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REVIEW ARTICLE

WHAT IS COVERED BY "CANCER REHABILITATION" IN PUBMED? A REVIEW OF RANDOMIZED CONTROLLED TRIALS 1990–2011

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Objective: **This focused review examines randomized controlled studies included by the term "cancer rehabilitation" in PubMed. The research questions concern the type of interventions performed and their methodological quality.**

Design: **Using the Medical Subject Headings (MeSH) terms: *neoplasm AND rehabilitation*, all articles with randomized controlled studies that included adult cancer patients, written in English, were extracted from PubMed. Papers covering physical exercise, psychiatric/psychological treatment or social support only were excluded as they had been reviewed recently. Abstracts and papers were assessed by 3 pairs of reviewers, and descriptive information was extracted systematically. Methodological quality was rated on a 10-item index scale, and the cut-off for acceptable quality was set at ≥8.**

Results: **A total of 132 (19%) of the 683 identified papers met the eligibility criteria and were assessed in detail. The papers were grouped into 5 thematic categories: 44 physical; 15 art and expressive; 47 psycho-educative; 21 emotionally supportive; and 5 others. Good quality of design was observed in 32 studies, 18 of them uni-dimensional and 14 multi-dimensional.**

Conclusion: **Published randomized controlled studies on cancer rehabilitation are heterogeneous in terms of content and samples, and are mostly characterized by suboptimal design quality. Future studies should be more specific and well-designed with sufficient statistical strength.**

Key words: rehabilitation; cancer patients; randomized controlled trials; PubMed; review.

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INTRODUCTION

With ongoing improvements in prognosis for major cancer types from the early 1970s, the rehabilitation of cancer patients (RCPs) has become of clinical importance. An accepted definition of RCPs is provided by DeLisa in 2001: "*Cancer rehabilitation* is a concept that is defined by the patient and involves helping a person with cancer to obtain maximum physical, social, psychological, and vocational functioning within the limit by the disease and its treatment" (1, p. 970). The World Health Organization's (WHO) report on disability subsequently presented a wider definition of *rehabilitation* as "a set of measures that assist individuals who experience, or are likely to experience, disability to achieve and maintain optimal functioning in interaction with their environments" (2, p. 96).

Typically RCPs occurs for a specific period of time, and can involve both single and multiple interventions delivered by a single professional, or a team of rehabilitation workers. RCPs may be needed from the acute or initial phase immediately after recognition of cancer as well as later on in the post-acute and maintenance phases.

With these definitions, this study reviewed the content, results, and methodological quality of the randomized controlled trials (RCTs) on RCPs in PubMed. A further reason for carrying out this review was the recent request by Alfano et al. (3) concerning revitalization of the link between cancer survivorship and cancer rehabilitation, and their presentation of a new model of comprehensive cancer rehabilitation involving a multidisciplinary team of providers (3). At the same time a closely related request was raised from both Nordic and European quarters (4). Finally, a recent Cochrane review (5) of multidimensional rehabilitation programmes for adult cancer survivors had reached the same conclusions as Alfano et al.

The first RCT of RCPs was noted in PubMed in 1979, and at the end of 1989, 21 RCTs had been recorded in that database. However, the annual number of studies has increased and, as of June 2012, a total of 616 RCTs concerning RCPs are cited in PubMed. The PubMed database is delivered by the US National Library of Medicine, it is free of charge and easily available, and therefore widely used as a tool by clinicians and clinical researchers. Since RCTs have the highest evidence level and the number of such papers found was more than 600, we decided to study only RCTs of RCPs published in English and registered in PubMed from 1990 to 2011. Our study should be considered as a *focused review* not fulfilling all the specific methodologi-

cal demands needed for a systematic review according to the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) or Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) designs. We reviewed papers on RCPs using RCTs with the aim of answering the following research questions: (*i*) What kinds of interventions have been published? (*ii*) What characterizes the quality of the research designs used in these studies?

METHODS

Literature search

A search of PubMed was carried out in order to identify relevant articles related to RCPs. "Cancer rehabilitation" is not a Medical Subject Headings (MeSH) term, and therefore *neoplasm* was used as the main MeSH term, covering all cancer diagnoses, and *rehabilitation* as the second MeSH term. By using only 2 MeSH terms in combination the search was broadened optimally. The following limitations were also defined: studies of humans, RCTs, all adults aged ≥ 19 years, from 1 January 1990 to 31 December 2011, published in English.

Selection criteria

Studies with interventions involving medical and surgical treatments and procedures were excluded. Due to recent reviews, we also excluded interventions concerning the following themes: physical exercise alone, psychiatric/psychological treatment, social support only, or artificial nutrition only (6–9). Observational and case-control studies without randomization were excluded due to the number of RCT papers.

Reviewers' evaluating procedures

Six reviewers operated as 3 pairs of evaluators, and all reviewers held PhDs in oncology, 2 as doctors, and 2 as instructors in physical activities, 1 as a nurse, and 1 as a social worker. First, all abstracts were distributed at random (every third paper to each pair) between 3 pairs, and they were scanned for fulfilment of inclusion and exclusion criteria. If the criteria were unclear in the abstract, the full paper was examined. Each pair of reviewers resolved any disagreement between themselves by discussion. If they still disagreed the study was evaluated by one of the other pairs. Each pair read the full-text papers allotted to them by included abstracts, and eventual disagreements in the evaluations were settled in the same way as for the abstracts.

