PERGAMON

European Journal of Cancer 38 (2002) 1447–1457

European
Journal of
Cancer

www.ejconline.com

Review

Mind and cancer: does psychosocial intervention improve survival and psychological well-being?

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Received 5 December 2001; received in revised form 8 January 2002; accepted 8 April 2002

Abstract

The aim of this review was to evaluate the scientific evidence for an effect of psychosocial intervention on survival from cancer and well-being and in particular on anxiety and depression. A literature search yielded 43 randomised studies of psychosocial intervention. Four of the eight studies in which survival was assessed showed a significant effect, and the effect on anxiety and depression was also inconsistent, indicating three possible explanations: (i) only some of the intervention strategies affect prognosis and/or well-being and in only certain patient groups; (ii) the effect was weak, so that inconsistent results were found in the generally small study populations; or (iii) the effect was diluted by the inclusion of unselected patient groups rather than being restricted to patients in need of psychosocial support. Thus, large-scale studies with sound methods are needed in which eligible patients are screened for distress. Meanwhile, the question of whether psychosocial intervention among cancer patients has a beneficial effect remains unresolved. © 2002 Elsevier Science Ltd. All rights reserved.

Keywords: Cancer; Review; Intervention studies; Psychosocial; Social support; Psycho-oncology; Quality of life; Anxiety; Depression; Survival

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1. Introduction

Cancer is a potentially life-threatening disease and is often accompanied by major psychological distress. In a review of studies of cancer patients at various times during their disease, the prevalence of depression ranged from 4.5% up to 50% [1]. Additionally, the patients reported distress in other family members [2], adverse neuropsychological reactions to chemotherapy [3], sexual problems [4] and disruption of daily social, physical and cognitive functioning [5]. The diagnosis and treatment of cancer therefore have long-lasting, pervasive psychosocial effects on the lives of many patients. In an attempt to improve emotional adjustment and to prevent negative psychosocial effects, several intervention strategies have been used over the past 30–40 years. Furthermore, the results of two randomised studies of psychosocial intervention, by Spiegel and colleagues in 1989 [6] and Fawzy and colleagues in 1993 [7], which showed remarkable increases in the length of survival of breast cancer patients and of patients with malignant melanoma, respectively, led the public to believe that psychosocial support for cancer patients can affect their prognosis.

Even if reliable, valid associations can be established between psychosocial intervention and subsequent improvement in the length of survival, the mechanisms underlying this effect have yet to be determined. Several explanations have been proposed. Kiecolt-Glaser in 1999 [8] suggested that psychological stress is directly linked to immune downregulation, and that distress or depression is associated with a poorer repair of damaged DNA and alterations in apoptosis. These adverse effects are hypothesised to be amenable to psychosocial intervention. An indirect biological effect could be mediated by healthier behaviour after psychosocial intervention, i.e. reductions in smoking, alcohol abuse and sleep disturbances and improved nutrition, physical activity and compliance with medical regimens [9].

The purpose of this comprehensive review of randomised studies of psychosocial intervention is to elucidate the degree of evidence for enhanced survival and psychological well-being after participation in such intervention. In another paper, we review the role of psychosocial factors in the causation of cancer [10].

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PII: S0959-8049(02)00126-0

2. Material and methods

The Medline (1966–June 2001) and Psych-INFO (1974–June 2001) databases were searched with the keywords *psychotherapy* or *social* or *psychosocial* combined with *intervention* and *cancer*. Citations were also sought manually in the papers and reviews that were identified. We included only randomised studies of psychosocial interventions among cancer patients aged 18 years or more, which included an untreated control group and in which effects on prognosis and/or psychological well-being were reported. We excluded studies on interventions aimed exclusively at reducing the side-effects of treatment and studies that were randomised by time period. The search resulted in 45 studies that fulfilled these criteria. However, after careful evaluation, we decided to omit two publications by Grossarth-Maticek [11,12] in which inadequate descriptive information was provided about the material, methods and analyses; furthermore, the integrity of the data has been questioned [13]. This left 43 studies for review.

3. Results

3.1. *Effect of psychosocial intervention on prognosis*

The effect of psychosocial intervention on the length of survival of cancer patients has been assessed in eight randomised studies (Table 1). In four studies, the intervention was found to be positively correlated with survival from cancer, whereas four studies failed to find this association.

In a study from the USA in 1982 by Linn and colleagues [14], 120 men with advanced cancer were included. After randomisation, the intervention group received individual counselling when needed, often several times a week, for 1 year or until the patient died. Relatives were allowed to participate in the counselling on the patient's request. No difference in survival was observed after 1 year of follow-up between the intervention group and the control group. The intervention group reported significantly better quality of life than the control group, and, in addition, the intervention group reported significantly less depression after 3 months of intervention.

