)

## MEDLINE SEARCH STRATEGY

1. cancer*.mp.
2. exp Neoplasms/
3. tumo?r*.mp.
4. malignan*.mp.
5. exp Adenocarcinoma/
6. exp Leukemia/
7. leukaemia*.mp.
8. metastat*.mp.
9. exp Carcinoma/
10. exp Medical Oncology/
11. exp Sarcoma/
12. choriocarcinoma*.mp.
13. lymphoma*.mp.
14. teratoma*.mp.
15. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14
16. screen*.mp.
17. measure*.mp.
18. assess*.mp.
19. Questionnaires/
20. Diagnosis/
21. instrument.mp.
22. validat*.mp.
23. 16 or 17 or 18 or 19 or 20 or 21 or 22
24. distress*.mp.

25. Stress, Psychological/

26. Anxiety/ or exp Anxiety Disorders/

27. Depression/

28. depress*.mp.

29. exp Depressive Disorder/

30. Dysthymic Disorder/

31. Adjustment Disorders/

32. "Quality of Life"/

33. psychosocial.mp.

34. Depressive Disorder, Major/

35. 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34

36. (psychosocial adj3 (care* or support* or service*)).mp.

37. Counseling/

38. (psychological adj3 (support* or care* or service* or therap* or intervention*)).mp.

39. exp Psychotherapy/

40. Mental Health Services/

41. (psycho oncology or psychooncology).mp.

42. Supportive care.mp.

43. Support service*.mp.

44. Social Support/

45. 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44

46. Intervention Studies/

47. implement*.mp.

48. disseminat*.mp.

49. adopt*.mp.

50. practice*.mp.

51. organi?ational change*.mp.

52. diffusion.mp.

53. system* change*.mp.

54. quality improvement*.mp.

55. transform*.mp.

56. translat*.mp.

57. transfer*.mp.

58. uptake*.mp.

59. sustainab*.mp.

60. institutionali*.mp.

61. routin*.mp.

62. maintenance.mp.

63. capacity.mp.

64. incorporat*.mp.

65. adher*.mp.

66. program*.mp.

67. integrat*.mp.

68. scal*.mp.

69. Randomized Controlled Trial/

70. Non randomized controlled trial*.mp.

71. Random Allocation/

72. Evaluation Studies/

73. Pilot study.mp. or Pilot Projects/

74. Evaluation Studies as Topic/

75. Cohort Studies/

76. Controlled Before-After Studies/

77. Historically Controlled Study/

78. Cross-Sectional Studies/

79. (intervention$ adj5 stud$).mp.

80. feasibility pilot*.mp.

81. sequential cohort.mp.

82. Interrupted-time-series stud*.mp.

83. case series.mp.

84. program*.mp.

85. intervention*.mp.

86. Random*.ab.

87. exp clinical trial/

88. trial.ab.

89. double blind.ab.

90. single blind.ab.

91. experiment*.mp.

92. (pretest or pre test).mp.

93. (posttest or post test).mp.

94. (pre post or prepost).mp.

95. Before after.mp.

96. (Quasi-randomised or quasi-randomized or quasi-randomized or quazi-randomised).mp.

97. stepped wedge.mp.

98. Comprehensive cohort.mp.

99. Natural experiment.mp.

100. (Quasi experiment or quazi experiments).mp.

101. (Randomised encouragement trial or randomized encouragement trial).mp.

102. (Staggered enrolment trial or staggered enrollment trial).mp.

103. (Nonrandomised or non randomised or nonrandomized or non randomized).mp.

104. Interrupted time series.mp.

105. (Time series and trial).mp.

106. Multiple baseline.mp.

107. 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 6 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or 90 or 91 or 92 or 93 or 94 or 95 or 96 or 97 or 98 or 99 or 100 or 101 or 102 or 103 or 104 or 105 or 106

108. 15 and 23 and 35 and 45 and 107

109. psychology.mp. or Psychology/

110. social work*.mp.

111. 45 or 109 or 110

112. 15 and 23 and 35 and 107 and 111

# PRISMA 2009 Checklist

| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| **TITLE** | | | |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | 1 |
| **ABSTRACT** | | | |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | 2-3 |
| **INTRODUCTION** | | | |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | 5-7 |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | 7 |
| **METHODS** | | | |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | 7 |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | 7-9 |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | 9-10 |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | 9 |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | 10-11 |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | 10-11 |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | 11 |
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | 11-12 |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | 12 |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$) for each meta-analysis. | 12-13 |

# PRISMA 2009 Checklist



| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| Risk of bias across studies | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). | 12-13 |
| Additional analyses | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | N/A |
| **RESULTS** | | | |
| Study selection | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | 13, F1 |
| Study characteristics | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | 13-14 Tables 1, 3, 4, 5 |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | 15, Table 6 |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | 14-15 |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | 15-19 |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | 19 |
| Additional analysis | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | N/A |
| **DISCUSSION** | | | |
| Summary of evidence | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | 19-22 |
| Limitations | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | 19-22 |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | 22 |
| **FUNDING** | | | |
| Funding | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | 33 |

*From:* Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

BMJ Open

# INTERVENTIONS TO IMPROVE SCREENING AND APPROPRIATE REFERRAL OF CANCER PATIENTS FOR PSYCHOSOCIAL DISTRESS: SYSTEMATIC REVIEW



| | |
|---|---|
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| Primary Subject Heading: | Oncology |
| Secondary Subject Heading: | Evidence based practice, Health services research, Mental health |
| Keywords: | Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Protocols & guidelines < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Adult oncology < ONCOLOGY |
| | |

# INTERVENTIONS TO IMPROVE SCREENING AND APPROPRIATE REFERRAL OF CANCER PATIENTS FOR PSYCHOSOCIAL DISTRESS: SYSTEMATIC REVIEW

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**Keywords:** distress; screening; referral; cancer; review

**Word count:** 4644

## ABSTRACT

### Objectives

The primary aim of the review was to determine the effectiveness of strategies to improve clinician provision of psychosocial distress screening and referral of patients with cancer.

### Design

Systematic review.

### Data sources

Electronic databases (Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, PsycINFO and CINAHL) were searched until July 2016.

### Inclusion criteria

Population: adult cancer patients and clinical staff members. Intervention: Any strategy that aimed to improve the rate of routine screening and referral for detected distress of cancer patients. Comparison: no intervention controls, 'usual' practice, or alternative interventions. Outcome: (primary) any measure of provision of screening and/or referral for distress, (secondary) psychosocial distress, unintended adverse effects. Design: trials with or without a temporal comparison group including randomised and non-randomised trials, and uncontrolled pre-post studies.

### Data extraction and analysis

Two review authors independently extracted data. Heterogeneity across studies precluded quantitative assessment via meta-analysis and so a narrative synthesis of the results is presented.

**Results**

Five studies met the inclusion criteria. All studies were set in oncology clinics or departments and used multiple implementation strategies. Using GRADE, the overall rating of the certainty of the body of evidence reported in this review was assessed as very low. Three studies received a methodological quality rating of weak and two studies received a rating of moderate. Only one of the five studies reported a significant improvement in referrals.

**Conclusions**

The review identified five studies of predominantly poor quality examining the effectiveness of strategies to improve the routine implementation of distress screening and referral for cancer patients. Future research using robust research designs, including randomised assignment are needed to identify effective support strategies to maximise the potential for successful implementation of distress screening and referral for patients with cancer.