A registration form for major variables was developed, and data were extracted from each paper and rated according to predefined categories. Collected data were stored on separate extraction sheets for each paper, and then merged.

Identification of papers

The PubMed search identified 683 RCT papers, and based on the selection criteria 414 (61%) of the retrieved abstracts were excluded from further review. A set of 269 (39%) full-text papers was then left for evaluation, and 137 (51%) of these papers were excluded since closer inspection showed that they did not meet our selection criteria. This examination left 132 full-text papers for intensive studies (19% of the initially identified papers).

RESULTS

Characteristics of the randomized controlled trial papers

The characteristics of the studies were based on the total numbers of participants and, in all subgroups, the mean age, gender, and diagnosis were specified.

Of the 132 papers, only 11 (8%) used the term "rehabilitation" in the title. The number of participants in the groups varied from 10 to 921, with a total number of 16,331 reporting 184 different types of interventions (Table I). There were 40 studies with 130 or more participants (at least 65 in each group, which is the minimally necessary sample size when 2 groups are compared) and 92 with fewer than 130 participants (number not shown in tables). Only 16 (12%) studies were published between 1990 and 1999, 30 (23%) between 2000 and 2004, and 86 (65%) between 2005 and 2011.

Study interventions

Based on their content and interventions the studies were grouped into 5 thematic groups (Table I), as follows:

I. *Physical interventions* included physiotherapy, endurance exercise and strength, flexitouch, massage, elastic sleeve, finger acupressure, lymph drain, pelvic muscle exercise, reflexology, shoulder exercises, vacuum erection devices, yoga, and relaxation. This category contained 44 studies (33%) and 56 interventions (30%).

II. *Art and expressive interventions* concerned music therapy, art therapy, dance and movement, expressive writing, imagery, and reading, with 15 studies (11%) and 17 interventions (9%).

III. *Psycho-educative interventions* included self-care instructions, cognitive behavioural treatment, sleep education, and stress management, relating to 47 studies (36%) and 70 interventions (38%).

IV. *Emotionally supportive interventions* covered support groups, emotional support, support for family, and hope intervention programme with 21 studies (16%) and 33 interventions (18%).

Table I. *An overview of intervention types in the 132 selected papers*[a]

Group	Thematic groups	Studies *n* (%)	Interventions *n* (%)	Studies with quality score ≥ 8 *n* (%)
I	Physical interventions	44 (33)	56 (30)	9 (28)
II	Art and expressive interventions	15 (11)	17 (9)	1 (3)
III	Psycho-educative interventions	47 (36)	70 (38)	15 (47)
IV	Emotional supportive interventions	21 (16)	33 (18)	6 (19)
V	Other interventions	5 (4)	8 (5)	1 (3)
Total		132 (100)	184 (100)	32 (100)

[a]The first intervention listed in studies with 2 or more interventions (see Table II) decides the thematic group in this table.

V. Other interventions ($n = 5$) included food and nutrition (fish-oil, diet), lifestyle interventions, hypnosis, and smoking cessation contained by 5 studies (4%) and 8 interventions (5%).

Assessment of scientific quality

The rating of the methodological quality of the papers was based on the criteria published by Iles et al. (10, 11). Their approach included scoring of 10 quality items for each paper (Appendix I). Based on the scorings of the 2 reviewers, each paper was rated within a range of scores from 0 (poorest quality) to 10 (best quality). Since we mainly were interested in studies with good design quality, we applied a cut-off at the 75th percentile with total score of ≥ 8 as definition of "good quality" (GQ) paper. Accordingly, papers with scores < 8 were defined as "less good quality" (LGQ) papers.

Based on this dichotomy, 100 papers (76%) were classed as LGQ and 32 (24%) studies as GQ. Only the latter papers are described in further detail here.

The 32 GQ papers belonged to the following thematic groups: 9 to group I (3 also used interventions from other categories), 1 to group II, 15 to group III (2 also used interventions from other categories), 6 to group IV, and 1 to group V.

Characteristics of good quality studies

The 32 GQ studies assessed 50 interventions, and the characteristics of these interventions were as follows: 21 studies concerned 1 intervention (uni-dimensional) compared with standard or usual care, 11 studies compared 2 or more types of interventions (multi-dimensional) and, among them, only 4 compared the interventions with standard care (Table II). Three studies got maximum GQ ratings: Korstjens et al. (16) and Sharp et al. (18) in group I, and the study by Kissane et al. (40) in group III (Table II).

The GQ group consisted of 18 uni-dimensional (intervention compared with treatment-as-usual) and 14 multi-dimensional (2 or more interventions compared). The study by Sharp et al. (18) was uni-dimensional, while those by Korstjens et al. (16) and Kissane et al. (40) were multi-dimensional.

Other characteristics

As shown in Table II 17 of the studies assessed a mixed group of cancer diagnoses and 12 studies assessed interventions for breast cancer, 2 for prostate cancer, 1 study covered colorectal cancer and another lymphomas, each with both genders.

Respondents of both sexes were found in 16 studies, 13 studies examined females only, and 3 studies reported on males only.