In a study from the USA in 1989 by Spiegel and colleagues [6,15,16], 86 women with metastasising breast cancer were randomised to receive group therapy for 1 year and instruction in self-hypnosis to control physical pain or to no intervention. No significant difference in the degree of depression was observed at the end of the intervention, but the intervention group reported significantly less anxiety [15] and pain intensity [16] than the control group, although the frequency and duration of pain were similar in the two groups [16]. In an analysis 10 years later [6], the women in the intervention group were found to have lived an average of 18 months longer than the women in the control group ($P<0.0001$). Remarkably, the survival curve for the intervention group was found to be similar to that of white women with metastasing breast cancer who lived in the San Francisco area, where the study took place, whereas the curve for the control group showed appreciably worse survival [17]. Three explanations were proposed: (1) the women in this study differed somehow from the background population at baseline; (2) randomisation to the control group had a negative effect on survival; or (3) more women with a poor prognosis were randomised to the control group by chance [17]. Although this study was well conducted, it needed to be replicated, and this is currently under way in Canada and the USA.

In a study from the USA in 1993 by Fawzy and colleagues [7,18], 80 patients with malignant melanoma in stage I (no metastases) or stage II (metastases in local lymph nodes) were recruited, of whom 40 were randomised to psycho-educational group therapy once a week for 6 weeks. Data on well-being was provided by 66 patients, and information on survival and relapse-free interval was available for 74 patients, of whom 6 had an initial diagnosis of stage II malignant melanoma. The 68 patients with stage I malignant melanoma were equally distributed in the two groups. At the 6-year follow-up, a significant reduction in mortality was seen in the intervention group among these 68 patients when compared with the control group [7]. At the end of the intervention, non-significant differences in scores for anxiety, depression and mood disturbance were observed. The differences were more pronounced at the 6-month follow-up, the patients in the intervention group reporting significantly less depression and mood disturbance than the control group [18]. After randomisation, 25% of the patients in the control group dropped out of the study, which could possibly have biased the results.

In a study from Canada in 1994 by Ilnyckyj and colleagues [19], 127 patients with various cancers were stratified on sex, physical functioning and stage of disease before randomisation. The intervention consisted of weekly group sessions for 6 months. The sessions were professionally led for the first 3 months ($n=30$) or for the full 6 months ($n=31$). These two intervention groups were compared with a group of cancer patients who met weekly for 6 months with no professional leadership ($n=35$) and with a control group of patients who did not participate in group meetings ($n=31$). Owing to the withdrawal of a considerable number of patients from the group with no professional leadership, 21 patients who had not been randomised were added after 3 months. Survival at 11 years of follow-up was analysed both including and excluding these 21 patients. In both cases, no significant difference in survival was observed [19]. The time between diagnosis of the cancer and inclusion in the study was not reported.

Table 1
Randomised studies (published in 1982–2000), in which patients receiving a psychosocial intervention were compared with a control group and the effect on survival was assessed. Anxiety, depression and other findings (emotional adjustment, mood, quality of life and pain) were assessed at the end of the intervention or up to 1 month thereafter

Study location	Cancer site (no of patients)	Intervention	Duration of follow-up on survival	Survival	Findings		
					Anxiety	Depression	Other findings
Linn and colleagues 1982 [14] Florida, USA	Various cancer types, advanced stage, life expectancy of 3–12 months ($n=120$)	Individual counselling when needed for up to 1 year	1 year	NS	Not assessed	POMS depression subscale; NS[a]	Quality of life: Sum of a range of scales; $P<0.001$
Spiegel and colleagues 1989 [6,15,16] California, USA	Breast cancer with metastases ($n=86$)	1.5 h of supportive group therapy weekly for 1 year as well as instruction in self-hypnosis to control pain to half of the intervention group	10 years	$P<0.0001$	POMS tension-anxiety subscale; $P<0.01$	POMS depression subscale; NS	Mood: POMS TMD; $P<0.01$ Pain: Pain-rating scale, sensation; $P<0.02$ Pain-rating scale, suffering; $P<0.03$ Pain-rating scale, frequency; NS Pain-rating scale, duration; NS
Fawzy and colleagues 1993 [7,18,67] California, USA	Malignant melanoma, stage I and II ($n=80$)	1.5 h of psycho-educational group therapy weekly for 6 weeks	6 years	$P=0.0066$	POMS anxiety subscale; NS	POMS depression subscale; NS[b]	Mood: POMS TMD; NS[b]
Ilnyckyj and colleagues 1994 [19] Canada	Various cancer types and stages ($n=127$)	1 h of weekly supportive group sessions for 6 months either led for the first 3 months, for the full period or without leadership	11 years	NS	Not published	Not published	Not published
Cunningham and colleagues 1998 [20,21] Canada	Breast cancer with metastases ($n=66$)	2 h of supportive and cognitive behavioural group therapy weekly for 35 weeks and an intensive weekend coping skills training course	5 years	NS	Not assessed	Not assessed	Mood: POMS-SF; NS Quality of life: FLIC; NS
Edelman and colleagues 1999 [22,23] New South Wales, Australia	Breast cancer with metastases ($n=121$)	Cognitive-behavioural group therapy weekly for 8 weeks and a family night followed by 3 monthly sessions	5 years	NS	POMS anxiety subscale; NS	POMS depression subscale; $P=0.008$[c]	Mood: POMS TMD; $P=0.036$[c]
Kuchler and colleagues 1999 [24] Germany	Gastrointestinal cancer in different stages ($n=271$)	Individual psychotherapy every second day or more frequently if necessary during hospital stay	2 years	$P=0.002$	Not published	Not published	Not published
McCorkle and colleagues 2000 [25] Pennsylvania, USA	Various cancer types and stages ($n=375$)	Three home visits and five telephone calls by specialised nurses over a 4-week period after surgery	3.67 years	$P=0.001$	Not assessed	Not assessed at the termination of the intervention	Not assessed

