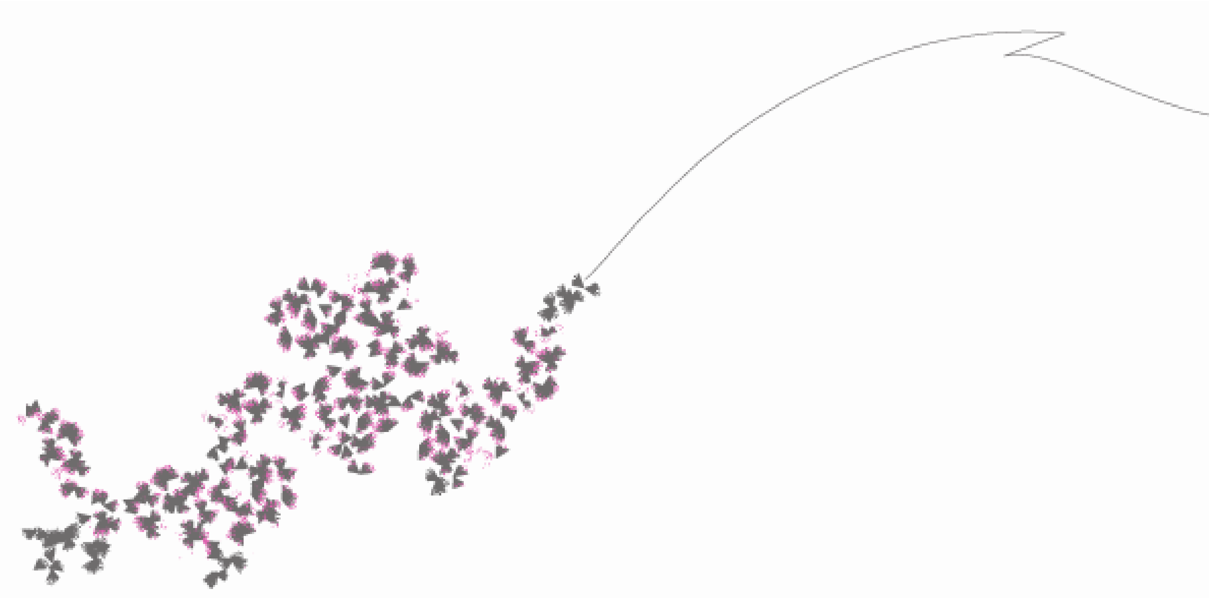

The effectiveness of psychosocial online interventions for cancer patients after initial treatment. A review of the literature.

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Abstract (English)

Background: Negative psychosocial consequences are common in conjunction with a cancer diagnosis. After completion of initial treatment, patients go through a transition from cancer patient to cancer survivor. This phase of re-entry is associated with a considerable psychosocial burden, affecting various aspects of patients daily life. To challenge those psychosocial disturbances, several approaches exist today. In recent years, the internet has become a popular medium of delivery for psychosocial interventions. Previous reviews however, did not clearly distinguish between cancer patients in initial treatment and cancer survivors.

Objective: The aim of this review was to investigate whether psychosocial online interventions are effective in improving psychosocial outcomes in cancer survivors. Furthermore, to explore the therapeutic approaches that have been used in psychosocial online interventions and whether a correlation becomes apparent between effectiveness and the underlying therapeutic approach.

Method: Searches were performed in PubMed and PsycINFO, to identify peer-reviewed articles that studied the effects of online psychosocial interventions for cancer survivors. Furthermore the grey literature was searched. Studies were eligible if they focused on adult cancer survivors and addressing at least one of our primary (Quality of Life, distress, depression, anxiety) or secondary (fatigue, pain, physical activity) outcomes.

Results: Finally, three studies were identified as eligible. All studies had a moderate risk of bias. Yet, only one intervention had the necessary power to draw conclusions about effectiveness. Significant treatment effects for one outcome were established in two interventions. Participants in this studies were screened on the presence of symptoms in advance. All of the three interventions were based on cognitive behavioural therapy.

Conclusions: It is concluded that a limited number of psychosocial interventions is offered to cancer survivors. For that reason, conclusions about the effectiveness could not be drawn. An indicator of effectiveness seemed to be, the inclusion of participants based on the presence of symptoms and the clear specification of theory-based outcomes, which the intervention aims to target. CBT seems to be the means of choice as the underlying approach of structured psychosocial online interventions for cancer survivors. More research in this field is needed to be able to draw strong conclusions about the effectiveness of those interventions.

Abstract (Dutch)

Achtergrond: Negatieve psychosociale gevolgen zijn veel voorkomend in samenhang met een kanker diagnose. Na afsluiting van de initiële behandeling, komen patiënten in een process van verandering. In plaats van patient gaan ze zich ontwikkelen naar een overlevende. Deze fase is gekenmerkt door opmerkelijke psychosociale belastingen, welke het dagelijks leven van de patienten beinvloeden. In de afgelopen jaren, is het internet populairder geworden als medium voor overdracht van psychosociale interventies. Voorafgaande reviews maakten echter geen verschil tussen patienten in initiële behandeling en overlevenden.

Doel: Doelstelling van deze review was, te onderzoeken of psychosociale online interventies effectief zijn in de verbetering van psychosociale uitkomstmaten. Bovendien, te kijken welke therapeutische benaderingen ten grondslag liggen aan dergelijke interventies en of er mogelijk een samenhang bestaat tussen effectiviteit en de therapeutische benadering.

Methode: Een systematische zoekstrategie in PubMed en PsycINFO heeft plaats gevonden, om relevante peer-reviewed artikelen te indentificeren. Bovendien vond een grey literature search plaats. Studies die gericht waren op volwassen kanker overlevenden en op ten minste éen van onze primaire (Quality of Life, distress, depressive, angst) of secundaire (vermoeidheid, pijn, fisieke aktiviteit) uitkomstmaten waren geschikt voor deze review.

Resultaten: Uiteindelijk voldeden drie studies aan de gestelde criteria. Alle studies hadden een moderate risk of bias, maar alleen éen studie had voldoende power om concrete conclusies te trekken. Significante behandelingseffecten zijn in twee studies gevonden, op éen uitkomstmaat. Deelnemers in deze studies worden van tevoren gescreened op de aanwezigheid van symptomen. Alle drie studies waren gebaseerd op cognitieve gedragstherapie.

Conclusies: Het kan geconcludeerd worden, dat slechts een beperkte aantal aan psychosociale online interventies bestaat. Om deze reden is het niet mogelijk om echt conclusies te trekken wat betreft de effectiviteit van dit sort interventies. Een indicator voor effectiviteit blijkt te

zijn, deelnemers op basis van aanwezigheid van symptomen te includeren in de interventies en dat theorie-gebaseerde uitkomstmaten van tevoren al gedefineërd worden. Cognitieve gedragstherapie blijkt de favoriete benadering te zijn als het gaat om gestructureerde psychosociale online interventies voor kanker patiënten. Om conclusies te kunnen trekken wat betreft hun effectiviteit is echter uitgebreider onderzoek op dit gebied nodig.

Introduction

In recent years there is a growing interest for psychosocial interventions delivered via the internet. Several studies have been conducted to test whether psychosocial online interventions are effective in a population of cancer patients and whether they are as effective as their face-to-face counterparts. Existing research points out that cancer survivors may experience social life disruptions and distress even decades post diagnosis (Bloom 2002). In this context, the following review aims to investigate, if psychosocial online interventions are effective in addressing the negative psychosocial impact of cancer in a population of cancer survivors irrespectively of the type of cancer. The term cancer survivor, refers in this review to the group of cancer patients that is living beyond cancer or living with progressive cancer, with the exception of patients in the terminal phase of the disease (Macmillan Cancer Support, 2013).