A similar number of studies took place at the time of primary treatment ($n = 12$) and the time after primary treatment ($n = 15$), while 4 studies were conducted during and after primary treatment, and for 1 study the time of assessment could not be identified (Table II). Only 1 of the papers was published in the 1990s (20), 8 between 2000 and 2004, and 23 between 2005 and 2011. Close to half of the GQ studies were from the USA

Table II. *First authors, component of interventions, characteristics and quality index score in each study according to categories I–V*

Ref Country	Component of the interventions	Numbers of studies, mean age, years, gender and diagnosis of the samples	Inclusion criteria clearly described Situation at baseline described	Measure time adequate Population criteria described	Used valid assessment tools Power calculated Follow-up	Non-responds described Intent to treat Blinded	Treatment setting[a]	Quality Index scores	Assessments[b]
Studies with contents in category I: Physical interventions									
Box et al., 2002 (13) Australia	Elective physiotherapy intervention. (IG 1) vs Instructions book for exercise. (IG 2).	$n = 65$ IG 1 = 37/IG 2 = 38 Mean age 56 Female Breast cancer	Yes Yes	Yes Yes	Yes Yes Yes	No No Yes	2	8	3
Cheung et al., 2003 (14) Hong Kong	Progressive muscle relaxes programme (IG 1)* vs standard care (SC)*.	$n = 59$ IG 1 = 29/SC = 30 Mean age 58 Male Prostate cancer	Yes Yes	Yes Yes	Yes Yes Yes	Yes Yes Yes	2	8	1
Lauridsen et al., 2005 (15) Danmark	Physiotherapy 2 weeks (IG 1) and 7 weeks (IG 2) after surgery.	$n = 139$ IG 1 = 67/IG 2 = 77 Mean age 54 Female Breast cancer	Yes Yes	Yes Yes	Yes Yes Yes	Yes Yes No	2	9	2

Table II. *Contd.*

Ref Country	Component of the interventions	Numbers of studies, mean age, years, gender and diagnosis of the samples	Inclusion criteria clearly described Situation at baseline described	Measure time adequate Population criteria described	Used valid assessment tools Power calculated Follow-up	Non-responds described Intent to treat Blinded	Treatment setting[a]	Quality Index scores	Assessments[b]
Korstjens et al., 2008 (16) The Netherlands	Physical training and cognitive-behaviour training (IG 1) vs physical training (IG 2).	*n*=147 IG 1=76/IG 2=71 Mean age=50 Male and female Mixed diagnosis	Yes Yes	Yes Yes	Yes Yes Yes	Yes Yes Yes	2	10	3
May et al., 2008 (17) The Nederlands	Physical training (IG 1) and physical training with cognitive behavioural training (IG 2).	*n*=147 IG 1=71/IG 2=76 Mean age 50 Male and female Mixed diagnosis	Yes Yes	Yes Yes	Yes Yes No	Yes Yes Unclear	2	8	3
Sharp et al., 2009 (18) UK	Psychological effects of reflexology in early breast cancer.	*n*=183 IG 1=66/IG 2= 61/ SC=62 Mean age=59 Female Breast cancer	Yes Yes	Yes Yes	Yes Yes Yes	Yes Yes Yes	2	10	1
Study with contents in category II: Art and expressive interventions									
Monti et al., 2006 (19) USA	Psychosocial group with mindfulness based art therapy (IG 1) vs wait-list group (IG 2).	*n*=111 IG 1=55/IG 2=56 Mean age 54 Female Mixed diagnosis	Yes Yes	Yes Yes	Yes Yes No	Yes Yes Yes	2	9	1
Studies with contents in category III: Psycho-educative interventions									
Greer et al., 1992 (20) UK	Adjuvant psychological therapy (IG 1) vs standard care (SC).	*n*=174 IG 1=72/SC=84 Mean age 52 Male and female Mixed diagnosis	Yes Yes	Yes Yes	Yes No Yes	Yes Yes Unclear	1	8	1
Wengström et al., 2001 (21) Sweden	Nursing intervention using Orem's self-care theory (promoting of behaviours) as a framework (IG 1) vs standard care (SC).	*n*=134 IG 1=67/SC=67 Mean age 61 Female Breast cancer	Yes Yes	Yes Yes	Yes No Yes	Yes Unclear Yes	4	8	1
Courneya et al., 2003 (22) Canada	Group psychotherapy with exercise 3–5 times week (IG 1) and weekly group psychotherapy (IG 2).	*n*=108 IG 1=60/IG 2=48 Mean age 52 Male and female Mixed diagnosis	Yes Yes	Yes Yes	Yes Yes No	Yes Yes Yes	3	9	3