**Systematic review registration** PROSPERO registration number CRD4 2015017518.

**Strengths and limitations of this study**

- The first review to systematically synthesise evidence of the effectiveness of strategies to improve the rate of routine distress screening and referral for cancer patients

- The review performed a comprehensive search of the literature, included controlled trials of any design, and was inclusive of non-English literature
- Few studies met inclusion criteria, and heterogeneity of study design, primary and secondary outcomes precluded quantitative synthesis

## INTRODUCTION

### Rationale

Psychosocial distress can be defined as an unpleasant experience of an emotional or psychological nature including depression, anxiety and other/mood/adjustment disorders[1]. Estimates of the prevalence of psychosocial distress vary due to the type and stage of cancer, patient age, gender and race, as well as the definition of distress used. Psychosocial distress can arise in response to cancer related factors such as diagnosis and cancer progression, pain and adverse effects of treatment. Psychosocial distress in cancer patients may lead to non-adherence to treatment, poorer quality of life and may negatively impact survival, as well as increase treatment burden to the oncology team and health system[1-4]. Therefore, recognizing and treating distress in cancer populations is an important health priority.

Professional associations and clinical guidelines including the National Comprehensive Cancer Network *Clinical Practice Guidelines in Oncology: Distress Management*[1] recommend that those responsible for the care of cancer patients routinely screen for distress and, as appropriate, refer for further assessment and support. Clinical practice guideline recommendations are based on evidence that screening improves the timely management of distress[3,5], and systematic reviews and meta-analyses that have demonstrated psychosocial intervention reduces distress (such as depression and anxiety[6,7], particularly when participants are prescreened[8].

The efficacy of distress screening for improving patient outcomes has been challenged in the literature. A recent systematic review failed to find evidence that distress screening improved distress outcomes among cancer patients[9]. Another systematic review that examined screening for distress in cancer settings found that those studies reporting a lack of benefit to distress screening in patients with cancer lacked appropriate follow-up care of distressed

patients, while trials that linked screening with mandatory referral or intervention showed improvement in patient outcomes [10]. Whilst screening itself may not be sufficient to improve patient outcomes, it is a necessary pre requisite to identify those patients who could benefit from evidence based treatment and guides clinical decision making[1]. Consequently, clinical guidelines recommend screening *and* referral protocols in cancer settings. It is clear that well-designed trials are needed to further evaluate the effectiveness of screening and referral on patient outcomes. However, in the absence of strong evidence from robust trials that suggest distress screening and referral should not be conducted, clinicians should be guided by clinical practice guidelines.

Despite clinical practice guideline recommendations, screening and referral of cancer patients for psychosocial distress is not routinely conducted by clinicians responsible for the clinical management of cancer [1,2,11]. Beginning in 2015, the American College of Surgeons Commission on Cancer (CoC) has required cancer centers to implement programs for distress screening as a criterion for accreditation[12]. A recent cross-sectional survey of 20 National Comprehensive Network (NCCN) Institutions reported only 60% of services conducted outpatient distress screening, and even fewer services reported screening all patients (30%) as outlined in the NCCN standards[11]. Systematic reviews of trials of strategies to improve depression or anxiety screening in primary care note that complex organisational interventions that incorporate multiple strategies are most effective in improving provision of care[13-15]. Such strategies include clinician education, opinion leaders, patient specific reminders, enhanced role of nurses, academic detailing, integrating screening into routine clinical reviews and a greater degree of coordination between services (for example between primary and secondary care) [13-15]. However, we are not aware of any previous systematic review of interventions to improve clinician routine provision of distress screening and

appropriate referral of cancer patients per-se. It is the discrepancy between these guideline recommendations and current practice that this review aims to address.

**Objectives**

The primary aim of this review was to assess for cancer patients the impact of trials of strategies to improve clinician delivery of psychosocial distress care compared to usual care on rates of psychosocial distress screening and referral for further assessment and/or psychosocial support.

The secondary aims of the review were to:

i) Describe the effectiveness of such interventions on reducing psychosocial distress of patients with cancer;

ii) Describe any unintended adverse effects of such an intervention

**METHODS AND ANALYSIS**

The review will be reported consistent with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Statement[16]. The details of the methods have been reported elsewhere[17] and the protocol is registered with PROSPERO (registration number CRD42015017518).

**Eligibility criteria**

Study characteristics

*Types of studies*

Original studies including randomised controlled trials and non-randomised trials were included. Exclusion criteria were trials without parallel comparison or control groups. Due to the limited number of studies (explained further in the results section) we later included

studies without parallel control groups including uncontrolled pre post studies. There were no restrictions based on length of follow-up, year of study publication or language. Studies could be published in peer review or grey literature.

*Participants*

Participants could include adult cancer patients and clinical staff members such as physicians and allied health professionals responsible for the care of cancer patients. Studies which examined screening for psychosocial distress and/or referral for carers of patients with cancer, or survivors of cancer, were excluded.

*Types of Interventions*

Interventions of strategies that aimed to improve the rate of screening procedures for psychosocial distress and/or rate of referral for appropriate psychosocial support in health care settings were included. There are a range of potential strategies that could improve the likelihood of implementation of distress screening and referral in healthcare settings. For example, The Cochrane Effective Practice and Organisation of Care (EPOC) taxonomy is a framework for characterising educational, behavioural, financial, regulatory and organisational interventions within the topic of 'implementation strategies'[18] and includes 22 sub-categories. Examples of strategies within the taxonomy include educational materials, performance monitoring, local consensus processes and educational outreach visits. Included interventions could be singular or multicomponent. Studies using clinical judgement of psychosocial distress alone, without use of a formal screening tool were excluded. Referral for psychosocial support was defined as any written or verbal offer or direction of a patient for further review, consultation, assessment or treatment with any health professional, including the primary oncology team or health service, offering psychosocial support such as psycho-oncology services. Studies were included if they implemented either distress

screening only or distress screening and appropriate referral. Studies where research staff conduct screening or referral were excluded.

*Comparisons*

Studies with no intervention controls, 'usual' practice periods or alternative intervention comparison groups were included.

*Outcomes*

Primary outcomes:

i) Any measure of the provision of screening for psychosocial distress (e.g. number or % of cancer patients screened).

ii) and/or any measure of the provision of referral for further assessment and/or psychosocial support (e.g. number or % of cancer patients referred) by a clinician responsible for the management of a cancer patient.

*Secondary outcomes:*

i) Any validated outcome measure of change in psychosocial distress levels in the patients (e.g. distress outcome assessments such as the Kessler Psychological Distress Scale).

ii) Any measure of adverse effects on patients, clinicians or health services; or barriers to performing screening such as displacement of other clinical priorities.

**Information sources**

Electronic databases

The following electronic databases were searched for potentially eligible studies published up until July 2016; the Cochrane Central Register of Controlled trials (CENTRAL) in the

Cochrane Library, MEDLINE, EMBASE, PsycINFO and CINAHL. The Medline search strategy (supplementary file) was adapted for other databases and included filters used in other systematic reviews for population (cancer patients)[19], screening for distress[20] and referral[21] and psychosocial support[22].

Other sources

Studies were also obtained from the following sources:

- Reference lists of included studies
- Hand searching of 3 relevant journals in the field (published in the last 5 years); Journal of the National Comprehensive Cancer Network, Psychooncology and Supportive Care in Cancer
- Hand searching of conference abstracts published in the preceding 2 years from the International Psycho-Oncology Society and the Society of Behavioural Medicine
- A grey literature search using Google Scholar (published online in the last 5 years – the first 200 citations was examined)

**Study selection**

The titles and abstracts retrieved by electronic searches were exported to a reference management database (Endnote version X6) to remove duplicates. Two reviewers independently screened abstracts and titles using a standardised screening tool that was pilot tested with a sample of articles before use. The abstracts of papers that were in a language other than English were translated using Google Translate. If considered eligible or eligibility was unclear, professional translation of the full paper was undertaken.