According to the World Health Organization (WHO) (2013), cancer is the leading cause of death in economically developed countries and the second leading cause in the developing world. Worldwide there were approximately 12.7 million new cancer cases in 2008 and an estimated 7.6 million deaths due to cancer. In consequence of the adoption of western lifestyles in less developed countries – poor diet, smoking etc. – the burden of cancer is estimated to be much larger in the future, with an estimated number of 13.1 million deaths due to cancer worldwide in 2030. At the same time, due to advances in the screening for cancer, early detection and treatment options, the number of long-term cancer survivors (> 5 years post diagnosis) is steadily increasing (American Cancer Society, 2007; American Cancer Society, 2011). Quite a number of cancer survivors face negative psychosocial consequences, in any form, due to the disease. The possible psychosocial obstacles will be discussed in this review. The above mentioned facts raise questions about the availability and effectiveness of existing psychosocial online therapies to deal with the possible negative psychosocial consequences of cancer.

The psychosocial impact of cancer

Besides possible death cancer may lead to many other problems –psychological, physical and social (Revenson, Wollman & Felton, 1983; Stein, Syrjala & Andrykowski, 2008). When talking about the psychosocial impact of cancer, the literature often refers to emotional or psychological distress (i.e. unpleasant emotions or feelings raising difficulties in the ability to cope with cancer effectively) and Quality of Life (QoL) (i.e. perception of position in life, social relationships, physical & psychological functioning and emotional well-being). In the acute phase of the illness the environment usually responds to the patient in a way of understanding, sympathy and compassion. After initial treatment the ill person turns into a survivor. As a consequence thereof the former carers expect a process of getting over it and moving on, any time soon. The obstacles, which will be discussed in the following, may exacerbate the way back to normal life, making it hard to construct meaning in future life or to accept changes to mind and body in conjunction with the diagnosis of cancer, the treatment, or possible post-operative sequelae (Little, Paul, Jordens & Sayers, 2002).

The time after initial treatment is dominated by uncertainty and fear of recurrence (Ferrell, Grant, Funk, Otis-Green & Garcia, 1998, Berg et al., 2011). If life, was previous to the disease especially burdened or quite the opposite, especially balanced and prosperous the likelihood of the development of depressive symptoms or demoralization increases (Schulz-Kindermann, 2013). In some patients anxious thoughts remain in a period of long remission and health-related worries manifest themselves over the course of time into more general forms of heightened distress, as anxiety or depression, who are commonly prevalent in cancer patients and survivors (Stark & House, 2000; Mullens, McCaul, Erickson & Sandgren, 2004; Miller & Massie, 2006; Miller & Massie, 2010). In a recent review Mitchell, Ferguson, Gill, Paul & Symonds (2013) found a pooled mean prevalence of depression ranging from 8-16% and a pooled mean prevalence of anxiety ranging from 13-24% in long-term cancer survivors.

On a physical level, a great number of cancer patients suffers from pain related to cancer. During treatment, pain could often be well-treated and tolerated by the patient, but the post-therapeutic persistence of pain as a result of the disease itself or its treatments inevitably affects nearly every aspect of patients' daily life and must therefore be seen as a source of distress (Cleeland, 1984 & 2000). Furthermore cancer-related fatigue (CRF) is a frequently mentioned byeffect, irrespectively of the type of cancer. It is reported from a majority of patients, that CRF belongs to the most disturbing symptoms associated with a cancer diagnosis, leading to increases in distress and great impairments in daily life (Hofman, Ryan, Figueroa-Moseley, Jean-Pierre & Morrow, 2007). Others have to deal with changes in body image due to indispensable surgery. These are, most often, patients suffering from breast-, colorectal- or bladder-cancer. According to DeFrank, Mehta, Stein & Baker (2007) 16-54% of female and 11-36% of male cancer survivors reported some dissatisfaction with their body image.

Cancer is an extreme experience, challenging the personal identity seriously. A great number of cancer survivors, 41-84% according to Taskila & Lindbohm (2007), succeeds in picking up life again. Others have to struggle with the above mentioned symptoms, making it harder for them to go back to work or fulfilling the former role in social life (Little, Paul, Jordens & Sayers, 2002; Main, Nowels, Cavender, Etschmaier & Steiner, 2005). To challenge this negative impact of cancer, psychosocial interventions can provide the cancer survivor with strategies and tools, to cope more effectively with the disease and its consequences.

Psychosocial interventions for cancer patients

In the past 30 years a considerable amount of psychosocial research has been done in the field of cancer. Hodges et al. (2010) pointed out that no clear definition exists of what a psychological or psychosocial intervention per se is. In their metareview they recommend authors of a review to subcategorize studies according to four useful treatment domains a) techniques applied in the intervention e.g. relaxation, education or modelling; b) the proposed mechanisms with which the intervention is about to bring change in terms of the desired outcome e.g. belief change; c) the method of delivery of the intervention e.g. self-help, psychoeducation, face-to-face individual psychotherapy; d) the target outcomes of the intervention e.g. distress, QoL, anxiety.

To name but a few, several approaches have been applied in cancer populations. Psychoeducation is a popular approach for the transfer of knowledge related to cancer and intended to give information about the diagnosis and its possible impact, to help the individual cope with the disease effectively (Simeit & Hoffmann, 2013). Moreover supportive-expressive therapy (SGT) has established itself in psychooncology. The aims of these approaches are the stabilization and relief of the cancer patient, respectively helping to get a deeper appreciation (Schulz-Kindermann, 2013). In a recent systematic review and meta-analysis, focusing on pain in breast cancer patients and survivors, statistically significant overall effects sizes were found for individual and group psychoeducation (Hedges' $g= 0.64$), for SGT ($g= 0.17$) and for relaxation, meditation and yoga ($g= 0.31$) (Johannsen, Farver, Beck & Zachariae, 2013). CBT likewise has proven to be an effective method to treat mental disorders in cancer populations. In the past, several studies have been conducted to highlight the effectiveness of CBT for cancer-related pain (i.e. Dalton, Keefe, Carlson & Youngblood, 2004), anxiety (i.e. Greer et al., 2012) or major depression (i.e. Brothers, Yang, Strunk & Andersen, 2011). In a narrative review by Ranchor et al. (submitted) it was found that CBT interventions, for cancer survivors, who have survived the disease for at least one year after diagnosis, may result in significant treatment effects in the short term. All of the above mentioned approaches can be provided in the context of group therapy as well as individual therapy. Some of them do not constitute a fixed programme themselves, but can contribute as a part of the whole intervention programme.

Psychosocial interventions - Online

With the internet becoming a common part of peoples daily lives and one of the primary sources of information acquisition, there is a growing alertness by researchers, to use this medium as a method of delivery for interactive health communication. Online interventions often are traditional evidence-based face-to-face methods which were transformed into online content. They have the possibility to overcome barriers and are furthermore time- and cost-effective. People living in rural areas with little or no access to mental health services in their region get the opportunity to participate in an intervention at home. Likewise online interventions can reach disabled and less mobile people in their homes. For some the attachment of a stigma prevents them from making use of mental health services (Meier, Fitzgerald & Smith, 2013; Mitchell & Murphy, 1998), seeing that others may expect the survivor to pick up life again and go on, instead of being disabled by any means (Little et al., 2002). In this sense, participation in an online intervention provides an opportunity to follow a therapy more anonymous and in privacy.