Table II. *Contd.*

Ref Country	Component of the interventions	Numbers of studies, mean age, years, gender and diagnosis of the samples	Inclusion criteria clearly described Situation at baseline described	Measure time adequate. Population criteria described	Used valid assessment tools Power calculated Follow-up	Non-responds described Intent to treat Blinded	Treatment setting[a]	Quality Index scores	Assessments[b]
Given et al., 2004 (23) USA	Cognitive behavioural education (IG 1) vs standard care (SC).	*n*=237 IG 1=118/SC=119 Mean age 60 Male and female Mixed diagnosis	Yes Yes	Yes Yes	Yes Yes No	Yes No Yes	1	8	1
Miaskowski, 2004 (24) USA	Psycho-educational for pain control (IG 1) vs standard care (SC).	*n*=174 IG 1=93/SC=81 Mean age 59 Male and female Mixed diagnosis	Yes Yes	Yes Yes	Yes Yes No	Yes No Yes	3	8	1
Yates et al., 2005 (25) Australia	Psycho-educational intervention (IG 1) consisting of individualized fatigue education and support programme delivered in the clinic and by phone vs standard care (SC).	*n*=109 IG 1=55/SC=54 Mean age (Unclear) Female Breast cancer	Yes Yes Yes	Yes Yes Yes	Yes Yes Yes	Yes No Yes	1	9	1
Rummans et al., 2006 (26) USA	Physical training, cognitive behavioural training, information and emotional support (IG 1) vs standard care (SC).	*n*=103 IG 1=49/SC=54 Mean age 60 Male and female Mixed diagnosis	Yes Yes Yes	Yes Yes Yes	Yes¨ Yes Yes	Yes No Unclear	1	8	3
Ream et al., 2006 (27) UK	Psycho-education providing psychological support and coaching participants in self-care (IG 1) vs usual care (SC).	*n*=103 IG 1=48/SC=55 Mean age 57 Male and female Mixed diagnosis	Yes Yes Yes	Yes Yes Yes	No Yes Yes	Yes Yes Yes	1	8	1
Zhang et al., 2006 (28) USA	Group counselling with combined pelvic floor muscle exercises (IG 1) and support group vs standard care (SC).	*n*=29 IG 1=14/SC=15 Mean age 62 Male Prostate cancer	Yes Yes Yes	Yes Yes Yes	Yes No Yes	Yes No Yes	2	8	1
Armes et al., 2007 (29) UK	Psycho-educative intervention (IG 1) vs standard care (SC).	*n*=55 IG 1=28/SC=27 Mean age 59 Male and female Mixed diagnosis	Yes Yes Yes	Yes Yes Yes	Yes Yes Yes	No No Yes	1	8	3
Hartmann et al., 2007 (30) Germany	Step-by-step inpatient rehabilitation (IG 1) vs conventional inpatient rehabilitation (SC).	*n*=197 IG 1=98/SC=99 Mean age 56 Female Breast cancer	Yes Yes Yes	Yes Yes Yes	Yes Yes Yes	Yes No No	3	8	3

Table II. *Contd.*

Ref Country	Component of the interventions	Numbers of studies, mean age, years, gender and diagnosis of the samples	Inclusion criteria clearly described Situation at baseline described	Measure time adequate Population criteria described	Used valid assessment tools Power calculated Follow-up	Non-responds described Intent to treat Blinded	Treatment setting[a]	Quality Index scores	Assessments[b]
Elkins et al., 2008 (31) USA	Mind-body therapy reducing the frequency and severity of hot flashes.	*n*=60 IG 1=30 /SC=30 Mean age 57 Female Breast cancer	Yes Yes	Yes Yes	No Yes Yes	Yes Yes Yes	2	9	1
Ruland et al., 2010 (32) Norway	Computer-supported interactive tailored patient assessment tool on patient care, vs standard care.	*n*=145 IG 1=70 /SC=75 Mean age=50 Male and female Lymphoma	Yes Yes	Yes Yes	Yes Yes Yes	Yes No Yes	1	9	1
Studies with contents in category IV: Emotional supportive interventions									
Herth, 2000 (33) USA	Theory driven nursing hope intervention programme (IG 1) and attention control group (IG 2) vs standard care (SC).	*n*=115 IG 1=38/IG 2=37/ SC=40 Mean age 54 Male and female Mixed diagnosis	Yes Yes	Yes Yes	Yes Yes Yes	Yes No Unclear	1	8	1
Cotay et al., 2007 (34) USA	Brief psychosocial telephone intervention (IG 1) vs standard care (SC).	*n*=305 IG 1=152/SC=153 Mean age 54 Female Breast cancer	Yes Yes	Yes Yes	Yes Yes Yes	Yes No No	1	8	3
Morey et al., 2009 (35) USA	Telephone counselling and mailed print-based diet and exercise intervention (IG 1) vs standard care (SC).	*n*=641 IG 1=319/SC=322 Mean age 73 Male and female Breast+colorectal+ prostate cancer	Yes Yes	Yes Yes	Yes Yes No	Yes Yes Yes	2	9	3
Lengacher et al., 2009 (36) USA	Mindfulness-based stress reduction (MBSR) for survivors of breast cancer vs standard care.	*n*=84 IG 1=41 /SC=43 Mean age=Unknown Female Breast cancer	Yes Yes	Yes Yes	Yes No Yes	Yes Yes No	2	8	3
Carson et al., 2009 (37) USA	Yoga of Awareness programme for menopausal symptoms in breast cancer survivors vs standard care.	*n*=37 IG 1=17 /SC=20 Mean age=54 Female Breast cancer	Yes Yes	Yes Yes	Yes Yes Yes	Yes No No	2	8	1
Sabariego et al., Epub 2011 (38) Germany	Cost-effectiveness of cognitive-behavioural group therapy for dysfunctional fear of progression in cancer patients.	*n*=174 IG 1=83 /SC=91 Mean age=54 Male and female Mixed diagnosis	Yes Yes	Yes Yes	Yes No Yes	Yes No Yes	2	8	1