NS, not significant; I, intervention groups; C, control group; M, males; F, females; POMS, Profile of Mood States (TMD = Total Mood Disturbance); POMS-SF, Profile of Mood States, Short Form; FLIC, Functional Living Index Cancer; STAI, Spielberger State/Trait Anxiety Inventory; CPBS, Cancer Patient Behaviour Scale; SADS, Schedule of Affective Disorders and Schizophrenia; Leeds SAA, Leeds self-assessment of anxiety; Leeds SAD, Leeds self-assessment of depression; ESI, The Effect of Illness Scale; GHQ-60, General Health Questionnaire; DAS, Death Anxiety Scale; HADS, Hospital Anxiety and Depression Scale; PAIS, Psychosocial Adjustment to Illness Scale; BSI, Brief Symptom Inventory; BDI, Beck Depression Inventory; EORTC QLQ-C30, European Organization of Research and Treatment for Cancer Quality of Life Questionnaire (core questionnaire); CES-D, Centre for Epidemiological Studies Depression Scale; MAACL, Multiple Affect Adjective Check List; SOSI, Symptoms of Stress Inventory; SCL-90-R, Symptom check list; SIP, Sickness Impact Profile; Spitzer's QLI, Spitzer's Quality of Life Index; PANAS, Positive and Negative Affect Scale; MOS SF-36, Medical Outcomes Study, short form, 36 items; CARES-SF, Cancer Rehabilitation and Evaluation Systems, Short Form.

[a] A significant effect was observed after 3 months of intervention, but was not sustained.

[b] A significant effect was observed after 6 months of follow-up.

[c] The effect was no longer significant 3 and 6 months after the end of the intervention.

A study from Canada in 1998 by Cunningham and colleagues [20,21] comprised 66 women with metastatic breast cancer who were stratified on the basis of age and location of metastases before randomisation. The intervention consisted of 35 weekly 2-h sessions of supportive and cognitive behavioural therapy. In addition, the 30 patients in the intervention group were offered an intensive weekend course of training in coping skills during the first 2–4 months of their group membership, and 19 patients took this course. The control group received a home study cognitive behaviour package. Well-being was assessed at baseline and after 4, 8 and 14 months. Patients in the intervention group experienced significantly more anxious preoccupation and less helplessness than the controls, but no improvements in mood or quality of life were recorded [21]. At the 5-year follow-up, no significant difference in survival was found between the two groups [20]. The survival curves of the two groups in this study closely resembled that of the intervention group in the study of Spiegel and colleagues [6]. The study of Cunningham and colleagues was well conducted, but offering the control group a home study cognitive behavioural package may have weakened the study, as the two groups may have tended to become more similar. In addition, this study, like most of these studies, had a relatively small sample size. The Kaplan–Meier plot of survival after the first metastases does not, however, indicate lack of strength as an explanation for the negative finding, as the survival curves of the intervention and control groups were identical [20].

In a study from Australia in 1999 by Edelman and colleagues [22,23], 121 women with metastatic breast cancer were randomised, the intervention group receiving eight weekly sessions of cognitive-behavioural therapy, a family night and three further monthly sessions. The intervention group showed reduced total mood disturbance and depression at the assessment immediately after therapy, but these improvements were not seen at the 3- and 6-month follow-ups [23]. No significant difference in survival was observed between the intervention group and the control group at the 5-year follow-up [22]. A major drawback of this well-conducted study is that 19 of the 62 patients who were randomised to the intervention group subsequently dropped out. This may have weakened the study, as the survival analysis was done on an ‘intention-to-treat’ basis. An analysis of survival after exclusion of the drop-outs did not alter the result.