Since the year 2000, a number of reviews has been written, concerning psychosocial online interventions for cancer patients. The spectrum of online interventions, investigated in earlier reviews is broad. It reaches from non-guided to guided online social support groups for cancer patients (Finfgeld, 2000; Hong, Peña-Purcell & Ory, 2012). Others reviewed interventions based on person-centred therapy, cognitive (behaviour) therapy and mindfulness-based therapies or composites of different methods (Ryhänen, Siekkinen, Rankinen, Korvenranta & Leino-Kilpi, 2010; Ventura, Ohlén & Koinberg, 2012). Some did not solely focus on cancer but comprised other chronic conditions as well (Andersson, Ljótsson & Weise, 2011; Kuijpers, Groen, Aaronson & van Harten, 2013; Paul, Carey, Sanson-Fisher, Houlcroft & Turon, 2013).

The effectiveness of psychosocial online interventions: The results, regarding the effectiveness, were diverse in most of the reviews. Ventura et al. (2012) found positive effects of several interventions on a number of outcomes e.g. coping and QoL. Albeit, the methodological designs, implementations or evaluations of the interventions often left much to be desired. Furthermore, a great deal of interventions could not be termed a fixed programme. Others found positive effects on health literacy, but diverse effects on other outcomes such as QoL or anxiety (Ryhänen, 2010) Paul et al. (2013) found, that the data of the available studies regarding cancer patients, did not suggest that web-based approaches were particularly effective in reducing psychosocial disturbance. However, the design of those studies did not so much focus on intervention content and was largely self-directed. Kuijpers et al. (2013), in their review, found no positive effects on patient empowerment and physical activity for the one reviewed study focusing on cancer. Hong et. al (2011) found positive effects for coping and QoL, although none of them significant in the reviewed RCTs.

None of the previous reviews made a precise distinction between cancer patients in initial treatment and cancer survivors. With regard to the effects found, a great deal of reviews not only covers cancer, but other chronic conditions as well. In none, but one review (Paul et al., 2013) the psychosocial outcomes that actually should reflect the effectiveness of the interventions are clearly stated in advance and in the methodology. One review pretends to focus on cancer survivors (Hong et al., 2011), but a definition of the term cancer survivor lacks. In a majority of studies, participants either still were in initial treatment at the time of the intervention, or it was uncertain. In the other reviews, focusing on cancer exclusively, no consideration was bestowed upon this criterium, whether they still were in initial treatment or whether they already had completed initial treatment and could be termed a survivor. As for the quality of the investigated studies, none but one (Kuijpers et al. 2013) has made use of a risk of bias analysis to distinguish the studies in terms of the quality of the methodology. In addition, none of the previous reviews explicitly postulated that participants had to take part in a program online, meaning that they had to play an active role - as it is the case in face-to-face interventions.

Given the notable heterogeneity of the available reviews, it becomes clear, that it would be necessary to do another review, to investigate the effectiveness of psychosocial interventions for cancer survivors. Making sure that qualitative guidelines for this review allow for the drawing of conclusions about the effectiveness in this population.

Objective of this review

This review aims to investigate whether psychosocial online interventions are effective in a population of cancer survivors. The primary outcomes to reflect the effectiveness were improvement in Quality of Life, reduced distress, depression and anxiety - corresponding to the psychological adaptations associated with cancer. Secondary outcomes were fatigue, pain and physical activity - corresponding to the more physical functioning of cancer survivors. With reference to the main objective, related aims were the revelation of approaches that were used to target the negative psychosocial consequences in terms of primary or secondary outcomes and, to explore whether effectiveness correlates with the used approach.

Method

Criteria for considering studies for the review

Types of studies: Included in the review, were randomized controlled trials (RCT), studies with a pre-post-test design not randomizing participants into groups and uncontrolled clinical trials. Based on the fact that research in the area of online interventions is relatively novel, we have decided to include studies handling a less robust research design than RCTs. The lack of a control condition and the inadequate concealment of participants was considered as part of the risk of bias assessment.

To be accepted for the review studies had to be published in a peer-reviewed journal between January 1990 en May 2013.

Types of participants: Studies had to focus solely on adult cancer survivors as defined by the Macmillan Cancer Support (2013). According to the Macmillan Cancer Support, a cancer survivor is someone who is “living with or beyond cancer”. A cancer patient, who has completed initial treatment, for any cancer site, with no apparent evidence of active disease or who has had cancer in the past or is living with progressive cancer disease and may be receiving treatment, but is not in the terminal phase. A cancer survivor, in any case, has completed initial treatment At least 80% of participants in any of the interventions had to have completed initial treatment, because as mentioned earlier the needs and stressors vary in the stages post-diagnosis, in treatment and post-treatment (Little et al., 2002).

Participants could be diagnosed with any type of cancer, earlier research highlights that it is unnecessary to argue about special clinical programs for different cancer sites, because most psychosocial issues remain stable for one cancer type over another (Zabora, Brintzenhofeszoc, Curbow, Hooker & Piantadosi, 2001).

Studies focusing on healthcare professionals were excluded, also studies including participants diagnosed with cancer in childhood. Finally studies focusing on participants with chronic health conditions other than cancer were excluded.

Types of interventions: Interventions were included if they were available online and addressing the negative psychosocial impact of cancer, as related to the primary and secondary outcomes. In the context of this review the included studies could best be categorized in terms of the target outcomes (Hodges et al., 2010), which should reflect the effectiveness of the intervention. Although they all have to be delivered via the internet, the method of delivery could vary. As long as participants had to play an active role in the interventions, as it is the case in face-to-face psychosocial interventions, because *‘‘the quality of the patient’s participation in therapy stands out as the most important determinant of outcome’’* (Orlinsky, Grawe and Parks, 1994, p. 361). Furthermore, the intervention has to be a fixed programme allowing for participation in at least more than one session.

Thus, studies focusing on information giving only or pure online support groups, guided or non-guided, were excluded, due to the fact that they do not allow for active participation in a fixed program.

Interventions focusing on specific cancer-related side effects were included as long as the primary aim of the study was related to the primary and secondary outcomes of this review.

Search strategy for identification of studies

An online literature search on two databases, namely PubMed and PsychINFO was performed to identify eligible studies (between January 1990 and April 2013) for the review. Studies had to be reported either in English or German. The search was performed by a Master degree student using free text searches of title and abstract and MeSH terms. See Appendix 1 for the search methods.

Furthermore a hand search was performed on the basis of the reference lists of identified studies and previous reviews of psychosocial online interventions for cancer patients and studies that cite the earlier identified studies.

Data collection and analysis

Selection of relevant studies: In *step 1*, a sensitive but not specific search of the internet was performed and all titles and abstracts that should be taken into consideration were downloaded. They were checked, in *step 2*, for duplicates and false positives (evidently not fulfilling our criteria) - which were removed. In *step 3*, full-text copies were downloaded from the remaining titles, and subsequently checked on the basis of our criteria for eligibility (primary & secondary outcomes, type of intervention, etc.), except for the criterion of being a cancer survivor. Finally in *step 4*, the remaining studies were checked for information about the criterion of being a cancer survivor.

In a great number of papers, participants could not be identified as a cancer survivor and it remains unclear if, and how many participants were in initial treatment at the time of the intervention. To make sure that papers do or do not fulfil our criteria to be termed a cancer survivor, or that only a small percentage of participants (< 20%) still was in initial treatment at the start of the intervention, authors were contacted via email to get the necessary information.