Table II. *Contd.*

Ref Country	Component of the interventions	Numbers of studies, mean age, years, gender and diagnosis of the samples	Inclusion criteria clearly described Situation at baseline described	Measure time adequate Population criteria described	Used valid assessment tools Power calculated Follow-up	Non-responds described Intent to treat Blinded	Treatment setting[a]	Quality Index scores	Assessments[b]
Studies with contents in category V: Other interventions									
Demark-Wahnefried et al., 2007 (39) USA	Tailored intervention promoting healthy diet and exercise behaviour (IG 1) vs non-tailored intervention promoting healthy diet and exercise behaviour IG 2).	*n*=543 IG 1=271/IG 2=272 Mean age 57 Male and females Breast+prostate cancer.	Yes Yes	Yes Yes	Yes Yes No	Yes Yes Yes	3	9	3
Studies with combination of contents from 2 or 3 categories									
Kissane et al., 2003 (40) Australia	Categories III and I Cognitive existential group therapy and relaxation classes (IG 1) vs Relaxation classes only (IG 2).	*n*=303 IG 1=154/IG 2=149 Mean age 45 Female Breast cancer	Yes Yes	Yes Yes	Yes Yes Yes	Yes Yes Yes	2	10	3
Stanton et al., 2005 (41) USA	Categories III and IV 1) Standard National Cancer Institute print material or 2) standard print material and peer-modelling videotape (IG 1) or 3) standard print material, videotape, 2 sessions with trained cancer educators and informational videotape (IG 2).	*n*=558 IG 1=279/IG 2=279 Mean age 59 Female Breast cancer	Yes Yes	Yes Yes	Yes Yes No	Yes Unclear Yes	2	8	3
Carmack et al., 2006 (42) USA	Categories V and III Live style programme (IG 1) and Cognitive educational support program (IG 2) vs usual care (SC).	*n*=134 IG 1=43/IG 2=43/ SC=48 Mean age 69 Male Colorectal cancer	Yes Yes	Yes Yes	Yes Yes Yes	Yes Unclear Yes	1	9	3
Johansson et al., 2008 (43) Sweden	Categories II, I and III Individual psychological support (IG 1), group rehabilitation (IG 2) and Individual psychological support with group rehabilitation (IG 3) vs standard care (SC).	*n*=481 IG 1=134/IG 2=104/ IG 3=117/SC *n*=126 Mean age 64 Male and female Mixed diagnosis	Yes Yes	Yes Yes	Yes Yes Yes	Yes Unclear No	1	8	1
Goedendorp et al., 2010 (44) The Netherlands	Categories I and IV Physical activity to diminish fatigue during cancer treatment compared with cognitive behaviour therapy and brief nursing intervention in standard care.	*n*=240 IG 1=77 /IG 2=82 / SC=81 Mean age=56 Male and female Mixed diagnosis	Yes Yes	Yes Yes	Yes Yes Yes	Yes No No	1	8	3

[a]1. During treatment, 2. After treatment, 3. During & after treatment, 4. Unclear. [b]1. "Well-being", 2. Functional, 3. Combination of 1 and 2.
Total number of participants. *n*=6,094 (min/max group, *n*=29/641). IG: intervention group; SC: standard care.

($n = 14$), 13 from Europe, and 5 from other parts of the world (Table II).

Measurements used in the good quality studies

Several instruments were used to assess the interventions used in the GQ studies, and we grouped these instruments into 2 main categories of measurements: (*i*) instruments used to assess well-being as outcome were used in 16 studies (quality of life, lifestyles, social relationships, psychological and cognitive measurements, etc.); (*ii*) instruments used to assess functional outcome were used in 15 studies (shoulder movement, physical activity, physiotherapy with lymphoma, etc.). Of these 32 studies, well-being instruments were used in 16 studies, functional instruments in one study, and a combination of both in 15 studies.

DISCUSSION

The main finding of this review is that papers registered in PubMed published as RCTs on cancer rehabilitation are heterogeneous in terms of samples and outcomes. The studies are mostly characterized by "less than optimal" design quality. Due to the heterogeneity of the research design, numbers of participants, genders and measurements, it was not feasible to perform any systematic or meta-analysis, hence we report the findings in a focused manner. Therefore, we also recommend that the design of future studies of RCPs should be more specific, multidimensional and well-planned.

This review, exploring RCTs studies of RCPs registered in PubMed, included full-text reading of 132 RCTs. Thematically these papers were divided into 5 groups, among which the groups of Physical and Psycho-educational interventions were the largest, with 44 and 47 studies, respectively. Groups II–IV have content focusing on general lifestyle improvement, increased well-being or reduction of "distress", defined as a unpleasant emotional experience of psychological (cognitive, behavioural, emotional), social, and/or spiritual nature (12), while group I mostly focuses on functional measures.

Only 32 of the studies reach GQ score concerning design. A common weakness in many studies was the lack of description or explanation of the baseline disability, which the study wanted to change by its interventions. The authors seem to presuppose that all cancer patients have similar problems, mostly with lifestyle issues.