In a study from Germany in 1999 by Kuchler and colleagues [24], 271 patients with a primary diagnosis of gastrointestinal cancer (oesophagus, stomach, liver/gallbladder, pancreas, colorectum) were stratified by sex before randomisation. The intervention consisted of individual psychotherapy during the hospital stay, a therapist visiting each patient every second day or more frequently if necessary. Quality of life was measured several times, but the results were not reported. A significant difference in survival was observed between the intervention group and the control group after 2 years of follow-up ($P=0.002$). After randomisation, 34 patients in the control group requested transfer to the intervention group, and 10 patients in the intervention group requested transfer to the control group. As an ‘intention-to-treat’ analysis was used, the patients remained in their originally assigned groups. Owing to the cross-over, the true prognostic effect of the intervention was probably underestimated.

A study from the USA in 2000 by McCorkle and colleagues [25] comprised 375 postsurgical cancer patients aged 60 years or more. The intervention consisted of three home visits and five telephone calls from specialised nurses over 4 weeks. The patients in the intervention group and their family caregivers received comprehensive clinical assessments, monitoring and teaching, and the nurses functioned as a liaison with healthcare settings and providers in the provision of technical and psychological support. No significant differences in the degree of depression were observed between the two groups at the 3- and 6-month follow-ups. A significant positive effect on survival was reported after 44 months of follow-up ($P=0.001$).

In summary, two of the four studies that found a positive effect on survival and also assessed psychological well-being found a beneficial effect during follow-up [6,7], whereas two of the four studies that failed to find an effect on survival and assessed well-being reported a positive effect that did not persist [14,22].

3.2. *Effect of psychosocial intervention on well-being*

In addition to the eight studies summarised above, 35 randomised studies have addressed the effect of psychosocial intervention on well-being, without assessing survival [26–61]. In 30 studies, well-being was assessed within 1 month of termination of the intervention. Only these studies are summarised in Tables 2 and 3, because the follow-up was comparable. The tables show studies in which one or more intervention strategies, respectively, are compared with a control situation.

3.2.1. *Populations*

The populations studied were heterogeneous with respect to sex, cancer type, stage of disease and other treatment. Breast cancer was the only site that was examined in more than three studies. Anxiety and/or depression were measured in five studies of breast cancer patients [42,48,49,51,56]. The results were inconsistent, the more recent studies tending to show no effect [48,49].

Table 2
Randomised studies (published in 1982–2001) of the effect of psychosocial intervention on anxiety, depression and other findings (emotional adjustment, mood, quality of life, and pain) at the end of the intervention or up to 1 month thereafter

Study location	Cancer site (no. of patients)	Intervention	Findings		
			Anxiety	Depression	Other findings
Johnson 1982 [26] Minnesota, USA	Type and stage not reported ($n=52$)	1.5 h education in groups twice a week for 4 weeks: "I can cope"	STAI; $P=0.00009$	Not assessed	Not assessed
Jacobs and colleagues 1983 [27] California, USA	Hodgkin's disease, stage not reported ($n=34$)	1.5 h peer supportive group therapy weekly for 8 weeks	CPBS; NS	CPBS; NS	Quality of life: CPBS; NS
Forester and colleagues 1985 [29] New York, USA	Various cancer types, stage not reported ($n=100$)	Individual psychotherapy weekly for 10 weeks during radiation therapy	Not published	Not published	Emotional adjustment: SADS; $P<0.01$
Rimer and colleagues 1987 [30] Pennsylvania, USA	Various cancer types and stages, life expectancy of a minimum of 3 months ($n=230$)	15 min counselling from an oncology nurse and printed material about pain management	Not assessed	Not assessed	Pain: McGill–Melzack's Present Pain Index; $P=0.07$
Ali and Khalil 1989 [31] Egypt	Bladder cancer, stage not reported ($n=30$)	1/2–1 h preoperative information	STAI; $P<0.001$	Not assessed	Not assessed
Hagopian and Rubenstein 1990 [32] Pennsylvania, USA	Various cancer types and stages ($n=55$)	Weekly telephone calls from a project nurse during radiation therapy	STAI; NS	Not assessed	Not assessed
Lerman and colleagues 1990 [33] Pennsylvania, USA	Various cancer types and stages, life expectancy of a minimum of 6 months ($n=48$)	30 min relaxation training before starting chemotherapy	Multiple Affect Adjective Checklist, Anxiety subscale; NS ($P=0.07$)	Multiple Affect Adjective Checklist, Depression subscale; NS	Not assessed
Bindemann and colleagues 1991 [34] Scotland, United Kingdom	Various cancer types and stages, life expectancy of a minimum of 6 months ($n=80$)	25 min relaxation training at 13 sessions in 12 weeks	Leeds SAA; M: $P<0.003$, F: $P<0.0001$ ESI anxiety severity; M: $P<0.0009$, F: $P<0.0001$ STAI: significant (P values not published)	Leeds SAD; M: NS, F: $P<0.001$ ESI depression severity; M: NS, F: $P<0.0004$	Emotional adjustment: GHQ-60; M: $P<0.001$, F: $P<0.009$
Connor 1992 [35] California, USA	Various cancer types, terminal stage ($n=24$)	One individual session with a therapist for denial-related coping ability	DAS; NS	Not assessed	Not assessed
Greer and colleagues 1992 [36] England, United Kingdom	Various cancer types and stages, life expectancy of a minimum of 12 months ($n=174$)	1 h or more individual cognitive-behavioural treatment for approximately six times in 8 weeks	HADS Anxiety Scale; $P=0.019$	HADS Depression Scale; NS	Emotional adjustment: PAIS; NS
Pruitt and colleagues 1993 [38] Texas, USA	Various cancer types, stage not reported ($n=31$)	1 h individual education on coping and communication weekly for 3 weeks during radiotherapy	BSI Anxiety subscale; NS	BSI Depression subscale; $P=0.02$	Emotional adjustment: BSI General Severity Index; NS
Berglund and colleagues 1994 [39,40] Sweden	Various cancer types, stage not reported ($n=199$)	2 h physical training, information, and education on coping techniques at 11 sessions in 7 weeks	HADS Anxiety Scale; NS	HADS Depression Scale; NS	Quality of life: Scale not published; NS Pain: Scale not published; NS
Brandberg and colleagues 1994 [41] Sweden	Malignant melanoma, stage I ($n=149$)	Information in a brochure and an 1.5 h group meeting	HADS Anxiety; NS	HADS Depression; NS	Not assessed