Descriptive data: The following descriptive data were collected from the papers.

design of the trial: Randomized controlled trials ,quasi-experimental trials or uncontrolled clinical trials

methodology: inclusion & exclusion criteria, follow-up assessments (time after the end of the intervention)

participants: age, gender, type of diagnosed cancer & cancer stage, referring to the development of the disease e.g. stage I = early form, stage IV = metastasized cancer

intervention: type of psychosocial intervention, period & duration of the intervention, number of sessions, support of the intervention (moderator, individual tailored or automated feedback)

outcomes: quality of life, distress, depression, anxiety, pain, physical activity as measured by standardized, validated questionnaires & interviews, means and standard deviations (pre- & post-intervention and follow-up), effect sizes, sample size, drop-out rates

time since completion of initial treatment

Risk of bias assessment of included studies

To rate the risk of bias in the studies identified for inclusion we handled the 10-item rating scale developed by Newell (2002). Additionally, 5 items were added. These items were recently developed to rate the risk of bias in a Cochrane review of psychological interventions for cancer patients who survived the disease for at least one year (Ranchor et al., submitted).

The scale was designed to rate the risk of drawing incorrect conclusions about the effectiveness of a psychological intervention on the basis of invalid data or results. A review of internally invalid studies may sophisticate the conclusions drawn by virtue of the analysis. The 5 items added by Ranchor et al. (submitted) were indicated with an asterix.

The risk of bias items:

random selection of patients;

concealment of allocation;

except trial intervention, other treatments equivalent;

recording of non-study interventions during the study period*;

blinding of patients to intervention conditions (i.e., are the patients aware of the treatment they receive and are they aware whether they are assigned to an intervention group or to a control group?);

blinding of care providers to intervention conditions (i.e., are the care givers aware of whether they provide care to an intervention group or to a control group?);

blinding of assessment of outcomes;

use of a manualized treatment or a session-by-session description of the protocol*;

monitoring of care providers adherence;

monitoring of patients adherence to treatment*;

specification of primary outcomes*;

report of detailed loss-to-follow-up information;

extent to which patients were not included in the analysis;

equivalence of treatment groups at baseline on variables of primary importance*;

conduct of intention-to-treat analyses.

Handling of risk of bias data: According to Newell (2002) all items have to be rated and encoded on a scale from 0 to 3. The answer categories are:

3 = entirely fulfilled;

2 = mostly fulfilled;

1 = mostly not fulfilled;

0 = not fulfilled at all or information is missing.

After rating the 15 items, mean item scores were derived. All item scores were summed up and divided by the number of items and afterwards interpreted in terms of risk of bias. The interpretation of mean item scores happened as follows:

≥ 2	= low risk of bias;
2 – 1	= moderate risk of bias;
< 1	= high risk of bias.

Results

Selection of studies

In the first step, 963 papers were identified and titles and abstracts downloaded. After scanning the titles and abstracts in step 2, 875 papers were removed because they did not focus on psychosocial interventions for adult cancer survivors. From the remaining 88 studies, full-text copies were downloaded and rated in terms of fulfilment of the intervention criteria (step 3). Another 74 studies were removed and two studies were included as part of the grey literature. The 16 remaining studies were checked for the criteria of being a cancer survivor (step 4). Most of the studies did not made clear, whether participants still were in treatment at the time of the intervention. Three studies (Duffecy et al., 2013; Ritterband et al., 2011; Yun et al., 2012) could clearly be identified as having included cancer survivors as the target population. Five studies (Beatty, Koczwara & Wade, 2011; Changrani et al., 2008; Carpenter, Schmitz, McGregor & Doorenbos, 2012; David, Schlenker, Prudlo & Larbig, 2012; Klemm, 2012) were directly excluded because a greater deal of participants was still in treatment at the time of the intervention. Authors of 8 studies were contacted to get further information about the intervention, whether or not participants still were in treatment at the time of the intervention. If a part of participants still was in initial treatment, this part had to be less than 20 %.. Authors of seven studies responded (Baker et al. 2011; Gustafson et al., 2001&2008; Hawkins et al., 2010; Lieberman et al., 2003; Owen et al., 2005 & Winzelberg et al., 2002) but none of the studies were eligible for inclusion, due to the fact that none of the authors could offer more precise data. One author did not respond to the request (Ruland et al., 2013) and the article was therefore excluded. See appendix 2 for a flow diagram of the selection of studies.

Due to the fact, that only three studies (Ritterband et al.,2011; Yun et al., 2012; Duffecy et al., 2013) were identified for the analysis and that two of the three studies were not adequately powered this analysis is narrative as opposed to systematic.

Characteristics of the selected studies

To get an overview, the main characteristics are shown in table 1. More detailed information about the studies are presented in appendix 3.

Time since treatment completion: In one intervention participants had to have completed initial treatment more than one month before the start of the intervention (Ritterband et al., 2011) and in another study participants had to have completed initial treatment within the 24 month before the intervention (Yun et al., 2012). In one study participants had to be cancer survivors, but no further information were given about the time since initial treatment completion (Duffecy et al., 2013).

Cancer type and stage: All of the three studies focused on various cancer sites, a great deal of participants however suffered from a breast cancer diagnosis. In two studies participants were in the disease stages I – III (Ritterband et al., 2011 & Yun et al., 2012) and in one studies in stage I – IV (Duffecy et al., 2013).

Socio-demographic characteristics: In all studies the proportion of female participants is higher (> 70%) than the proportion of male participants. The mean age in two studies is around 55 years (Ritterband et al., 2011 & Yun et al., 2012) and in one study around 45 years (Duffecy et al., 2013).

Type of psychosocial intervention: The theoretical background of the three interventions is based on cognitive behavioural therapy (CBT). They all focus on the individual. One intervention focused on individuals suffering from insomnia as related to their cancer diagnosis (Ritterband et al., 2011) and one intervention focused on cancer-related fatigue (Yun et al., 2012). The third intervention addresses depressive symptoms in cancer survivors (Duffecy et al., 2013).

Primary & secondary outcomes: Merely one study clearly stated primary and secondary outcomes to test the effectiveness of the intervention (Yun et al., 2012). Measured were, in terms of the outcomes defined for this review – QoL, depression, anxiety, pain and fatigue. One study did not made a difference of outcomes in terms of primary or secondary (Ritterband et al., 2011). Here, QoL, depression, anxiety and fatigue were the outcomes of interest. The last study was intended to measure the feasibility and acceptability of the intervention and additionally the effectiveness on depressive symptoms (Duffecy et al., 2013). From the outcomes, which were originally defined to reflect effectiveness of the psychosocial online interventions in this review, several were not outcome of interest in any of the studies – distress and physical activity.

Risk of bias analysis & main outcomes

The results of the risk of bias assessment and the main outcomes of the interventions are presented in table 2. All three reviews had a moderate risk of bias ranging from 1.3 (Duffecy et al., 2013) to 1.9 (Ritterband et al., 2010 & Yun et al., 2012). Participants were screened for the presence of symptoms in advance, in all studies. Positive outcomes for depressive symptoms were found by Duffecy et al. (2013) and Ritterband et al. (2011). Those outcomes were not significant. Yun et al. (2012) and Ritterband et al. (2011) found positive outcomes

Table 1

Study Characteristics – an overview

Author	TSD	Age	Total N at start	Gender	Cancer site	Cancer stage	Intervention type	Delivery to whom	Primary & secondary outcomes in this review						
	Time since completion treatment	Mean age		% female					QoL	distress	depression	anxiety	fatigue	pain	physical activity
Duffecy (2013)	unknown	45.5	48	87	various	mixed	CBT	individual			X				
Ritterband (2011)	> 1 month mean: 3.9 years	56.7	28	85.7	various	mixed	CBT-I for insomnia	individual	X		X	X	X		
Yun (2012)	within 24 month	53.5	273	72.9	various	mixed	CBT cancer related fatigue	individual	2		2	2	1	2	

1= primary outcome; 2 = secondary outcome; X = not clear
CBT-I = Cognitive Behavioural Therapy for Insomnia

on QoL, anxiety and fatigue. But significant treatment effects were found for fatigue only. See appendix 4 for the detailed risk of bias analysis.