The full texts of manuscripts were obtained for all potentially eligible trials for further examination and independently screened by two reviewers. For all manuscripts, the primary

reason for exclusion was recorded and is documented in Figure 1. Discrepancies regarding study eligibility were resolved by discussion and consensus.

**Data extraction**

Two review authors (KM and EF) independently extracted data from the included trials using a pre-piloted data extraction form that was developed based on recommendations from the *Cochrane Handbook for Systematic Reviews of Interventions*[23]. Discrepancies regarding data extraction were resolved by discussion and consensus.

Data items

Data was sought for the following variables:

- Authors, year and journal
- Study eligibility, study design, health care provider type (e.g. nurses), country, health care setting (e.g. oncology clinic)
- Patient characteristics and demographics including cancer site, cancer stage, age, sex, cancer treatment type, treatment status (pre/undergoing/post)
- Characteristics of the intervention, including the duration, intervention strategies, screening instrument
- Trial primary and secondary outcomes, including sample size, the data collection method, validity of measures used, any measures of client uptake or use of psychosocial support services following referral, effect size, measures of change in distress
- Number of participants per experimental condition
- Information to allow assessment of risk of study bias

**Methodological quality assessment bias**

Two review authors (KM and EF) independently assessed the risk of bias of all included trials using the Effective Public Health Practice Project Quality Assessment Tool (EPHPP) for quantitative studies[24]. The use of the EPHPP tool was a post hoc change from protocol due to the study designs included in the review. This tool covers any quantitative study design and includes components of intervention integrity. Any discrepancies were resolved through discussion. The EPHPP assesses six methodological dimensions: selection bias, study design, confounders, blinding, data collection methods, and withdrawals and dropouts. These domains are rated on a three-point scale (strong, moderate, weak) according to pre-defined criteria and procedures recommended for tool use, and then given an overall global rating. Those with no weak ratings were given an overall rating of strong, those with one weak rating were given an overall rating of moderate and those with two or more weak ratings across the six domains were given an overall weak rating. Two additional methodological dimensions provided by the tool are intervention integrity and analyses and these were also completed by the reviewers.

**Data analysis**

Summary measures

The small number of studies and differences in study design and primary and secondary outcomes reported in the included studies precluded the use of summary statistics to describe treatment effects. As such, the findings of included trials are described narratively.

Grading the strength of evidence

As recommended by the *Cochrane Handbook for Systematic Reviews of Interventions*[23], the overall quality of evidence on primary outcomes is presented using the GRADE (Grades of Recommendation, Assessment, Development and Evaluation) approach, which involves consideration of within-study risk of bias (methodological quality), directness of evidence,

heterogeneity, precision of effect estimates and risk of publication bias. The overall quality of evidence was rated by two review authors (KM and EF) at four levels: high, moderate, low and very low.

## RESULTS

A total of 18 542 citations were identified (after duplicates were removed) (Figure 1) for abstract and title screening. Just one study met the eligibility criteria (i.e. parallel control/comparison group). As such, and in an attempt to provide some evidence to guide researchers and practitioners regarding methods to improve patient distress screening and referral of cancer patients, we relaxed the design criteria and post-hoc rescreened all 18 542 citations and included studies with controlled trial designs without parallel control groups including uncontrolled pre post studies. The full text of 185 manuscripts were sought for further assessment against the review inclusion criteria (Figure 1). Of these, 178 were considered ineligible following the trial screening process. Seven publications describing 5 trials were included in the review.

### Included studies

#### *Types of studies*

A description of the trial characteristics of included studies is provided in Table 1. One study was conducted in Japan[25], one in the Netherlands[26-28], one in Germany[29], one in Belgium[30] and one in Australia[31]. Studies were published between 2009 and 2014. There was considerable heterogeneity in the participants, interventions and outcomes (clinical heterogeneity) of included studies.

#### *Health providers*

All studies were set in oncology clinics or departments. In regards to the healthcare providers responsible for conducting the distress screening and/or referral, one study targeted nurses[31],

one targeted radiation oncologists[26-28], one required pharmacists to perform the screening[25], one study involved both specialised breast care nurses and doctors[29] and one study utilised oncologists[30].

***Interventions***

All trials used multiple implementation strategies. The EPOC subcategories used to classify the implementation strategies employed by included studies in the review are provided in Table 2. The interventions employed in the included studies, as well as the specific EPOC subcategories identified in each study are presented in Table 3. Using EPOC taxonomy descriptors, all trials included educational materials and educational meetings, with two trials using only these strategies[30-31]. One trial utilised these strategies with the addition of educational outreach visits[26-28]. One study used a combination of educational materials, educational meetings, educational outreach visits and reminders[25]. One study tested an intervention consisting of organizational culture, continuous quality improvement, educational materials, educational meetings and reminders[29].

***Outcomes***

The primary and secondary outcomes are presented in Tables 4 and 5. Implementation of distress screening and/or referral was primarily assessed using reviews of patient medical records[25-29,31], however one study did not report the data collection method[28]. None of the studies reported which staff completed the medical record reviews. All trials reported the rates of referral for supports for those patients identified as distressed, however none of the studies examined the improvement in rates of distress screening. Change in distress levels were reported in one study[26-28]. No studies included a measure of potential adverse effects.

***Study design characteristics***

One of the included studies was a cluster randomised controlled trial[26-28], three were pre post studies[25,30,31] and one was a prospective consecutive study[29]. The cluster randomized

controlled trial compared an intervention to a usual care control[26-28], three studies compared a screening program period to a usual care period[25,30,31], and one trial compared a screening program phase to a two-phase non-screening period[29].

**Methodological quality assessment**

Individual ratings for each study against the six methodological criteria from the EPHPP tool and the assigned global rating are reported in Table 6. Overall, three studies received a methodological quality rating of weak[29-31] and two studies received a rating of moderate[25-28]. For three of the four non-randomised studies[29-31], it was unclear whether confounders were adequately adjusted for and for the majority of studies, blinding of outcome assessors or study participants was not described. While most studies reported medical record reviews for the data collection method, no reference was made to their validity or reliability as an outcome measure, nor was a description of who conducted the audits provided, resulting in weak ratings for all studies. All studies were judged as using analyses as appropriate to study design.

**Effects of intervention on distress screening and/or referral**

None of the included trials reported on the effects of strategies to improve rates of distress screening provision. Only one of the five studies reported a significant improvement in rate of referrals[27]. Zemlin et al.[29] reported a significant positive trend for the proportion of patients that were informed/offered psycho-oncological interview ($t = 22.40$, $df = 2$, $p < 0.001$). The effects of interventions are presented according to the implementation strategies (classified using the EPOC taxonomy) employed by included studies.

***Educational materials and educational meetings***

Two studies examined the impact of educational materials and educational meetings only on distress screening or referral[30,31]. Thewes et al. [231]conducted a pre post trial testing the feasibility and acceptability of introducing a routine psychological screening program using the Distress Thermometer (DT) to improve screening rates and timeliness of referral to psychosocial services in three rural outpatient oncology clinics in Australia. Nursing and psychosocial staff participated in a two-hour training session (educational meetings and educational materials) covering the rationale for screening, the screening instrument and the study procedure. The impact of the intervention on distress screening was not explicitly reported (i.e. the control period rates of screening). Five of eight cases (according to predefined PSYCH-6 cutoff criteria) and ten of 19 cases (according to DT cutoff) were referred to a social worker or psychologist in the control and intervention periods respectively. Due to the small number of cases, significance testing of differences between the pre-screening and screening phases was not conducted.