(*continued on next page*)

Table 2 (*continued*)

Study location	Cancer site (no. of patients)	Intervention	Findings		
			Anxiety	Depression	Other findings
Marchioro and colleagues 1996 [42] Italy	Breast cancer without metastases ($n=36$)	50 min individual cognitive psychotherapy weekly + family counselling once every second month during chemotherapy (9 months)	Not assessed	BDI; $P<0.0001$	Quality of life: FLIC; $P=0.0001$
De Wit and colleagues 1997 [43] The Netherlands	Various cancer types and stages, experiencing pain, life expectancy of a minimum of 3 months ($n=313$)	1/2–1 h education in pain management and two telephone calls 3 and 7 days postdischarge by project nurses	Not assessed	Not assessed	Quality of life: EORTC QLQ-C30; NS Pain: EORTC QLQ-C30 Pain symptom; $P=0.05^a$/NS^b McGill's Pain Questionnaire Present Pain Intensity; $P<0.001^a$/NS^b, Average Pain Intensity; $P<0.01^a$/NS^b, Worst Pain Intensity; NS
McQuellon and colleagues 1998 [46] North Carolina, Tennessee and Virginia, USA	Type and stage not reported ($n=150$)	A clinic tour, general information, and a question and answer session with an oncology counsellor	STAI State Anxiety; $P<0.0001$ STAI Trait Anxiety; $P<0.013$	CES-D; $P<0.001$	Mood: Brief POMS TMD; $P<0.0001$
Speca and colleagues 2000 [47] Canada	Various cancer types and stages ($n=90$)	1.5 h meditation training in groups weekly for 7 weeks + home practice	POMS Anxiety subscale; $P<0.001$	POMS Depression subscale; $P<0.01$ SOSI Depression; NS	Mood: POMS TMD; $P<0.001$
Fukui and colleagues 2000 [48] Japan	Breast cancer, lymph node metastasis positive and/or histological or nuclear grade 2-3 ($n=50$)	1.5 h psycho-educational and supportive group therapy weekly for 6 weeks	HADS Anxiety subscale; NS POMS Tension/anxiety subscale; $P=0.03$ (Level of significance; 0.01)	HADS Depression subscale; NS, POMS Depression subscale; $P=0.04$ (Level of significance; 0.01)	Mood: POMS TMD; 0.003
Classen and colleagues 2001 [49] California, USA	Breast cancer with metastases ($n=125$)	1.5 h supportive-expressive group therapy weekly for 1 year or more	POMS Tension/anxiety subscale; NS	POMS Depression subscale; NS	Mood: POMS TMD; NS ($P=0.02$ when removing the last observation within 1 year from death)

For abbreviations, see footnote to Table 1.

[a] Did not receive visits from a district nurse.

[b] Received visits from a district nurse.