A narrative review of the selected studies

To make assumptions about the effectiveness of the three interventions it is necessary to note that that effectiveness of treatment was measured in terms of Group-by-Time interaction tests and tests within study conditions.

Duffecy et al. (2013): Thirty-one survivors of any type of cancer were randomized into either „Project Onward“ an Individual Internet Intervention (III) + Internet Support Group (ISG) building the intervention condition or into an III only, the control condition. Originally the intervention was designed for cancer survivors, suffering from depression as a consequence of the disease and indicated by a Hospital Anxiety and Depression Scale (HADS) score of > 8. This inclusion criterion was abandoned, since recruitment went dragging. The thought behind the intervention design was the creation of greater adherence to the program by adding a support group. The 8-week program consisted of eight lessons using different cognitive behavioural techniques. The main outcomes mentioned were feasibility & acceptability of the program, supportive accountability and improvement in depressive symptoms. The study was not adequately powered to detect significance. Of the outcomes of interest to this review, depression was the only one measured, with the HADS. Among participants meeting a HADS >8 score, the intervention group as well as the control group showed large within treatment reductions on the HADS ($d = 1.27$ & 0.89, respectively). The full sample showed similar results ($d = 0.72$ & 0.38). Those results indicate an effect of III itself with a slightly greater effect size for the III plus ISG. In the full sample, non-depressed survivors participated and it was unclear, how they were distributed over the groups. In general, no significant time *x* treatment effect could be found, due to the lack of adequate power.

Ritterband et al. (2011): Twenty- eight cancer survivors of any cancer site, meeting the

DSM-IV TR criteria of insomnia, were randomized to either the intervention group or a waitlist control group. The 9-week individually tailored, interactive intervention was based on CBT for insomnia (CBT-I) and called *Sleep Healthy Using The Internet* (SHUTi). It was especially designed for cancer survivors suffering from insomnia targeting automatic thoughts and behaviours that frequently perpetuate insomnia. The program consisted of five treatment components – sleep restrictions, stimulus control, cognitive restructuring, sleep hygiene and relapse prevention. Six outcomes were considered, of which three were of interest to this review, fatigue, mood and quality of life. Instruments used were the Short Form-12 (SF-12) to measure QoL, the HADS to measure anxiety and depression (mood) and the Multidimensional Fatigue Symptom Inventory – Short Form (MFSI-SF) and a sleep diary to measure fatigue. A significant group x time interaction was found for fatigue (p < 0.01, d= 1.16). Participants in the internet group had significantly improved fatigue scores. Positive outcomes were also found for anxiety (d= 0.42), depression (d= 0.54) and QoL mental (d= 0.48), QoL physical (d= 0.21). However, none of the positive outcomes reached significance.

Yun et al. (2012): Two hundred seventy-three cancer survivors of any cancer site, suffering from cancer-related fatigue (CRF) were randomly assigned into an internet-based, individually tailored education program for CRF, called “Health Navigation” or a waitlist control group. The 12-week intervention covered six strategic areas – energy conservation, physical activity, nutrition, sleep hygiene, pain control and distress management and is based on CBT. The Brief Fatigue Inventory (BFI) and the Fatigue Severity Scale (FSS) were used to measure fatigue. To measure quality of life the EORTC-Quality of Life Questionnaire-30 (EORTC-QLQ-30) was used; for depression and anxiety the HADS and for pain, the Brief Pain Inventory (BPI). Significant time *x* treatment effects were found in the decrease of fatigue on the BFI and the FSS (p= < 0.001) in the intervention group. Furthermore anxiety (d= 0.33) and QoL (d= 0.26) showed a significant improvement, which was lost after applying the Bonferroni-procedure.

Table 2

Studies included in the analysis with risk of bias and the main Outcomes

Author	Risk of bias	Primary outcome specified	Screening presence symptoms	QoL	distress	depression	anxiety	fatigue	pain	physical activity
Duffecy et al.	moderate (1.3)	No	Yes			+				
Ritterband et al.	moderate (1.9)	No	Yes	+		+	+	+ (*)		
Yun et al.	moderate (1.9)	Yes	Yes	+		=	+	+ (*)	=	

= indicating Null findings; + indicating a positive outcome; (*) significant: $p < 0.01$; *blanket* outcome not measured in study

Discussion

The objective of this review was the measurement of effectiveness of psychosocial online interventions in a population of cancer survivors. Related aims were the revelation of approaches that were used to target the negative psychosocial consequences in terms of primary or secondary outcomes and, to explore whether effectiveness correlates with the used approach. To address this objective, only a limited number of studies could be identified. Outcomes which were intended to measure the effectiveness were distress, quality of life, anxiety, depression, pain, fatigue and physical activity. Three studies could be identified as entirely fulfilling the criteria for this review. The fact, that the number of studies in this review is limited and that the review is narrative instead of systematic, precludes from drawing conclusions with regard to the effectiveness of psychosocial online interventions for cancer survivors after initial treatment – which was the main objective of this review. Some patterns could be revealed as indications with respect to effectiveness, at the utmost.

Searching the literature for psychosocial online interventions for cancer patients provides a great number of interventions at first sight. When focusing on survivors in particular this impression changes. Merely, three studies fulfilled the eligibility criteria for inclusion into this review. One intervention was designed to target depressive symptoms in cancer survivors (Duffecy et al., 2013). The second intervention was designed to treat insomnia in cancer survivors (Ritterband et al.,2011) and the third intervention aimed to reduce cancer-related fatigue in a population of cancer survivors (Yun et al., 2012). Studies were homogeneous with regard to age of the study population, gender, cancer site, cancer stage and type of intervention and heterogeneous with respect to sample size. All interventions were accessible for all cancer sites. Yet, most of the participants suffered from breast cancer. Mean age in all three studies was between 45 and 56 years. Indicating that older people participate in online interventions as well. All studies were conducted between 2011 –

2013 and revealed a moderate risk of bias.

Quality of Life, distress, depression and anxiety, were the primary outcomes that were selected to reflect effectiveness, in challenging the negative psychosocial impact of cancer. QoL was outcome of interest in the interventions of Ritterband et al. (2011) and Yun (2012). The results indicated a positive trend in terms of improvement of QoL. Yet, no significant group *x* time interactions or within-group treatment effects were found for this outcome. Distress was not a target outcome in any of the interventions. As opposed to this, depression was outcome of interest in all of the three studies. Positive outcomes were found in the interventions by Duffecy et al. (2013) and Ritterband et al. (2011). Duffecy found positive within-group treatment effect sizes in the intervention group (III + ISG) as well as in the control group (III). Although, effect sizes were smaller in the control group. Likewise, positive outcomes related to depressive symptoms were found in Ritterbands' intervention group and not in the waitlist control group. However, no statistically significant group *x* time interactions or within-group treatment effects have been found. Yun et al. (2012) found no intervention effects on depressive symptoms. Anxiety was part of the outcome measure in the studies by Ritterband and Yun. Here again, the outcomes showed a positive trend but were not statistically significant.