Bauwens et al.[30] conducted a pre post study to evaluate the impact of systematic screening with the Distress Barometer (DB) on detection rates of elevated distress and on rates of psychosocial referral at an oncology centre in Belgium. Oncologists were instructed in using the DB and given a written explanation (educational materials) on how to interpret the DB results in a collective 1 hour session (educational meetings). As this study did not aim to improve rates of distress screening, but focused on oncologist detection of distress and subsequent referral, all patients were screened using the DB in both conditions. Consequently, the rates of distress screening prior to the study, conducted by oncologists or other professional staff, compared to the study period are unknown. In the usual care period, using oncologists' judgement, referral was considered necessary for 5.4% of all patients. In the DB condition, referral was considered necessary for 41.6% of all patients. Of those patients for whom referral was considered necessary, 40% (6/15) in the usual care period and

69% (85/123) in the DB condition were actually referred to psychosocial care. The authors did not conduct an analysis to determine if there was a significant difference in these rates, however concluded that the implementation of screening using the DB led to increased numbers of referrals to psychosocial professionals.

***Educational materials, educational meetings and outreach visits***

Braeken et al.[26-28] conducted a cluster randomised controlled trial to study the effect of the implementation of the Screening Inventory Psychosocial Problems (SIPP) on the number and types of referrals of cancer patients to psychosocial caregivers in a radiation oncology department in the Netherlands. Radiation oncologists were randomised to a control or intervention group. Those in the intervention group were trained by a researcher and two social workers with experience in using and interpreting the SIPP during a 1 hour training session (educational meetings, educational materials and educational outreach visits). The study found no significant intervention effects were observed for the total number of patients referred to psychosocial care providers at any of the assessment time points (first three months, the last nine months and the total study period).

***Educational materials, educational meetings, educational outreach visits and reminders***

Ito and colleagues[25] conducted a pre post trial to examine the usefulness of a screening program (using the distress and impact thermometer; DIT) modified for cancer patients undergoing radiotherapy at an outpatient cancer treatment center in Japan. Prior to the screening phase, all pharmacists attended a 2 hour lecture and (educational meetings) given by a trained psychiatrist (who also met with the pharmacists monthly; educational outreach visits) and underwent role play training to learn how to implement the DIT and referral for those patients scoring above the predetermined cutoff, (educational materials). When providing instructions to patients beginning chemotherapy and at the second visit, pharmacists invited patients to complete the DIT and a screening program sheet was

completed by the pharmacists (reminders). The proportion of patients screened prior to the implementation of the screening program using the DIT or other measure was not assessed and 84.8% of patients were screened using the DIT in the intervention phase. The proportion of patients referred to the Psychiatric Service (and were subsequently confirmed to have major depression or adjustment disorder) during the screening program period compared to the usual care period was not significantly different between the two periods (2.7% during the program-period vs 1.0% during the usual care-period, $p = 0.46$).

***Educational materials, educational meetings, reminders, organizational culture, continuous quality improvement***

One study examined the effect of educational materials, educational meetings, reminders, organizational culture and continuous quality improvement on improvement in distress screening or referral. The trial by Zemlin et al.[29] was a prospective consecutive study that aimed to integrate psycho-oncological early detection and diagnostics as an integral part of everyday practice routines of acute inpatient care within the multidisciplinary diagnosis and care chain of breast cancer patients at a gynaecology clinic in Germany. Prior to the introduction of the program, certified training courses were held for clinicians, gynaecologists and psychotherapists as well as other professional groups (educational meetings, educational materials, organizational culture) and every three to four months, cross-departmental meetings between psychology and gynaecology departments were held (continuous quality improvement). The authors described the trial in three phases; in phase one, breast care nurses and doctors asked the patient about their interest in a psycho-oncological consultation where they felt necessary, and in phase two the nurses asked this of patients on the day of their admission. In phase three, the nurses conducted screening using the Hospital Anxiety and Depression Scale (HADS) with all patients and passed the HADS sheet to the physician (reminders). A predetermined cutoff indicated if referral was required.

The proportion of patients screened with the HADS during phase three was 100%. The proportion of patients screened in phase one or two using the HADS or other measure was not assessed. The authors reported a significant positive trend for the proportion of patients offered referral for psycho-oncological care between phase one and three ($t = 22.40$, $df = 2$, $p < 0.001$).

**Secondary outcomes**

***Psychosocial distress***

Only one study compared patients' levels of distress at follow up using the distress screening measure implemented. Braeken et al.[26-28] found no significant intervention effects as measured by the HADS for patients' psychological distress at three months or 12 months after baseline, nor dichotomous distress outcomes (no distress or at least moderate distress) at three months, or 12 months after baseline.

***Reported adverse consequences***

No study explicitly assessed whether the intervention had adverse effects.

**Quality of the evidence**

Using GRADE, the overall rating of the certainty of the body of evidence reported in this review was assessed as very low. The primary outcomes examined were downgraded one level to reflect high risk of bias and further downgraded two levels due to clinical heterogeneity and inconsistency in reporting either rates of distress screening or referral across both control and intervention periods. Since indirectness and imprecision also lowers the quality of the evidence, we downgraded two further levels on that basis. We found the quality of evidence to be of weak to moderate quality due to risk of bias using the EPHPP (Table 6), which identified a number of limitations, particularly among the pre post studies in regards to controlling for potential confounders.

## Discussion

This review sought to assess the impact of trials of strategies to improve clinician provision of: screening of cancer patients for psychosocial distress; and referral for further assessment and/or psychosocial support where necessary. The review identified just one trial that met the prospectively registered inclusion criteria of having a parallel control trial design. When these criteria were relaxed to include those with a non-parallel control group a further four trials were included. Largely due to study designs (i.e. mostly pre-post), none of the included studies were able to provide quality evidence for the effectiveness of screening procedures in improving in rates of distress screening. The intervention in just one trial was effective in significantly improving the rates of referral for psycho-oncological support for distressed patients. Such findings highlight the sparse evidence base for this important element of cancer patient care, and leave health services and cancer professionals with little clear guidance of strategies to improve provision of these elements of care to their patients.

Our findings are consistent with previous systematic reviews of trials aiming to improve depression or anxiety screening in primary care that have found that improvement in care provision is more likely when complex organisational change strategies are used, such as coordination between departments, enhanced role of nurses and performance feedback, in addition to clinician education[13-15]. The findings of the review highlight that the implementation of routine psychosocial screening and referral in cancer is complex and more rigorous research is needed. The trial by Zemlin et al.[29] was the only study included in the review to adopt a comprehensive implementation approach, and the only to report significant improvement in offer of referral of cancer patients for distress. Implementation strategies employed by other trials were primarily based on one off training and resource provision, suggesting that such support is insufficient. Comprehensive implementation strategies may be more likely to improve care given their greater capacity to address various barriers to

screening and referral. Interestingly, Zemlin et al[29] was the only study to describe strategies employed to change the organisational culture of the healthcare setting, specifically, defining responsibilities and tasks between the specialist disciplines and the medical and nursing staff involved in the treatment team, training certificates, as well as regular meetings to facilitate communication. It may be that simpler interventions are less effective in implementing routine provision of this care because they fail to address the organisational culture of the setting. Strengthening team communication[25] and making clinicians more aware of their role and responsibilities in distress screening and referral for cancer patients [27] may improve the rates of this care delivery. Further research identifying they key barriers to such care, and the best strategies to address them in cancer services is therefore warranted.

Surprisingly, none of the included studies examined the impact of strategies employed (e.g. training) to improve the rate of clinician provision of psychosocial distress screening. Due to the majority of study designs not employing a parallel comparison group, the review does not provide quality evidence regarding the effectiveness of implementation strategies to improve screening or referral. Such a finding is of concern. Screening is a necessary pre-requisite to appropriate referral of cancer patients to psychological support. As screening for psychosocial distress in cancer populations is low across jurisdictions[32], improving this form of care should represent a priority. Previous studies have used novel technologies to prompt screening by clinicians[33-35]. Such approaches should be examined in robust trial designs in cancer settings that allow for their impact on improving the rate of routine clinician provision of distress screening to be determined.