Table 3
Randomised studies (published in 1986–2000), in which two kinds of psychosocial intervention were compared with each other and with a control group. Anxiety, depression and other findings (emotional adjustment, mood, quality of life, and pain) were assessed at the end of the intervention or up to 1 month thereafter

Study location	Cancer site (no. of patients)	Intervention	Findings		
			Anxiety	Depression	Other findings
Cain and colleagues 1986 [50] Connecticut, USA	Gynaecological cancer, stage not reported, life expectancy of a minimum of 12 months ($n=80$)	(1) Individual or (2) group counselling and support weekly for 8 weeks: "I can cope"	Hamilton Anxiety Scale; $P=0.02$ (I_2 equals C, I_1 is better)	Hamilton Depression Scale; NS	Emotional adjustment: PAIS; NS
Davis 1986 [51] Canada	Breast cancer, stage I ($n=25$)	(1) Biofeedback, relaxation or (2) cognitive therapy with training in coping techniques and relaxation in 13 group sessions for 8 weeks	STAI State anxiety; NS	Not assessed	Not assessed
Telch and Telch 1986 [52] California, USA	Various cancer types and stages ($n=41$)	(1) 5 h education on coping techniques or (2) supportive group therapy weekly for 6 weeks	POMS Tension/anxiety; $P<0.001$[a], (NS for I_1 versus I_2)	POMS Depression Scale; $P<0.001$ ($P<0.01$ for I_1 versus I_2)	Mood: POMS TMD; $P<0.001$[a] ($P<0.01$ for I_1 versus. I_2)
Burish and colleagues 1991 [53] Tennessee, USA	Various cancer types, stage not reported ($n=60$)	(1) 1.5 h individual coping preparation before chemotherapy or (2) 45 min relaxation training at three sessions during chemotherapy	MAACL Anxiety; NS	MAACL Depression; $P<0.05$ for I_1 versus C, NS for I_2 versus C	Not assessed
Evans and Connis 1995 [54] Seattle, USA	Various cancer types, stage II ($n=78$)	(1) Group support or (2) group cognition/behavioural training weekly for 8 weeks during radiation therapy	SCL-90-R Anxiety Scale; $P<0.05$ for I_1 versus C	SCL-90-R Depression Scale; $P<0.05$[a] CES-D; NS	Emotional adjustment: SCL-90-R Global Severity; $P<0.05$ for I_1 versus C
Johnson 1996 [55] New York, USA	Prostate cancer, localised ($n=62$)	(1) Three tape-recordings and written material giving concrete information or (2) giving instructions in self-care and coping during radiation therapy	Not assessed	Not assessed	Emotional adjustment: SIP; NS Mood: POMS Bipolar Profile; NS
Mantovani and colleagues 1996 [57] Italy	Various cancer types, mainly stage III-IV ($n=74$)	(1) Support from volunteers 2–3 times (6 h) weekly or (2) with simultaneous 1 h psychotherapy weekly for about 6 months. All participants had psychopharmacological treatment	STAI State anxiety and Anxiety-traits; $P<0.001$	BDI; $P<0.001$	Quality of life: Spitzer's QLI; NS, FLIC; $P<0.001$ Pain: Scott Huskisson's visual analogue; $P<0.001$
Braden and colleagues 1998 [58] Arizona, USA	Breast cancer, all stages ($n=193$)	(1) 1.5 h group self-help sessions weekly for 6 weeks or (2) 6 weekly telephone calls aimed at uncertainty management or (3) both interventions simultaneously	Not assessed	Not assessed	Emotional adjustment: PANAS Negative Affect; $P<0.01$ for all interventions versus control ($P<0.01$ for I_1 versus I_2)
Walker and colleagues 1999 [59] Utah, USA	Breast cancer, stage I or II ($n=44$)	(1) Emotional expression in writing once or (2) three times at the completion of radiotherapy	Not assessed	Not assessed	Mood: PANAS Negative affect; NS, PANAS Positive affect; NS
Helgeson and colleagues 1999 [60] Pennsylvania, USA	Breast cancer, stage I, II or III ($n=312$)	(2) 1 h education or (2) 45 min peer discussions or (3) education and peer discussions in groups weekly for 8 weeks	Not assessed	Not assessed	Emotional adjustment: MOS SF-36 mental health component; NS, Positive affect scale; NS, Negative affect scale; NS
Herth 2000 [61] Minnesota, USA	Different cancer types with first recurrence ($n=115$)	(1) 2 h mix of information, cognitive-behavioural therapy and psychotherapy aimed at enhancing hope or (2) 2 h information in groups weekly for 8 weeks	Not assessed	Not assessed	Quality of life: CARES-SF; $P=0.036$ for I_1 versus. I_2, $P=0.032$ for I_1 versus C

[a] P values for I_1 versus C and I_2 versus C were both significant.

The hypothesis that only patients with severe psychological distress benefit from psychosocial intervention was supported by the results of five studies that included only patients who were found on screening to be suffering from psychological distress [36,38,52,54,57]: all these studies found a significant effect on anxiety and/or depression (Tables 2 and 3).