Fatigue, pain and physical activity were the secondary outcomes to reflect effectiveness of the interventions. Statistically significant treatment effects were found for fatigue in the two studies, having fatigue as a target outcome. Fatigue was no outcome of interest in the study by Duffecy et al.. Pain was one of the secondary outcomes in the study by Yun et al. but no treatment effects have been found for this outcome. Physical activity was, just as distress, not an outcome of interest in any of the studies.

In sum, positive outcomes have been found for QoL, depression, anxiety and fatigue. A significant treatment effect however, was only detected for the outcome variable fatigue. In the following, several possible explanations for the mostly non-significant findings will be discussed.

In all of the studies, patients were screened in advance, for the presence of symptoms, on at least one outcome. On those screened outcome variables, positive results were obtained, yet not significant in any case. Two out of three interventions, targeted a population of cancer survivors, with the presence of symptoms on one of our secondary outcomes – fatigue (Ritterband et al., 2011 & Yun et al.,2012). Showing significant group *x* time interactions for the decrease of fatigue in cancer survivors. The other intervention (Duffecy et al., 2013) screened for the presence of depressive symptoms right at the outset, but stopped at a given point in time, during the recruitment phase. A slightly greater effect size was found in the population of participants, which indeed was screened for depressive symptoms. Ventura et al. (2012) concluded that the definition of theory-based outcomes that adequately test the effectiveness of an intervention are inevitable. After the definition of those outcome variables, the processes that may bring change on those variables have to be found. To measure if the chosen processes are effective in challenging the target outcome, it is necessary to know if the target outcome played a role at the start of the intervention. This means, not every cancer survivor perceives the presence of e.g. cancer-related fatigue as stressful as some other cancer survivor might do (Stein et al., 2008). Besides, not every cancer survivor develops a depression or an anxiety disorder as a consequence of the disease. A cancer survivor, who is not suffering from depressive symptoms, right at the start of an intervention targeting depression in cancer, is not likely to show improvements in depressive symptoms over the course of the intervention. To be able to draw conclusions about the effectiveness of an intervention on the target outcomes, it is necessary to screen participants for the presence of symptoms, as related to the defined outcomes, in advance.

Another possible explanation for the non-significance of results is the sample size of the studies. Adequate power to detect significant differences was constituted by only one intervention (Yun et al., 2012).

Related to the main objective, this review aimed to get an overview of the approaches that have been used to target the negative psychosocial consequences of cancer, online. Furthermore, to check for a possible relationship between effectiveness and the used theoretical background. Although the search for eligible studies was open-minded in terms of the theoretical background of the studies, it turned out that all studies included into this review were based on CBT. Given the limited number of studies, no conclusions could be drawn with respect to the theoretical framework. Considering that CBT is evidence based practice in the face-to-face treatment of many psychiatric disorders (Hofmann, Asnaani, Vonk, Sawyer & Fang, 2012) it seems reasonable that researchers choose for this therapeutic approach. In addition CBT provides a solid foundation for the building of a structured programme. Even though, other therapeutic approaches hold promise as well. The transfer of knowledge about cancer, by use of psychoeducation, is a popular face-to-face approach to improve the individuals' coping strategies (Simeit & Hofmann, 2013). Supportive-expressive approaches also showed positive outcomes on mood and affective disturbances (Boutin, 2007) and peer support can help reduce depressive symptoms in cancer patients (Pfeiffer, Heisler, Piette, Rogers & Valenstein, 2011). It may be an opportunity, for that reason, to combine different therapeutic approaches or to at least add some strategies to the CBT approaches.

No assertions can be made about the late effects of the interventions, because in none of the studies a long-term follow-up measurement was established. It is however possible that a significant effect on one outcome variable, such as fatigue, will have a positive effect on the other outcomes in the long-term. In a systematic review Brown & Kroenke (2009) found a positive correlation between depression and cancer-related fatigue.

In conclusion, all of the three studies were based on CBT, all had a moderate risk of bias, but only two produced significant treatment effects on one of our secondary outcomes and patients in this studies were included into the intervention based on the presence of symptoms.

Limitations

A possible limitation of this review is the missing of an inter-rater reliability analysis. Only one person responsible did the literature search and decided which articles should be included into the review and which not. For future reviews it is recommended to do such an analysis to get more certainty that all available and relevant literature is included in the review.

A further point of discussion is the definition of the term cancer survivor, which is vague and diverse in the literature. Other definitions exist, in which cancer patients are termed survivors from the point of initial diagnosis on (NCCS, 2013). For clarification, in this review, the definition of the Macmillan Cancer Support has been used, and a cancer survivor had to have finished initial treatment.

Recommendations

During the literature search it became apparent that, most of the authors did not make a difference between participants being a survivor or still undergoing initial treatment. From the 16 studies being eligible for inclusion into the review, five clearly did not fulfil the criteria of participants being a survivor. Seven authors were contacted via email, of whom six replied and stated that is was either unclear if participants still were in initial treatment or that it was certain that both groups were part of the intervention. It is clearly recognizable that for most of the authors this criterion is of no consideration. One author replied, that at first the intervention was designed for patients in initial treatment, but it turned out that a great deal of patients already had completed initial treatment (Gustafson et al. 2001 & 2008). Another stated that the intervention was designed to be most useful to patients if they got access as close to diagnosis as possible (Hawkins et al. 2010) and that the percentage of participants who actually had completed treatment was likely very small. To our understanding, effectiveness of an intervention is not measurable if this criterion is not taken into consideration. As already mentioned in the introduction, the needs and stressors of patients in these different stages vary. Shortly after diagnosis and in initial treatment the threat of the potentially life-threatening diagnosis itself provides anxious thoughts about possible death or future dysfunctions. Moreover, questions about the best treatment option and its possible adverse effects, characterize the stressors in this acute phase of the disease. After initial treatment these stressors seem to transform into fear of recurrence, financial difficulties, resulting from sick leave or high medical care costs or physical late or long-term effects of the disease, etc. (Stein, Syrjala & Andrykowski, 2008). The initial situation for the start of psychosocial treatment differs completely for cancer survivors from patients undergoing initial treatment, because they have survived the disease, for now, and they got the possibility to take up life again. In terms of the design of psychosocial online intervention, in the future, a careful separation of patients with respect to the disease trajectory is necessary. Thus, interventions for patients in treatment on the one hand, and interventions for survivors on the other hand.

CBT provides an adequate evidence based therapeutic approach for building a structured programme, which can be translated into online content. In future research, sections of other therapeutic face-to-face approaches can be added. This would be necessary to get a broader understanding of what an effective psychosocial treatment is, for cancer survivors.

As mentioned above, it seems worth consideration to use existing evidence-based CBT programmes for e.g. depression or anxiety to target those symptoms in cancer survivors - online. Instead of measuring a great deal of outcome variables, just focusing on a few variables. And for those defined variables, screening should take place in advance. Paul et al. (2013) in their review found, that online CBT interventions were effective in several chronic conditions. They found no data which suggest effectiveness in reducing psychosocial disturbance in cancer patients, but highlight that the reviewed interventions in this population did not so much focus on intervention content and were largely self-directed.

Certain study protocols have been published in 2012, concerning psychosocial online interventions for cancer survivors (Krebber et al., 2012; Sansom-Daly et al., 2012; van den Berg, Gielissen, Ottewanger & Prins, 2012). These protocols sound promising with regard to the realization of RCTs targeting the negative psychosocial consequences of cancer in a population of cancer survivors. In all of the three study protocols, the interventions are based on cognitive behavioural therapy.