A number of methodological aspects of the study warrant highlighting and should be considered when interpreting the study findings. As far as the authors are aware, this is the first systematic review to examine the impact of interventions of strategies to improve the rate of clinician provision of distress screening and appropriate referral in cancer patients.

The review was prospectively registered, followed a peer reviewed protocol and included a comprehensive search strategy examining over 18000 citations. There was substantial clinical and methodological heterogeneity in the included studies. Classification of EPOC taxonomy implementation strategies was also difficult due to the lack of detail reported on intervention components in the studies. Furthermore, only one of the studies was a randomised controlled trial. Such characteristics of the included studies precluded quantitative synthesis of the effects of these strategies.

**Conclusions**

The findings of this review suggest that there is considerable scope to improve implementation of psychosocial distress screening and referral in cancer settings in order to establish a strong evidence base for future successful interventions. Implementation of psychosocial distress screening and appropriate referral needs to be employed using a systematic method and assessed with appropriately controlled studies in order to determine the most effective approaches. Better reporting of outcomes and more detailed description of intervention components need to be prepared.

**Figure 1. PRISMA Flow Diagram**

## Table 1. Trial characteristics

| Study | Design | Study dates | Single-centre or multicentre | Setting | Country | Aim | Patient inclusion criteria | No. of patients | Mean age in years (SD) | Gender (male) | Tumour site/Tumour stage | Cancer treatment type/Stage of treatment |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Thewes et al. 2009[31] | Pre post | NR. | Multicentre - 3 rural outpatient oncology clinics | Outpatient oncology clinics. | Australia | (i) Prospectively investigate the feasibility and acceptability of introducing a routine psychological screening program for rural oncology clinics; (ii) explore the impact of screening on rates and timeliness of referral to psychosocial services; and (iii) provide pilot data on the acceptability and utility of the DT as a screening tool within the rural Australian setting. | (i) Newly diagnosed with malignant disease; (ii) 18 years of age or older; (iii) able to give informed consent; and (iv) able to read English proficiently. | Unscreened cohort – 40. Screened cohort – 43. | 60.0 (10.5 SD). | 54.0% | Colorectal 22.9%, Breast 30.1%, Lung 14.5%, Other 13.2%, Haematological 9.6%, Skin 6.0%, Unknown primary 3.6%.<br><br>Localised/locally advanced 71.1%, Advanced or metastatic 28.9%. | Surgery 75.9%, chemotherapies 66.3%, RT 53%, endocrine therapies 32.5%.<br><br>Newly diagnosed patients. |
| Braeken et al. 2009[26], 2013[27] & 2013[28] | Cluster randomised controlled trial | April 2008 – October 2010. | Single | Institute Verbeeten (BVI) - a radiation oncology department (Tilberg). | The Netherlands | To study the effect of the SIPP on the number and types of referrals of cancer patients with psychosocial problems to psychosocial caregivers. | i) Receiving RT; ii) most common cancer types such as lung, prostate, bladder, rectum, breast, cervix, endometrial, skin and Non-Hodgkin; iii) 18 years of age or older; and iv) no metastases. Exclusion criteria: i) receiving palliative treatment, ≤ 10 fractions of RT; ii) unable to read and speak Dutch; and iii) unable to complete questionnaires. | Control group – 300. Intervention group – 268. | Control group 62.4 (10.7 SD), intervention group 62.4 (10.8 SD). | Control group 47.0%, intervention group 31.7%. | Prostate/Bladder 24.1%, Lung 11.3%, Breast 50.0%, Cervix/Endometrial 1.6%, Rectum 9.0%, Non-Hodgkin Lymphoma 1.7%, Skin 2.3%. | 100% RT.<br><br>SIPP before the first consultation prior to RT and SIPP2 before the consultation at the end of RT. |
| Ito et al. 2011[25] | Pre post | UP: April 1 - September 30, 2006. PP: April 1 | Single | Outpatient treatment center of the NCCH- | Japan | To examine the usefulness (rate of referral) of a screening program modified for outpatients | All consecutive cancer patients who began chemotherapy at the outpatient treatment | UP – 478. PP – 520. | UP 61.4 (10.8 SD), | UP 54.0%, PP | Lung 20.0%, Colon/rectum 18.2%, Breast 13.8%, Hematopoietic and | Chemotherapy.<br><br>Patients beginning chemotherapy at the outpatient |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | - September 30, 2007. | | E (Kashiwanoha, Kashiwa, Chiba). | | with cancer who are undergoing chemotherapy. | center of NCCH-E in Japan. | | PP 62.8 (10.9 SD). | 56.7%. | lymphatic tissue 12.8%, Stomach 7.9%, Pancreas 10.2%, Esophagus 5.5%, Liver, bile duct, gall bladder 4.6%, Head and Neck 2.8%, Other 4.0%.<br><br>Reported for PP only: Stage I 2.5%, Stage II 9.6%, Stage III 20.8%, Stage IV or recurrent 67.1%. | treatment center of the NCCH-E. |
| Zemlin et al. 2011[29] | Propsective consecutive study | NR. | Single | Clinic for Gynaecology of the University of Marburg Hospital (Marburg). | Germany | To examine whether a screening and computer-based psycho-oncological clinical pathway can improve the diagnosis of breast cancer patients requiring psycho-oncological support according to current guidelines. | Breast cancer patients who were in stationary treatment. | Phase 1 - 236, Phase II – 384, Phase III - 247. | 59.5 (12.2 SD). | 0.6% | Breast 100%.<br><br>Stage 0 (Ductal carcinoma in situ) 11.6%, Stage I 43.7%, Stage II 25.5%, Stage III 7.8%, Stage IV 11.2%. | Screening occurred on day of admission.<br><br>Stage of treatment NR. |
| Bauwens et al. 2014[30] | Pre post | UP: May 2010. DB period June 2010. | Single | Oncology Centre of the University Hospital (UZ Brussel). | Belgium | To evaluate the impact of systematic screening with the DB on detection rates of patients with elevated distress and on rates of psychosocial referral compared to usual practice. | i) Ambulatory patients; ii) 18 years and older; iii) diagnosed with cancer; iv) sufficiently fluent in the languages of the study (Dutch or French); and iv) not affected by a cognitive disorder. | UP – 278, DB period – 304. | 58.92 (13.03 SD). | 32.0% | Breast 43.9%, Lung 10%, Colon 8.6%, Prostate 3.4%, Gynaecological 7.7%, Skin 9.5%, Brain 7.4%, Other 9.5%<br><br>Local disease 33%, Locoregional disease 38.6%, Advanced disease 28.4% | No treatment 24.3%, surgery 3.1%, RT 1.7%, chemotherapy 43.3%, medication 18.9%, RT + chemotherapy 2.1%, chemotherapy + medication 5.8%, RT + medication 0.7%<br><br>Diagnosis 2.1%, active treatment curative intent 22.7%, active treatment palliative intent 53.0%, cured 9.8%, remission (partial/complete) 3.3%, palliative care 0.3%, wait and see 5.0%, recent recurrence 3.8%. |

NR, not reported; DT, Distress Thermometer; UP, usual care period; PP, program period; DB, Distress Barometer; NCCH-E, National Cancer Center Hospital East; DT, Distress Thermometer, SIPP; Screening Inventory Psychosocial Problems; RT, Radiotherapy.