3.3.2. *Intervention strategies*

In studies in which different intervention strategies were compared, no clear pattern emerged. A randomised study from the USA in 1986 by Cain and colleagues [50] involved a comparison of individual and group counselling and support. The patients were women with newly diagnosed gynaecological cancers, and the two intervention groups were compared with a control group. At the end of the 8-week intervention, the patients given individual counselling reported significantly less anxiety than those receiving group counselling or the control group, and, at the 6-month follow-up, the patients in both intervention groups reported significantly less anxiety and depression than women in the control group [50] (Table 3). The intervention used in the studies of F.I. Fawzy and colleagues in 1990 [18] (Table 1) and N.W. Fawzy in 1995 [44] (not in table) in the USA was similar, but was used in a group setting in the former study and in an individual setting in the latter. Patients in the intervention group in the group setting improved their coping skills, whereas no significant effect on coping was observed in the individual setting [62].

A study in the USA, by Telch and Telch in1986 [52], showed that training in coping techniques was more effective than supportive therapy, whereas another study in the USA, by Evans and Connis in 1995 [54], found the opposite to be true (Table 3).

With regard to the effectiveness of various intervention strategies used in the studies that were reviewed in reducing anxiety and/or depression, of the studies in which psychological education was used, eight showed a positive effect [23,26,36,38,42,50,52,54], and four showed no effect [18,39,48,51]. Long-term (>6 months) psychotherapeutic intervention had a positive effect on well-being in two studies [15,57] and no effect in two others [14,49]. Likewise, a short-term psychotherapeutic intervention had a positive effect on well-being in two studies [52,54] and no effect in two others [32,35]. Short-term provision simply of information had a beneficial effect in three studies [31,46,53] and no effect in one other study [41]. As information is part of psychological education, these two strategies appear to be more effective than supportive psychotherapy, regardless of duration, showing the importance of including education and information in psychosocial interventions.

3.2.3. *Timing and intensity of intervention*

The optimal timing of an intervention has not been fully elucidated. In many reports, the time between diagnosis and intervention was not given, probably because the patient population was heterogeneous in this regard. In a study from Canada by Edgar and colleagues in 1992 [63], the same intervention was provided immediately after the initial diagnosis of cancer and 4 months later. The group that received the intervention later was significantly less depressed, anxious and worried 8 months after inclusion and continued to be less worried about their illness than the group given early intervention 4 months later.

In another study in Canada, by Cunningham and colleagues in 1995 [64], a 6-week intervention consisting of supportive therapy and training in coping strategies was compared with the same intervention provided during an intensive weekend programme. At 6 and 19 weeks of follow-up, no difference in well-being was found between the two groups.

To the best of our knowledge, these are the only studies in which timing and intensity of intervention were compared; however, they were not included in our review, as no untreated control group was included.

4. Discussion

4.1. *Survival*

The eight studies of the effect of interventions on survival were generally well conducted, but three had a sample size of fewer than 90 persons [6,7,20], which would have increased the possibility that a positive or detrimental effect would be observed on the basis of a few atypical patients. The two studies with a sample size greater than 250 both showed improved survival [24,25], but the follow-up in these two studies was less than 4 years, which reduces the conclusiveness of the results. Two other studies that showed a benefit with regard to survival had follow-up periods of 10 [6] and 6 years [7].

No consistent pattern of an effect on survival emerged with the different intervention strategies. In the study of McCorkle and colleagues in 2000 [25], the intervention was not only psychosocial, but also included clinical assessment. The results may therefore indicate an effect on prognosis of optimised medical treatment.

It has been proposed that psychosocial intervention affects the prognosis only of patients with early-stage cancer, as the natural course of more advanced stages might obviate a possible effect of psychosocial factors. Indeed, except for one study of patients with diseases in various stages [19], all studies failing to find an effect on survival included late-stage patients [14,20,22]. The four studies that found an effect on survival of psychosocial intervention [6,7,24,25] included patients with late-stage cancer [6], patients with cancers known to have a poor prognosis [24], a study population that was heterogeneous in terms of stage [25] and patients with early-stage cancer [7], thus precluding any clear conclusion.

It seems unlikely that an intervention that does not affect psychological well-being could affect survival, and this perception is supported by the finding that studies that showed no persistent effect on well-being also did not show a beneficial effect on survival [14,22]. It had also been proposed that intervention does not enhance survival but, rather, that randomisation to a control group decreases the length of survival. Patients who are randomised to the control group in psychosocial intervention studies might be disappointed that they are not receiving an intervention that they consider might have been helpful. However, in a study in Sweden by Berglund and colleagues [65], in which 73 non-participants were compared with 199 cancer patients participating in a randomised study of the effect of psychosocial intervention and physical training, no negative effect of randomisation to the control group was observed on psychosocial variables over time when controls were compared with non-participants.

None of the studies included in this review showed that any effect on prognosis was mediated by alteration of the immune system. However, a positive effect on survival was observed in the study of patients with malignant melanoma [7], an immune-related cancer form [66]. This was the only study in which immune parameters were assessed [7,67]. Although changes in these parameters were indeed observed, these were unrelated to survival [7]. As changes in health behaviour were not measured in any of the studies, the possible mechanism is unknown.