Another common weakness was the absence of statistical power considerations concerning sample sizes, which is of crucial importance for interpretation of group comparisons concerning outcome variables. Our analyses showed that 92 (70%) of the studies had less than 130 participants usually needed for safe comparison of 2 groups (65×2). If studies with smaller group sizes show significant statistical group differences, they are of clinical significance, but there is a considerable risk of lacking significant differences due to small sample size (type II statistical error).

Based on the explanations given by the authors of the papers evaluated, most of them focused on supportive interventions for cancer patients rather than rehabilitation, and almost half of the studies were conducted during the period of primary cancer treatment. Most of the authors claimed to fulfil the criteria of *rehabilitation* interventions, although they did not fulfil the definition of RCPs given by DeLisa (2, p. 96). We find it challenging that lifestyle interventions are classified as RCPs, although we admit that the WHO definition accepts as rehabilitation all interventions that reduce disability to achieve and maintain optimal functioning in interaction with the environment.

Most of the authors stated that their interventions improved health for the participants during the study period. On the other hand, the long-term effects of the interventions are unknown, since the majority of studies had either no follow-up or just a short follow-up period. The samples frequently showed selection bias and since they regularly lack attrition analyses, their external validity is open for discussion.

Using an index score for evaluating the quality of the studies, we categorized only 24% as GQ studies. This means that 3 out of 4 studies had considerable problems, either of design, material, methods or statistics. We consider this to be a high proportion, but we do not have data from related fields of investigation. Our findings also support the recommendations reported by Scott et al. (5) in their systematic review of multidimensional rehabilitation programmes, namely that researchers designing RCTs for RCPs should be more aware of methodological issues in the future. In addition there is a need to report more systematically and in more detail on sampling, statistical power, attrition, as well as diseases and treatment characteristics, such as time from diagnosis to interventions, cancer treatment received, and disease and treatment status during the intervention period.

Furthermore, functional impairment, assessment tools, and inclusion and exclusion criteria were less than optimally described and could definitely be improved and become more standardized. These suggestions are in line with the recent papers on the Nordic and European perspective on RCPs (3) and from the USA (2).

We may speculate whether the heterogeneity of interventions classified as RCTs in PubMed may be consequences of the rather wide and unspecific definitions of RCTs presented in the Introduction. The inclusiveness of the WHO definition of rehabilitation supports such heterogeneity (11), even if that definition requires disability as the basis for rehabilitation. The content of this definition states that the aim of rehabilitative interventions is to mobilize the patient's optimal functional level to participate in the community.

In many of the studies reviewed there is lack of description of the levels of impairment before the start of the interventions. The main idea of many interventions seems to be secondary prevention addressing risk factors for a future disease burden caused by the cancer and/or its treatment, rather than to deal with defined needs for rehabilitation due to limitations in physical, psychological, social functions, or their combination.

The WHO definition indicates that rehabilitation can address a variety of functions with a consequent need for several

types of interventions, and our findings based on the PubMed database confirmed such a plurality. On the other hand, this plurality may be considered problematic, since RCPs thereby loses more of its cancer-specific content. In addition, many cancer patients have complex functional impairments, which require a combination of rehabilitative efforts, and we found very few studies addressing such combinations.

Another perspective is related to PubMed methods of classification and characterization of the content of RCPs. This might be one explanation for the inclusion of studies in our search that barely concern rehabilitative interventions at all.

Study imitations and strengths

Using PubMed as the only database is a limitation of our study. However, PubMed is a major literature base in medicine, and frequently used, since it is free and easily accessible, and it is therefore worth exploring. The review must be considered as focused rather than systematic, identifying RCTs that will be consulted by clinicians. Coverage of studies in English only may be considered a limitation, since relevant papers could have been published in other languages.

It was not possible to report the effectiveness of all the interventions, since different studies concerned different groups of cancer patients, sexes, age groups, and times in the cancer trajectory. For example, among studies offering the same type of interventions, some reported socio-demographics and detailed cancer information, while others did not. Due to limited methodological descriptions in the studies reviewed, we have hardly been able to discuss the long-term positive or negative impacts of the interventions on the cancer patients' impairments.

Conclusion

This review highlights those RCTs under the heading of RCPs in PubMed and recognizes that they cover a heterogeneous set of uni- and multi-dimensional interventions that we classified into 5 thematic groups. We observe that these interventions are more focused on secondary prevention, lifestyle, and supportive care than on rehabilitation in the strict sense. Based on our design quality index, only 24% of the included papers reached "good quality" concerning research design and methodology. We therefore recommend that future studies of RCPs should assess more specific factors related to the rehabilitation of cancer patients.