**Table 2. Definition of EPOC subcategories**

| EPOC subcategory | Definition |
|---|---|
| Educational materials | Distribution to individuals, or groups, of educational materials to support clinical care, i.e. any intervention in which knowledge is distributed. For example, this may be facilitated by the internet, learning critical appraisal skills; skills for electronic retrieval of information, diagnostic formulation; question formulation. |
| Educational meetings | Courses, workshops, conferences or other educational meetings. |
| Educational outreach visits or academic detailing | Personal visits by a trained person to health workers in their own settings, to provide information with the aim of changing practice. |
| Reminders | Manual or computerised interventions that prompt health workers to perform an action during a consultation with a patient, for example computer decision support systems. |
| Organisational culture | Strategies to change organisational culture. |
| Continuous quality improvement | An iterative process to review and improve care that includes involvement of healthcare teams, analysis of a process or system, a structured process improvement method or problem solving approach, and use of data analysis to assess changes. |

## Table 3. Intervention description

| Study | Healthcare providers | Distress screening tool | Referral criteria | Training | Intervention | Control/Comparison | EPOC subcategories |
|---|---|---|---|---|---|---|---|
| Thewes et al. 2009[31] | Nurses | The DT - a single item screening measure that identifies level and causes of distress.<br><br>Respondents are asked to indicate their level of distress in the past week on an 11-point scale ranging from 0 ('None') to 10 ('Extreme'). | Screening cohort - for individuals who scored above the cut-off score (≥5), nursing staff were encouraged to assess problems and concerns and explore the patient's interest in receiving referral to psychosocial staff using the skills and strategies discussed in the initial training session. | Nursing and psychosocial staff participated in a 2 hour training session covering the screening procedure and suggestions for how to discuss the results of screening with patients who scored above cut-off. | Distress screening was completed immediately before an initial oncologist rural clinic appointment or chemotherapy education session. | All participants completed the SPHERE-Short at baseline; a 12-item questionnaire measuring common psychological and somatic distress developed and validated in Australia. The SPHERE- Short has 2 subscales: PSYCH-6 and somatic symptoms. A score of ≥2 on the PSYCH-6 subscale indicates a likely case of psychological disorder. | Educational materials, educational meetings. |
| Braeken et al. 2009[26], 2013[27] & 2013[28] | Radiation oncologists | The SIPP - a short, valid and reliable 24-item self- reported questionnaire that systematically identifies psychosocial problems in Dutch cancer patients. Items are rated on a 3-point scale of 0 (no) to 2 (yes). Higher scores indicate poorer functioning. | Intervention: Potential referral to a psychosocial caregiver was based on the scores of the SIPP in combination with the radiation oncologist's judgement.<br><br>Control: According to the radiation oncologist's judgement about the presence or absence of psychosocial problems in patients. | Before the start of the study, the radiation oncologists in the experimental condition were trained in using and interpreting the SIPP during a 1 hour training session.<br><br>Training was given by the researcher and two social workers with experience in using and discussing the SIPP. | Patients received the SIPP just before the first and last consultation with the radiation oncologist. Psychosocial problems were discussed with the patient during the consultation and referral to a psychosocial caregiver occurred only with the permission of the patient.<br><br>The radiation oncologists were stratified according to general percentages of incoming patients they referred in 2006–2007 and then randomised to experimental or control condition. | Care as usual - no recent guidelines for the systematic assessment of psychosocial problems in cancer patients existed at the Institute Verbeeten. The radiation oncologist was able to refer patients to psychosocial caregivers (social workers) at the Institute Verbeeten based on their clinical judgement. | Educational materials, educational meetings, educational outreach visits. |
| Ito et al. 2011[25] | Pharmacists | The DIT - a 2 item, self-administered rating scale.<br><br>Each 'distress' and 'impact' question is scored using an 11-point Likert scale, with scores ranging from 0 to 10 and a high score indicating an unfavourable status. | PP - if a patient scored equal to or more than each cut-off point (≥ 4 for distress and ≥ 3 for impact) the screening result was regarded as positive. | Before implementing the screening program, all the pharmacists attended a 2 hour lecture given by a trained psychiatrist regarding the epidemiology, impact, risk factors, under-recognition, and appropriate management of psychiatric disorders in cancer patients. Additionally, the pharmacists underwent role-play training to learn | Pharmacists providing instructions to patients beginning chemotherapy at their first and second visit also provided information regarding the Psychiatric Service using a brief pamphlet and invited the patients to complete the DIT. The pharmacist then completed the screening program sheet, which is a record of the patient's DIT scores.<br><br>The pharmacist recommended a consultation with the Psychiatric Service | UP was not described in detail. | Educational materials, educational meetings, educational outreach visits, reminders. |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | how to implement the DIT and to give recommendations for psychiatric referral. | to all the patients with a positive screening result and recorded the screening results on the medical chart. | | |
| Zemlin et al. 2011[29] | BCN's and doctors | The HADS - scores of more than 13 indicate clinically suspected psychological distress. | Phase I – BCN's and doctors asked the patient about their interest in a psycho-oncological consultation where they felt necessary.<br><br>Phase II – BCN's asked all patients about their interest in a psycho-oncological consultation on day of admission.<br><br>Phase III – patients were referred to a psycho-oncological interview if i) they scored > 13 on the HADS; ii) the doctor had a clinical impression that the patient required referral; or iii) the patient desired referral. | Certified training courses for clinicians, gynaecologists and psychotherapists as well as other professional groups of the inpatient and outpatient network were carried out. | In Phase III, all patients completed the HADS questionnaire. The BCN evaluated the HADS and informed the patients about the possibility of a psycho-oncologic initial interview. The BCN passed the evaluated HADS sheet to the physician. For those patients with psycho-oncological need (threshold HADS score and/or clinically suspected treatment oriented psychological distress) the doctors recommended a psycho-oncological interview. Each patient with a desire for psycho-oncological care was logged and offered initial interview (regardless of HADS score). | In Phase I, BCN's and doctors asked the patient about their interest in a psycho-oncological consultation where they felt necessary. In addition, all patients received information on psychosocial support options. | Organizational culture, continuous quality improvement, educational materials, educational meetings, reminders. |
| Bauwens et al. 2014[30] | Seven oncologists | The DB - comprises three parts:<br><br>1. The DT (described above). The VAS was slightly adapted by using a background colour effect with anchors labelled 'no distress' through 'moderate distress' and 'extreme distress'.<br><br>2. The CCS, which consists of 10 items that are rated on a coloured 5-point scale. Patients are required to rate how much each of a list of sources of distress has been troubling them lately.<br><br>3. Additional Wish-Needs Questions: 4 additional questions regarding complaints and needs for further medical information and/or support. | UP condition - oncologists used their own VAS assessment of distress to decide on an eventual referral. Whereas in the DB condition, the cut-off point for the DB (Distress Thermometer ≥4 and elevated CCS was used by the oncologists for this purpose. | In a collective 1 hour session held shortly before the DB condition, oncologists were instructed in using the DB and were given a written explanation on how to interpret DB results. | Two week period<br><br>DB condition - The DB was administered before the consultation with the oncologist.<br><br>Also in the DB condition, oncologists had a form with three other yes/no questions: (2) if they considered referral necessary, (3) if they actually gave an advice for referral and (4) if referral was accepted by patients. | 2 week period<br><br>UP condition - The DB was administered after the consultation with the oncologist.<br><br>Also in the UP condition, oncologists had a form with four other questions: (1) their rating of patients' distress on a VAS (0–10), (2) if they considered referral necessary, (3) if they actually gave advice for referral and (4) if referral was accepted by patients. | Educational materials, educational meetings. |

BCN, breast care nurse; DT, Distress Thermometer; DIT, Distress and Impact Thermometer; HADS, Hospital Anxiety and Depression Scale; DB, Distress Barometer; VAS, Visual Analogue Scale; CCS, Coloured Complaint Scale; PP, program period; UP, usual care period; SIPP; Screening Inventory Psychosocial Problems; SHPERE-Short, Somatic and Psychological Health Report Short form; PSYCH-6, psychological symptoms.