4.2. *Well-being*

The comparability of the results of the studies on well-being is reduced by differences in the time between diagnosis of cancer and inclusion in the study, in patient populations, in intervention strategies and in outcomes. Furthermore, most of the studies suffered from methodological flaws. The randomisation procedure and the characteristics of non-responders were often not adequately described. The ‘intention-to-treat’ principle may not have been followed in some of the analyses, which would violate the principle of randomisation and possibly result in an overestimate of the benefit, if only highly motivated patients experiencing a beneficial effect were included in the analyses. Few reports indicated whether the outcome was assessed by persons involved in the intervention (a possible source of interviewer bias), and long-term follow-up was rare.

The results of the studies were not consistent, as 15 of 25 studies in which anxiety and depression were assessed immediately after the end of the intervention (Tables 1–3) showed a significant positive effect [15,23,26,31,34, 36,38,42,46,47,50,52–54,57]. The fact that the majority of the studies gave positive results may be a result of publication bias, as some studies with negative results may not have been published. Some of the ‘positive’ effects of intervention may have been chance findings, as many of the studies included multiple scales and thereby made multiple comparisons, with a strong probability of chance findings. In one study, a significant effect on one scale of depression was not found on another [54]. Most of the findings were, however, in the predicted direction, and the lack of significance in some studies might have been due to lack of power, as the study populations were generally small.

Of the five studies in which more than 100 patients were included and anxiety and depression were measured [36,40,41,46,49], two showed a positive effect at the end of the intervention [36,46]. However, similar outcomes were assessed on a range of different scales, so that the results of one study cannot be extended to another. In general, methods have improved over the past decade; however, consideration only of studies conducted during that period revealed the same degree of inconsistency as in the total group of studies, precluding a clear conclusion [34–49,53–61].

A meta-analysis conducted in 1995 of published randomised studies of psychosocial intervention included 15 of the studies described above [68]. The analysis showed a significant, small-to-moderate effect on emotional adjustment, which covered a number of scales of mood state, fear and anxiety, depression, denial or repression, self-esteem, locus of control, satisfaction with medical care, other attitudes, personality traits and other types of emotional adjustment or distress. It is not clear whether outcomes such as satisfaction with treatment accounted for most of the effect, or if anxiety and depression had an independent effect. A meta-analysis conducted in 1999 of studies published before 1993 of psychological interventions among cancer patients included nine of the studies described above and several non-randomised studies [69]. A moderate positive effect was found on anxiety when the results for a total sample of 1023 patients were pooled, although the size of the effect was reduced when only randomised studies of high quality and with a sample size of more than 40 patients were included. A moderate positive effect for depression was found for a pooled sample of 1101 patients, but with the inclusion of only the randomised studies of high quality and those with a sample size of more than 40 patients the size of the effect was reduced to a clinically negligible value. Group therapy tended to be more effective than individual therapy, and psycho-educational interventions appeared to be particularly effective. Furthermore, short-term interventions seemed to be more effective than long-term ones, and the most experienced therapists tended to be the most effective. The effect on anxiety and depression tended to be greater in patient groups who were found on screening to suffer from psychological distress, when compared with unscreened populations [69]. Although it is difficult to conduct a meta-analysis of heterogeneous studies, the results of this meta-analysis are convincing and supports our conclusion that psychosocial intervention may have a weak effect on well-being and may be most relevant in populations screened for psychological distress.

5. Conclusion

The results of a large number of studies fail to demonstrate a conclusive effect of psychosocial intervention on survival and psychological well-being. Several explanations are possible. First, different intervention strategies were used in different studies, and perhaps only some of them affect prognosis and/or well-being and in only certain patient groups. Secondly, the effect may be weak, accounting for the inconsistent results found for the generally small study populations. Thirdly, the effect of the interventions may have been diluted by the inclusion of unselected patient groups rather than being restricted to selected groups of patients in need of psychosocial support.

In order to make progress in this field of research, large-scale studies are needed that allow evaluation of a possibly small effect. Identifying patients in need of psychosocial intervention by screening for psychological distress or available social support could enhance any effect on well-being. Sound methods regarding the randomisation procedure and assessment of outcomes should be used, and international collaboration might be considered in order to increase the study size and the comparability of the findings. Future studies on survival should address the possible mechanisms underlying an improved prognosis.

If the effect of psychosocial intervention on endpoints such as survival, anxiety and depression is found to be weak, it may have other, more subtle benefits, which are difficult to measure, but which might justify implementation of psychosocial programmes in the clinical treatment of cancer patients. Meanwhile, the issue of possible beneficial effects of psychosocial intervention for cancer patients remains unresolved.

Acknowledgements

The study was financially supported by The Danish Cancer Society, Psychosocial Research Foundation (Grant 97 225 58), The Health Insurance Fund (Grant 11/047-97), Mogens and Else Wedell-Wedellsborg's Fund (Grant 579), and The IMK General Fund (Grant 30206-081).

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