REFERENCES

1. DeLisa JA. A history of cancer rehabilitation. Cancer (Suppl) 2001; 4: 970–974.
2. World Health Organization. World report on disability 2011. Geneva: World Health Organization. ISBN: 978 92 4 068521 5.
3. Alfano CM, Ganz PA, Rowland JH. Cancer survivorship and cancer rehabilitation: Revitalizing the link. J Clin Oncol 2012; 9: 904–906.
4. Hellbom M, Bergelt C, Bergenmar M, Gijsen B, Loge JH, Rautalahti M, et al. Cancer rehabilitation: A Nordic and European perspective. Acta Oncol 2011; 50: 179–186.
5. Scott DA, Mills M, Black A, Cantwell M, Campbell A, Cardwell CR, et al. Multidimensional rehabilitation programmes for adult cancer survivors. Cochrane Database Syst Rev 2013; 3: CD007730.
6. Lowe SS, Watanabe SM, Cournrya KS. Physical activity as a supportive care intervention in palliative cancer patients: a systematic review. J Support Oncol 2009; 1: 27–34.
7. Ballard-Barbash R, Friedenreich CM, Courneya KS, Siddiqi SM, McTiernan A, Alfano CM. Physical activity, biomarkers, and disease outcomes in cancer survivors: a systematic review. J Natl Cancer Inst 2012; 104: 815–840.
8. Laoutidis ZG, Mathiak K. Antidepressants in the treatment of depression/depressive symptoms in cancer patients: a systematic review and meta-analysis. BMC Psychiatry 2013; 13: 140.
9. Raijmakers NJ, vanZuylen L, Costantini M, Caraceni A, Clark J, Lundquist G, et al. Artificial nutrition and hydration in the last week of life in cancer patients: a systematic literature review of practices and effects. Ann Oncol 2011; 7: 1478–1486.
10. Iles RA, Davidson M, Taylor NF. Psychosocial predictors of failure to return to work in non-chronic non-specific low back pain: a systematic review. Occup Med 2008; 65: 507–517.
11. Iles RA, Davidson M, Taylor NF. Systematic review of the ability of recovery expectations to predict outcome in non-chronic non-specific low back pain. J Occup Rehabil 2009; 29: 25–40.
12. Distress management v. 2.2013. National Comprehensive Cancer Network 2013.
13. Reul-Hirche HM, Bullock-Saxton JE, Furnival CM. Shoulder movement after breast cancer surgery: results of a randomized controlled study of postoperative physiotherapy. Breast Cancer Res Treat 2002; 75: 35–50.
14. Cheung YL, Molassiotis A, Chang AM. The effect of progressive muscle relaxation training on anxiety and quality of life after stoma surgery in colorectal cancer patients. Psychooncol 2003; 12: 254–266.
15. Lauridsen MC, Christiansen P, Hessov I. The effect of physiotherapy on shoulder function in patients surgically treated for breast cancer: a randomized study. Acta Oncol 2005; 44: 449–457.
16. Korstjens I, May AM, van Weert E, Mesters I, Tan F, Ros MJ. Quality of life after self-management cancer rehabilitation: a randomized controlled trial comparing physical and cognitive-behavioral training versus physical training. Psychosom Med 2008; 70: 422–429.
17. May AM, Van Weert E, Korstjens I, Hoekstra-Weebers JE, Van Der Schans CP, Zonerland M, et al. Improved physical fitness of cancer survivors: a randomized controlled trial comparing physical training with physical and cognitive-behavioural training. Acta Oncol 2008; 47: 825–834.
18. Sharp DM, Walker MB, Chaturvedi, Upadhyay S, Hamid A, Walker AA, et al. A randomised, controlled trial of the psychological effects of reflexology in early breast cancer Eur J Cancer 2010; 2: 312–322.
19. Monti DA, Peterson C, Kunkel EJ, Hauck WW, Pequignot E, Rhodes L, et al. A randomized, controlled trial of mindfulness-based art therapy (MBAT) for women with cancer. Psychooncol 2006; 15: 363–373.
20. Greer S, Moorey S, Baruch JD, Watson M, Robertson BM, Mason A, et al. Adjuvant psychological therapy for patients with cancer: a prospective randomised trial. BMJ 1992; 304: 675–680.
21. Wengström Y, Häggmark C, Forsberg C. Coping with radiation therapy: effects of a nursing intervention on coping ability for women with breast cancer. Int J Nurs Pract 2001; 7: 8–15.
22. Courneya KS, Friedenreich CM, Sela RA, Quinney HA, Rhodes RE, Handman M, et al. The group psychotherapy and home-based physical exercise (group-hope) trial in cancer survivors: physical fitness and quality of life outcomes. Psychooncol 2003; 12: 357–374.
23. Given C, Given B, Rahbar M, Jeon S, McCorkle R, Cimprich B, et al. Effect of a cognitive behavioral intervention on reducing symptom severity during chemotherapy. J Clin Oncol 2004; 22: 507–516.