In most of the studies the majority of participants suffered from breast cancer. It would be desirable to pay more attention to other cancer sites as well. The focus on breast cancer leads to the fact that female participants were overrepresented in the existing studies. According to Zabora, Brintzenhofeszoc, Curbow, Hooker & Piantadosi (2001) and as mentioned earlier, participants could be diagnosed with any type of cancer and that earlier research highlights that it is unnecessary to argue about special clinical programs for different cancer sites, because most psychosocial issues remain stable for one cancer type over another. If more research has been done in this field, it seems however reasonable, to have a look at interventions related to a particular cancer site.

In addition, future studies have to be adequately powered to allow for the drawing of conclusions with regard to the effectiveness of the interventions.

A further difficulty with online interventions is the delicate controllability of adherence to the programme. Good user tracking systems have to be implemented to make sure that participants use the intervention in the way it is meant to - without seriously violating the privacy. A step in this direction has been done by Duffecy et al. (2013). They combined elements of CBT with elements from supportive-expressive therapy. Participants had to work on modules during the intervention, but had the possibility to take part in group discussions. This platform for group discussions had a further meaning, it was meant to strengthen adherence of participants to the program. The thought behind this platform was, that users are more likely to adhere if they were accountable to another person. The average number of logins in the treatment group was 20.8 (+/- 17.7) and for the control group 12.5 (+/- 12.5). This difference, between groups, was not significant. This may be, due to the small sample size of the intervention. A trend toward greater adherence was displayed, however.

The risk of bias analysis revealed a moderate risk of bias for all three studies. The items of the Risk of Bias analysis were taken over from Newell (2002) and Ranchor (submitted). Those items were originally established for psychological face-to-face interventions and it is questionable if the items, with respect to blinding, are reasonable in the context of online interventions. Leaving those items out of the analysis would have resulted in a low risk of bias in two studies (Ritterband et al., 2011 & Yun, 2012). Considering that most of the time the control group is a waitlist control group, that the interventions are mainly automated and patients are at home and unaware of their condition, this may be reconsidered in future reviews. But further research in this field is needed.

In conclusion, not much research has been done in the field of psychosocial online interventions for cancer survivors. Although, several treatment effects could be found in the three interventions, the limited number of studies precludes from drawing strong conclusions about the effectiveness. A great deal of cancer survivors however, has to struggle with negative psychosocial consequences of cancer. Since the number of cancer survivors is steadily increasing, there is a need of appropriate care. In the past, several interventions have proven to be effective in targeting those negative psychosocial consequences, such as depression, anxiety or sleep disturbances. In face-to-face therapy and as well in web-based interventions. Those existing interventions should be customized for the needs of cancer survivors. In this context, an indicator of effectiveness seemed to be, the inclusion of participants based on the presence of symptoms and the clear specification of theory-based outcomes, which the intervention aims to target..

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Appendices

Appendix 1

Search strategies:

Pubmed:

exp Neoplasms/ OR (tumor OR tumor OR oncol*) OR cancer.tw

AND

exp Psychotherapie/OR (cognitive therapy OR psychosocial intervention OR psychosocial).tw. OR (health education OR self-help groups OR peer to peer OR peer groups OR psychosocial support).tw. OR quality of life intervention OR (psychological coping OR psycological adaptation).tw

AND

(online OR web-based OR internet-based OR computer-assisted OR online supported OR internet).tw.

AND

treatment outcome OR efficacy OR effectiveness OR effects OR cost effectiveness

AND

yr= "1990/01/01-present"

((((((tumor OR tumour OR neoplasm OR oncol*)) OR cancer[Text Word]) AND (psychotherapy OR cognitive therapy OR psychosocial intervention OR psychosocial OR health education OR quality of life OR self-help groups OR peer to peer OR peer groups OR psychosocial support OR psychological coping OR psychological adaptation[Text Word])) AND (online OR web-based OR internet-based OR computer-assisted OR online supported OR internet[Text Word])) AND (treatment outcome OR efficacy OR effectiveness OR effects OR cost effectiveness)) AND ("1990/01/01"[Date - Publication] : "3000"[Date - Publication])

resulted in 854 articles

PsycINFO:

Neoplasms OR cancer OR tumor* OR tumour OR oncol* OR chronic disease

AND

psychotherapy OR cognitive therapy OR psychoeducation OR health education OR psychosocial intervention AND (peer "to" peer OR peer groups OR social support OR psychosocial support OR self-help groups

OR

(adjustment OR adaptation OR coping AND intervention OR therapy OR treatment)

AND

online OR web-based OR internet-based OR computer-assisted OR electronic support OR internet

AND

treatment outcome OR effectiveness OR efficacy OR cost effectiveness OR effects

AND

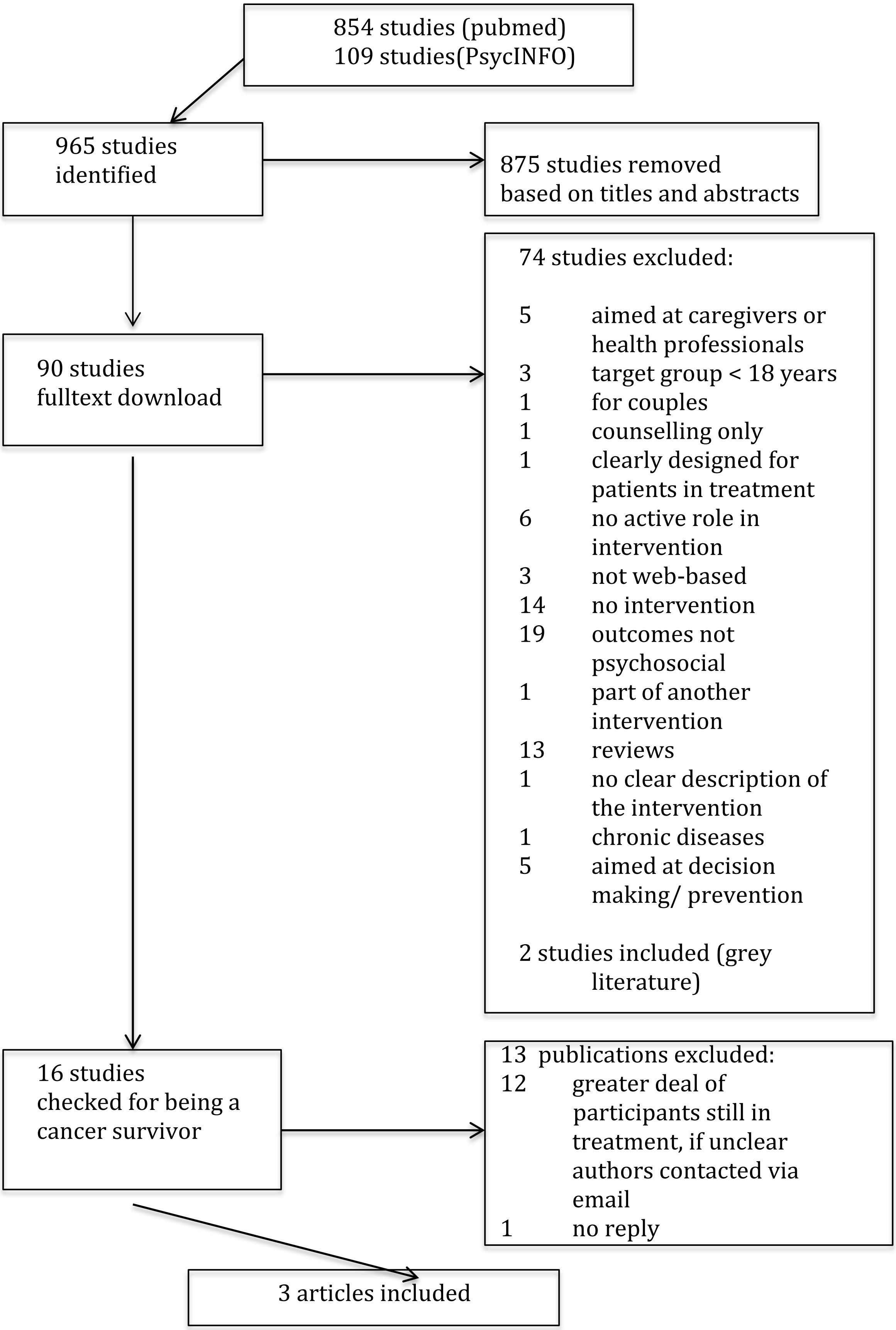
(PY 1990 – 2013)