## Table 4. Primary outcomes

| Study | Distress screening | | Referral | |
|---|---|---|---|---|
| | Measure; data collection method | Results | Measure; data collection method | Results |
| Thewes et al. 2009[31] | Proportion of patients screened.<br><br>NR. | Pre-screening phase – proportion of patients screened (using any distress screening tool) was not reported.<br><br>Screening phase – all patients were screened using the DT. | Proportion of patients referred in the pre-screening phase compared to the screening phase.<br><br>Review of referral records and databases. | Pre-screening phase - Of the 8 PSYCH-6 cases in the pre-screening phase, 6 were referred to a CCC and 5 to a social worker/psychologist.<br><br>Screening phase – 10/19 (53%) patients that met the DT cutoff were referred to a social worker or psychologist (11 of 14 PSYCH-6 cases were referred to the CCC and 8 to a social worker/psychologist). |
| Braeken et al. 2009[26], 2013[27] & 2013[28] | Proportion of patients screened.<br><br>NR. | Control group – proportion of patients screened (using any distress screening tool) was not reported.<br><br>Intervention group – 263/268 (98%) were screened using the SIPP before the first consultation. 250/268 (96%) were screened using the SIPP before end of radiotherapy consultation. | The number of referrals of patients with psychosocial problems to psychosocial workers at the Institute Verbeeten and/or to external health care providers (e.g. psychologists, psychiatrists). Three dichotomous outcome variables (yes/no) during the first 3 months, the last 9 months, and the total study period.<br><br>Measured at 3 and 12 months after baseline assessment with a self-developed questionnaire by the patient and from registration records of the psychosocial caregivers at the Institute Verbeeten. | First 3 months - Control group 29/300 (9.7%) vs intervention group 34/268 (12.7%) patients referred (NS).<br><br>Last 9 months – Control group 24/300 (8%) vs intervention group 19/268 (7.1%) patients referred (NS).<br><br>Group differences in these outcomes were analysed using Generalized Estimating Equations with patients at level 1 and radiation oncologists at level 2. All models were adjusted for baseline differences with respect to gender and cancer diagnosis. Analyses were taken on an intention-to-treat principle.<br><br>Generalised Estimating Equations found that numbers of referrals did not differ significantly between the intervention and control group at 3 months (β =-0.16, SE±0.34, p=0.32), 9 months (β =0.22, SE±0.28, p = 0.22) or overall months (β =-0.04, SE±0.28, p = 0.44). |
| Ito et al. 2011[25] | Proportion of patients screened.<br><br>NR. | UP – proportion of patients screened (using any distress screening tool) was not reported.<br><br>PP – 441/520 (84.8%). | Proportion of patients referred to the Psychiatric Service and treated for MDD or AD among all the outpatients who had begun a new chemotherapy regimen within 3 months of their visit to the outpatient clinic.<br><br>Data extracted from patients' medical charts and the computerized database of the electronic medical record at NCCH-E. | Retrospective cohort analysis (Chi-squared test comparing patients treated during the PP with historical control data gathered during the UP).<br><br>UP – 5/478 (1.0%) vs PP – 15/520 (2.7%) patients referred to the Psychiatric Service with subsequent confirmed and treated for MDD or ADs ($p$ = .46). |
| Zemlin et al. 2011[29] | Proportion of patients screened.<br><br>NR. | Proportion of patients screened in Phase I or II screened (using any distress screening tool) was not reported.<br><br>All patients in Phase III were screened using the HADS. | Proportion of patients offered referral for psycho-oncological interview.<br><br>Medical records. | Univariate data analysis.<br><br>Cochran-Armitage test.<br><br>Phase I – 194/236 (82.2%) vs Phase II 344/384 (89.6%) vs Phase |

| | | | | |
|---|---|---|---|---|
| | | | | III 236/247 (95.5%) were informed/offered the psycho-oncological interview. There was a significant positive trend for the proportion of patients informed about the psycho-oncological care available (t = 22.40, df = 2, $p$ <0.001). |
| Bauwens et al. 2014[30] | Proportion of patients screened.<br><br>NR. | UP condition – all patients were screened with the DB after consult with oncologist (therefore not used as part of the referral decision).<br><br>DB condition – all patients were screened with the DB prior to consult with the oncologist. | Necessary referrals (UP condition: referrals necessary as per oncologists' VAS ratings, DB condition: referrals necessary for all patients with distress according to the DB).<br><br>Self-assessment. | UP condition – 13.8% of patients with elevated distress (or 5.4% of all patients), DB condition - 100% of patients with distress (or 41.6% of all patients). |
| | | | Referrals made (UP condition: proportion of patients for whom referral was considered necessary by the oncologists and were actually referred to psychosocial care, DB condition: proportion of patients with elevated distress that were referred).<br><br>Self-assessment. | UP condition – 6/15 patients, DB condition - 85/123 patients. |

NR, not reported; DT, Distress Thermometer; UP, usual care period; SIPP; Screening Inventory Psychosocial Problems; PP, program period; DB, Distress Barometer; MDD, Major Depressive Disorder; AD, Adjustment Disorder; NCCH-E, National Cancer Center Hospital East; VAS, visual analogue scale; CCC, cancer care coordinator; NS, not significant.

## Table 5. Secondary outcomes

| Study | Measure; data collection method | Results |
|---|---|---|
| Braeken et al. 2009[26], 2013[27] & 2013[28] | Extent of psychological symptoms at 3 months and 12 months after baseline.<br><br>Measured with the HADS and the GHQ-12 (assesses with 12 items whether the patient considers him- or herself better, the same, worse or much worse over the previous four weeks than he/she "usually" is. Total scores range from 0 to 12). Patients complete these self- reported questionnaires at baseline and at 3 and 12 months after the baseline period. | Mixed effects' modelling.<br><br>No significant intervention effects were observed for patients' extent of psychological distress. (3 months after baseline mean psychological distress score control group 2.85 vs intervention group 2.74, $p = 0.19$; 12 months after baseline mean psychological distress score control group 2.14 vs intervention group 1.96, $p = 0.12$). |
| | Group differences in the proportion of dichotomous distress outcome (no or at least moderate distress) at 3 months and 12 months after baseline.<br><br>Measured with HADS and GHQ-12. | Generalised estimating equations.<br><br>No significant intervention effects were observed for proportion of patients with distress (3 months after baseline control group 39% vs experimental group 38.4%, $p = .036$; 12 months after baseline control group 24.7% vs intervention group 24.3%, $p = 0.39$). |

HADS, Hospital Anxiety and Depression Scale; GHQ-12, Goldberg's General Health Questionnaire-12 item version.

**Table 6. Ratings of methodological quality: strong (S), moderate (M) and weak (W)**

| **Study** | *Selection bias* | *Study design* | *Confounders* | *Blinding* | *Data collection* | *Withdrawals* | *Global rating* |
|---|---|---|---|---|---|---|---|
| Thewes et al. 2009[31] | Moderate | Moderate | Weak | Moderate | Weak | Moderate | Weak |
| Braeken et al. 2009[26], 2013[27] & 2013[28] | Moderate | Strong | Strong | Moderate | Weak | Strong | Moderate |
| Ito et al. 2011[25] | Moderate | Moderate | Strong | Moderate | Weak | Moderate | Moderate |
| Zemlin et al. 2011[29] | Moderate | Moderate | Weak | Moderate | Weak | Moderate | Weak |
| Bauwens et al. 2014[30] | Moderate | Moderate | Weak | Weak | Weak | Weak | Weak |

## AUTHORS' CONTRIBUTIONS

KM and LW conceptualised the review with input from BB, AB, SAH, AKB, GC, CW, JB, DB, EF. KM and EF conducted screening, data extraction and methodological quality analysis. KM and LW drafted the manuscript. All authors contributed to subsequent drafts and have approved the final version of the manuscript.