24. Miaskowski C, Dodd M, West C, Schumacher K, Paul SM, Tripathy D, et al. Randomized clinical trial of the effectiveness of a self-care intervention to improve cancer pain management. J Clin Oncol 2004; 22: 1713–1720.
25. Yates P, Aranda S, Hargraves M, Mirolo B, Clavarino A, McLachlan S, et al. Randomized controlled trial of an educational intervention for managing fatigue in women receiving adjuvant chemotherapy for early-stage breast cancer. J Clin Oncol 2005; 23: 6027–6036.
26. Rummans TA, Clark MM, Sloan JA, Frost MH, Bostwick JM, Atherton PJ, et al. Impacting quality of life for patients with advanced cancer with a structured multidisciplinary intervention: a randomized controlled trial. J Clin Oncol 2006; 24: 635–642.
27. Ream E, Richardson A, Alexander-Dann C. Supportive intervention for fatigue in patients undergoing chemotherapy: a randomized controlled trial. J Pain Symptom Manage 2006; 31: 148–161.
28. Zhang AY, Strauss GJ, Siminoff LA. Intervention of urinary incontinence and quality of life outcome in prostate cancer patients. J Psychosoc Oncol 2006; 24: 17–30.
29. Armes J, Chalder T, Addington-Hall J, Richardson A, Hotopf M. A randomized controlled trial to evaluate the effectiveness of a brief, behaviorally oriented intervention for cancer-related fatigue. Cancer 2007; 110: 1385–1395.
30. Hartmann U, Muche R, Reuss-Borst M. Effects of a step-by-step inpatient rehabilitation programme on quality of life in breast cancer patients. A prospective randomised study. Onkologie 2007; 30: 177–182.
31. Elkins G, Marcus J, Stearns V, Perfect M, Rajab MH, Ruud C, et al. Randomized trial of a hypnosis intervention for treatment of hot flashes among breast cancer survivors. J Clin Oncol 2008; 31: 5022–5026.
32. Ruland CM, Holte HH, Røislien J, Heaven C, Hamilton GA, Kristiansen J, et al. Effects of a computer-supported interactive tailored patient assessment tool on patient care, symptom distress, and patients' need for symptom management support: a randomized clinical trial. J Am Med Inform Assoc 2010; 4: 403–410.
33. Herth K. Enhancing hope in people with a first recurrence of cancer. J Adv Nurs 2000; 32: 1431–1441.
34. Gotay CC, Moinpour CM, Unger JM, Jiang CS, Coleman D, Martino S, et al. Impact of a peer-delivered telephone intervention for women experiencing a breast cancer recurrence. J Clin Oncol 2007; 25: 2093–2099.
35. Morey MC, Snyder DC, Sloane R, Cohen HJ, Peterson B, Hartman TJ, et al. Effects of home-based diet and exercise on functional outcomes among older, overweight long-term cancer survivors: RENEW: a randomized controlled trial. JAMA 2009; 301: 1883–1891.
36. Lengacher CA, Johnson-Mallard V, Post-White J, Moscoso MS, Jacobsen PB, Klein TW, et al. Randomized controlled trial of mindfulness-based stress reduction (MBSR) for survivors of breast cancer. Psychooncol 2009; 12: 1261–1272.
37. Carson JW, Carson KM, Porter LS, Porter LS, Keefe FJ, Seewaldt VL.Yoga of Awareness program for menopausal symptoms in breast cancer survivors: results from a randomized trial. Support Care Cancer 2009; 10: 1301–1309.
38. Sabariego C, Brach M, Herschbach P, Berg P, Stucki G. Cost-effectiveness of cognitive-behavioral group therapy for dysfunctional fear of progression in cancer patients. Eur J Health Econ 2011; 5: 489–497.
39. Demark-Wahnefried W, Clipp EC, Lipkus IM, Lobach D, Snyder DC, Sloane R, et al. Main outcomes of the FRESH START trial: a sequentially tailored, diet and exercise mailed print intervention among breast and prostate cancer survivors. J Clin Oncol 2007; 25: 2709–2718.
40. Kissane DW, Bloch S, Smith GC, Miach P, Clarke DM, Ikin J, et al. Cognitive-existential group psychotherapy for women with primary breast cancer: a randomised controlled trial. Psychooncol 2003; 12: 532–546.
41. Stanton AL, Ganz PA, Kwan L, Bower JE, Krupnick JL, Rowland JH, et al. Outcomes from the Moving Beyond Cancer psychoeducational, randomized, controlled trial with breast cancer patients. J Clin Oncol 2005; 23: 6009–6018.
42. Carmack Taylor CL, Demoor C, Smith MA, Dunn AL, Basen-Engquist K, Nielsen I. Active for Life After Cancer: a randomized trial examining a lifestyle physical activity program for prostate cancer patients. Psychooncol 2006; 15: 847–862.
43. Johansson B, Brandberg Y, Hellbom M, Persson C, Petersson LM, Berglund G, et al. Health-related quality of life and distress in cancer patients: results from a large randomised study. Br J Cancer 2008; 99: 1975–1983.
44. Goedendorp MM, Peters ME, Gielissen MF, Witjes JA, Leer JW, Verhagen CA, et al. Is increasing physical activity necessary to diminish fatigue during cancer treatment? Comparing cognitive behavior therapy and a brief nursing intervention with usual care in a multicenter randomized controlled trial. Oncologist 2010; 10: 1122–1132.

APPENDIX I. Quality assessment of the papers

Evaluation of the scientific quality of the papers was made using adapted scores according to the criteria of Iles et al. (9–10) based on 10 items related to the design of the studies:

1. Are the inclusion/exclusion criteria clearly described?
2. Is the definition of the cancer patients' situation at baseline described clearly?
3. Is the measurement made at a suitable time in relation to the research questions?
4. Are the important criteria (medical and demographic) of the population described adequately?
5. Do the researchers use valid assessment tools?
6. Has the power of the study population been calculated?
7. Is a follow-up evaluation after the pre- and post-intervention presented?
8. Is the description of the non-responders adequate?
9. Do the researchers mention "intention to treat"?
10. Are the respondents blinded?

If item present, score 1, if not present, score 0, then sum scores of the 10 items to give the total quality score (range 0–10).