(cancer OR neoplasms OR tumor* OR oncol* OR chronic disease) AND (psychotherapy OR cognitive therapy OR psychoeducation OR health education OR psychosocial intervention) AND (peer "to" peer OR peer groups OR social support OR psychosocial support OR self-help groups OR (adjustment OR adaptation OR coping AND intervention OR therapy OR treatment)) AND ((online OR web-based OR internet-based OR computer-assisted OR electronic support OR internet)) AND (treatment outcome OR effectiveness OR efficacy OR cost effectiveness OR effects) AND (PY 1990 - 2013)

resulted in 109 articles

Appendix 2

Flow diagram of studies selected for inclusion in the review



74 studies excluded:

5	aimed at caregivers or health professionals
3	target group < 18 years
1	for couples
1	counselling only
1	clearly designed for patients in treatment
6	no active role in intervention
3	not web-based
14	no intervention
19	outcomes not psychosocial
1	part of another intervention
13	reviews
1	no clear description of the intervention
1	chronic diseases
5	aimed at decision making/ prevention

2 studies included (grey literature)

13 publications excluded:

12	greater deal of participants still in treatment, if unclear authors contacted via email
1	no reply

Appendix 3

Detailed description of studies that were included in the review

Duffecy et al. – moderate risk of bias

Cancer site(s)	breast	N= 14
	lymphoma	N= 8
	gynaecologic	N= 3
	lung	N= 2
	colon	N= 2
	sarcoma	N= 1
	thyroid	N= 1
Gender	Females	27 (87%)
	Males	4 (13%)
Age	total sample	27-68 years
Time since diagnosis		unknown
Selection	initially yes	participants were selected on the basis of a score of 8 or above on the Hospital Anxiety and Depression Scale (HADS). Recruitment with this criterion slow- so it was removed.
Sample	N= 91	Patients with cancer screened by an online screening program
	N= 31	enrolled and randomly assigned by a biostatistician
	N= 24	patients with data at all time points
Intervention	Intervention	*Project onward* Individual internet intervention (III) + skills management training for distress + internet support group (ISG)
	Control	unguided individual internet intervention (III)
Design	T0	at baseline
	T1, T2	mid-treatment & post-treatment
Adherence (number of logins)	intervention	21

	control	12
Outcomes	Depression	HADS
Results	Depression	not adequately powered to detect statistically significant differences both groups demonstrated reductions in depressive symptoms

Ritterband et al. – moderate risk of bias

Cancer site(s)	breast	N= 18
	other	N= 10
Gender	Females	24
	Males	4
Age	intervention	53.7 (10.8)
	control	59.6 (12.3)
Time since diagnosis	intervention	years since completion of active treatment, mean 4.6 (3.1)
	control	years since completion of active treatment, mean 3.2 (2.9)
Selection	yes	meeting the DSM-IV criteria of insomnia and additionally reporting poor sleep for at least 6 months, at least 3 nights per week and daytime consequences of the sleep disturbances.
Sample	N=171	patients assessed for eligibility
	N= 29	patients enrolled in the study
	N= 28	randomized to either intervention or control group
	N= 28	patients with data at all time points
Intervention	intervention	SHUTi based on validated face-to-face CBT-I and behaviour change model for internet interventions 6 cores in 9 weeks
	control	waitlist control group
Design	T0	prior to intervention
	T1	post treatment measure
Adherence (number of logins)	intervention	38 (16) 12/14 completed all 6 cores
Outcomes	QoL	SF-12
	depression	HADS
	anxiety	HADS
	fatigue	Multidimensional Fatigue Symptom Inventory – Short Form (MFSI-SF)

		sleep diary
Results	QoL	measure of mental QoL not significant ($p= 0.09$) adjusted effect size indicated small-to-medium treatment effect ($d= 0.48$) on the physical subscale also non-significant ($p= 0.52$) adjusted effect size indicated small treatment effect ($d=0.21$)
	depression anxiety	measure of depression and anxiety not significant ($p=0.09$) adjusted effect size for the total ($d= 0.52$) depression ($d= 0.54$), anxiety ($d=0.42$)
	fatigue	significantly improved fatigue scores

Yun et al. – moderate risk of bias		
Cancer site(s)	breast	N= 106
	stomach	N= 55
	colon	N= 36
	uterine	N= 31
	lung	N= 20
	thyroid	N= 25
Gender	Females	199
	Males	74
Age	intervention	71 > 45 years
	control	75 > 45 years
Time since diagnosis		unknown
Selection	yes	moderate to severe fatigue (worst fatigue in BFI) for at least 1 week
Sample	N= 1876	potential contactable participants
	N= 310	patients potentially eligible for the study
	N= 273	eligible and randomly assigned
	N= 243	patients with data at all time points
Intervention	intervention	*Health Navigation*, an internet-based, individually tailored education program for cancer-related fatigue (CRF) – CBT 12 weeks
	control	routine care in a waitlist control group
Design	T0	prior to the intervention
	T1	post-intervention
Adherence (number of logins)	intervention	unknown
Primary outcomes	fatigue	BFI FSS
Secondary outcomes	QoL	EORTC-QLQ-C30
	depression	HADS
	anxiety	HADS

	pain	BPI
Results	fatigue	significant decrease in global severity
	QoL	significantly greater increase in global QoL (Significance lost after Bonferroni corrections)
	depression	no significant results
	anxiety	significantly greater in HADS anxiety scores (Significance lost after Bonferroni corrections)
	pain	no significant results

Appendix 4

risk of bias items	Duffecy et al.	Ritterband et al.	Yun et al.
concealment of allocation adequate	3	3	3
random selection of patients	3	3	3
equivalence of intervention conditions (except trial intervention)	0	2	2
recording of non-study interventions during the study period*	2	0	0
blinding of patients to intervention conditions (i.e., are the patients aware of the treatment they receive and are they aware whether they are assigned to an intervention group or to a control group?	0	1	1
blinding of care providers to intervention conditions (i.e., are the care givers aware of whether they provide care to an intervention group or to a control group?)	0	1	1
blinding of assessment of outcomes	0	0	0
use of a manualized treatment or a session-by-session description of the protocol*	3	3	3
monitoring of care providers adherence	0	2	1
monitoring of patients adherence to treatment*	2	2	0
specification of primary outcomes*;	0	0	3
report of detailed loss-to-follow-up information	2	3	3
extent to which patients were not included in the analysis	0	3	3
equivalence of treatment groups at baseline on variables of primary importance*	2	3	3
conduct of intention-to-treat analyses	3	3	3
mean score	1.3	1.9	1.9