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## COMPETING INTERESTS

The authors declare that they have no competing interests.

## DATA SHARING STATEMENT

No additional data available.

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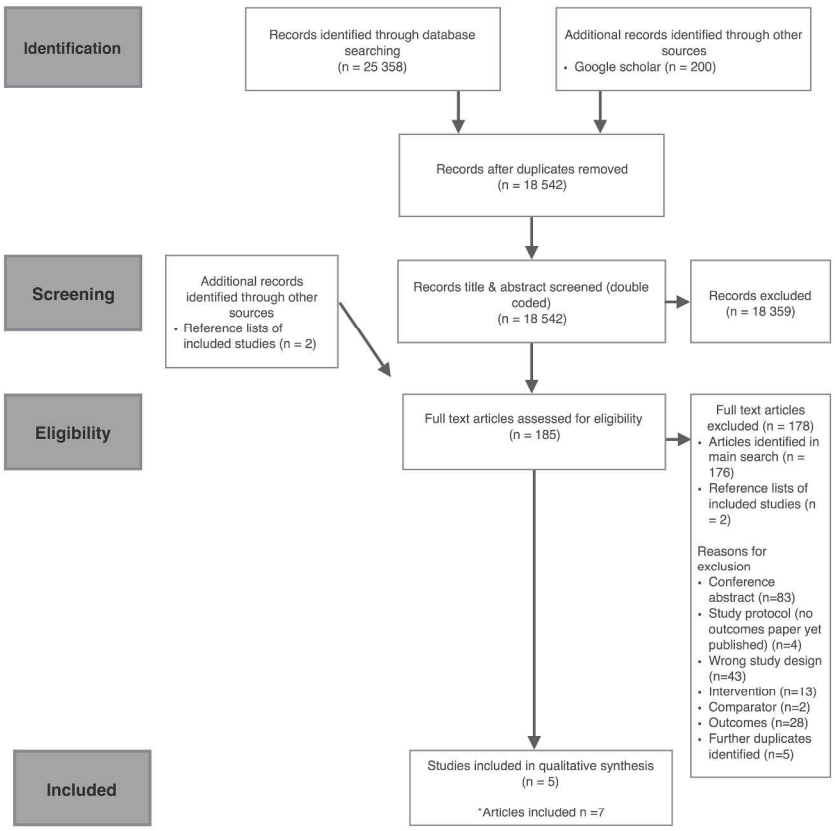


Figure 1. PRISMA Flow Diagram

296x420mm (300 x 300 DPI)

## MEDLINE SEARCH STRATEGY

1. cancer*.mp.
2. exp Neoplasms/
3. tumo?r*.mp.
4. malignan*.mp.
5. exp Adenocarcinoma/
6. exp Leukemia/
7. leukaemia*.mp.
8. metastat*.mp.
9. exp Carcinoma/
10. exp Medical Oncology/
11. exp Sarcoma/
12. choriocarcinoma*.mp.
13. lymphoma*.mp.
14. teratoma*.mp.
15. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14
16. screen*.mp.
17. measure*.mp.
18. assess*.mp.
19. Questionnaires/
20. Diagnosis/
21. instrument.mp.
22. validat*.mp.
23. 16 or 17 or 18 or 19 or 20 or 21 or 22
24. distress*.mp.

25. Stress, Psychological/

26. Anxiety/ or exp Anxiety Disorders/

27. Depression/

28. depress*.mp.

29. exp Depressive Disorder/

30. Dysthymic Disorder/

31. Adjustment Disorders/

32. "Quality of Life"/

33. psychosocial.mp.

34. Depressive Disorder, Major/

35. 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34

36. (psychosocial adj3 (care* or support* or service*)).mp.

37. Counseling/

38. (psychological adj3 (support* or care* or service* or therap* or intervention*)).mp.

39. exp Psychotherapy/

40. Mental Health Services/

41. (psycho oncology or psychooncology).mp.

42. Supportive care.mp.

43. Support service*.mp.

44. Social Support/

45. 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44

46. Intervention Studies/

47. implement*.mp.

48. disseminat*.mp.

49. adopt*.mp.

50. practice*.mp.

51. organi?ational change*.mp.

52. diffusion.mp.

53. system* change*.mp.

54. quality improvement*.mp.

55. transform*.mp.

56. translat*.mp.

57. transfer*.mp.

58. uptake*.mp.

59. sustainab*.mp.

60. institutionali*.mp.

61. routin*.mp.

62. maintenance.mp.

63. capacity.mp.

64. incorporat*.mp.

65. adher*.mp.

66. program*.mp.

67. integrat*.mp.

68. scal*.mp.

69. Randomized Controlled Trial/

70. Non randomized controlled trial*.mp.

71. Random Allocation/

72. Evaluation Studies/

73. Pilot study.mp. or Pilot Projects/

74. Evaluation Studies as Topic/

75. Cohort Studies/

76. Controlled Before-After Studies/

77. Historically Controlled Study/

78. Cross-Sectional Studies/

79. (intervention$ adj5 stud$).mp.

80. feasibility pilot*.mp.

81. sequential cohort.mp.

82. Interrupted-time-series stud*.mp.

83. case series.mp.

84. program*.mp.

85. intervention*.mp.

86. Random*.ab.

87. exp clinical trial/

88. trial.ab.

89. double blind.ab.

90. single blind.ab.

91. experiment*.mp.

92. (pretest or pre test).mp.

93. (posttest or post test).mp.

94. (pre post or prepost).mp.

95. Before after.mp.

96. (Quasi-randomised or quasi-randomized or quasi-randomized or quazi-randomised).mp.

97. stepped wedge.mp.

98. Comprehensive cohort.mp.

99. Natural experiment.mp.

100. (Quasi experiment or quazi experiments).mp.

101. (Randomised encouragement trial or randomized encouragement trial).mp.

102. (Staggered enrolment trial or staggered enrollment trial).mp.

103. (Nonrandomised or non randomised or nonrandomized or non randomized).mp.

104. Interrupted time series.mp.

105. (Time series and trial).mp.

106. Multiple baseline.mp.

107. 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 6 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or 90 or 91 or 92 or 93 or 94 or 95 or 96 or 97 or 98 or 99 or 100 or 101 or 102 or 103 or 104 or 105 or 106

108. 15 and 23 and 35 and 45 and 107

109. psychology.mp. or Psychology/

110. social work*.mp.

111. 45 or 109 or 110

112. 15 and 23 and 35 and 107 and 111

# PRISMA 2009 Checklist

| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| **TITLE** | | | |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | 1 |
| **ABSTRACT** | | | |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | 2-3 |
| **INTRODUCTION** | | | |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | 5-7 |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | 7 |
| **METHODS** | | | |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | 7 |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | 7-9 |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | 9-10 |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | 9 |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | 10-11 |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | 10-11 |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | 11 |
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | 11-12 |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | 12 |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$) for each meta-analysis. | 12-13 |

# PRISMA 2009 Checklist



| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| Risk of bias across studies | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). | 12-13 |
| Additional analyses | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | N/A |
| **RESULTS** | | | |
| Study selection | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | 13, F1 |
| Study characteristics | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | 13-14 Tables 1, 3, 4, 5 |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | 15, Table 6 |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | 14-15 |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | 15-19 |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | 19 |
| Additional analysis | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | N/A |
| **DISCUSSION** | | | |
| Summary of evidence | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | 19-22 |
| Limitations | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | 19-22 |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | 22 |
| **FUNDING** | | | |
| Funding | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | 33 |

*From:* Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097