Distress and unmet needs in cancer patients
van Scheppingen, Corinne

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Document Version
Publisher's PDF, also known as Version of record

Publication date:
2015

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):

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Patient Recruitment Rates in Psychosocial Interventions for Cancer Patients: a Systematic Review

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James C. Coyne
Adelita V. Ranchor
Abstract

**Background:** Detailed reporting of recruitment procedures and recruitment rates for clinical trials facilitate the evaluation of the generalizability of findings, the design of replication studies, and estimates of likely uptake when interventions are disseminated into routine care. This systematic review examines the completeness of reporting of the recruitment procedures and recruitment rates (i.e. eligibility, enrollment, and recruitment rates) of randomized controlled trials (RCTs) of psychosocial interventions for cancer patients. We also examined the relationship between intervention and trial characteristics and enrollment rates.

**Methods:** A systematic search in Medline, Embase, CINAHL and PsychInfo identified 97 eligible psychosocial RCTs from 2000-2013 that included fatigue, pain, distress, depression, anxiety and/or mood as primary outcome(s). Eligibility rate was defined as the ratio of number of patients being eligible to number of patients assessed for eligibility, enrollment rate as the ratio of number of patients randomized to number of patients eligible, and recruitment rate as the number of patients randomized to number of patients assessed for eligibility. We approached authors by email for missing information.

**Results:** We could calculate enrollment, recruitment, and eligibility rates for only 41%-77% of the studies. Studies that consecutively screened patients on the presence of complaints as recruitment strategy showed significantly lower eligibility and recruitment rates than studies not using screening. Studies with higher enrollment rates more often recruited by a physician and examined an individual rather than a group intervention.

**Conclusions:** Many psychosocial RCTs in cancer lack clear information about their recruitment procedures and recruitment rates, needed for the generalizability of findings. Current guidelines, such as CONSORT, should raise awareness of the importance of reporting details of the recruitment process and provide clear definitions.
6.1 Introduction

An understanding of how patients are recruited in clinical trials is important to evaluate to which target population the findings can be generalized, to facilitate the design of replication studies, as well as to estimate the likely uptake of interventions when they become disseminated and implemented in routine care. Unfortunately, many randomized clinical trials fail to reach their planned sample size (1,2), resulting in reduced statistical power or heterogeneity introduced by broadening of inclusion criteria or inconsistent sampling strategies. Poorly reported recruitment procedures and rates can also lead to unrealistic expectations about rates of uptake and the acceptability of interventions to patients. This latter issue takes on new importance as professional guidelines shift from calls for evaluation of interventions to calls for their widespread dissemination and implementation in practice (3,4).

Most clinical journals now endorse the use of the CONSORT guidelines (5-7). These guidelines give more attention to internal validity than to external validity and do not require authors to report sufficient information about their approach of the target population (8,9). Even when congruent with reporting guidelines, many reports of clinical trials do not provide sufficient information about their recruitment procedures and rates to ascertain external validity and clinical relevance of the findings (8-11).

So far, one systematic review examined the characteristics and methodological quality of 488 psychosocial intervention studies for cancer patients (including RCTs, other study designs, and unpublished dissertations) (11). For only 15% of the studies the authors could calculate ‘the proportion of potential participants who were excluded by in- and exclusion criteria, which was 34.3%’, and for only one-third they could calculate ‘the mean proportion of eligible patients not involved in the study, which was 27.4%’ (11). Put differently, the authors found a mean eligibility rate (the ratio of number of eligible patients to number of patients assessed for eligibility) of 65.7%, and a mean enrollment rate (the ratio of number of patients randomized to number of eligible patients) of 72.6%. Although these results provide important insights into these rates, a limitation is that the authors did not clearly define the rates, nor did they differentiate between studies using a consecutive or convenience sample of patients with and without screening, or evaluate factors associated with recruitment rates. The current review therefore updates and broadens this review by calculating the eligibility, enrollment, and recruitment rates (for definitions see table 1) and factors associated with higher enrollment rates. Enrollment rate was considered a key rate, as this rate contains important information about the amount of eligible patients being interested to participate in the trial. The higher the rate, the more attractive and accessible a trial is for a certain (pre-defined) group of patients. Factors associated with enrollment rate are likely the recruitment procedures (e.g. the use of a consecutive or convenience sample; screening on the presence of complaints; the type of recruiter and recruitment strategy)
(2,12) and intervention and trial characteristics. Evidence for a potential relationship between these factors has not been systematically reviewed.

This systematic review focused on randomized controlled trials (RCTs) of psychosocial interventions for cancer patients, aimed to alleviate fatigue, pain, distress, depression, anxiety and/or mood. Our three aims were: 1) to determine the completeness of reporting of the recruitment process, i.e. whether studies reported complete information about how their study sample was assembled; 2) to calculate eligibility, enrollment, and recruitment rates; and 3) to explore if intervention and trial characteristics were associated with higher enrollment rate.

6.2 Methods

6.2.1. Search strategy
We searched randomized controlled trials evaluating the efficacy of psychosocial interventions aiming at the alleviation of depression, distress, anxiety, mood, fatigue and/or pain between January 2000 and August 2013. Studies had to be reported in English, Dutch or German. The search was performed using Thesaurus terms and free text searches in titles and abstracts. Databases searched were Medline (through OVIDSP), Embase (through Embase.com), CINAHL and Psycinfo (through EBSCO). Two independent raters screened all titles and abstracts with the aim to exclude papers that obviously were not focused on psychosocial interventions for adult cancer patients. Full-texts of remaining papers were rated on the selection criteria described below. Disagreements were resolved by discussing whether or not including a paper.

6.2.2. Selection criteria

Types of interventions.
Original studies reporting the results of a psychological intervention, i.e. psycho-education, psychotherapy/counseling, cognitive behavioral therapy, relaxation and social support interventions were included. Interventions including only a single session and non-psychological interventions such as yoga, physical exercise, and medical procedures were excluded.

Outcomes of the intervention.
Studies were included that defined fatigue, pain, depressive symptoms, anxiety, distress, and/or mood as the primary outcome or as part of multiple outcomes and with no further specification of a primary outcome. A study was excluded when these were only secondary outcomes.

Patient population.
Studies were included if they focused exclusively on adult cancer patients. Studies focusing on a mixed population of patients with a chronic disease, including cancer,
were excluded. Also excluded were studies in which patients were selected from a larger study population (non-original studies). Studies focusing on couples were included as long as outcome assessment was performed at the level of individual cancer patients.

**Randomization.**
Studies were included that randomized at the level of patients. Cluster-randomized trials were excluded.

### 6.2.3. Data extraction

For each paper we filled out a flow diagram, guided by a figure of Gross *et al.* (9) (figure 1). This figure resembled the CONSORT flow diagram, but also explicitly included a box of ‘eligible’ patients and depicted the different rates of recruitment we wanted to examine. The following counts were extracted: target population, number of patients assessed for eligibility, number of patients eligible and number of patients randomized. If these specific terms were not found we searched for the following alternatives: Assessed for eligibility: ‘screened for eligibility’ (e.g. in medical records/ patient database), ‘screened’ (with a screening instrument), ‘considered for participation’, ‘approached’ (not only eligible), ‘contacted’ (not only eligible), ‘mailed/phoned/send a letter’ (not only eligible). Eligible: ‘identified’, ‘contacted’, ‘mailed/phoned/send a letter’, ‘met inclusion, exclusion or study criteria’. Randomized: ‘allocated to groups’, ‘agreed to participate’, ‘signed informed consent’. Two researchers independently coded recruitment data, method of recruitment and intervention and study characteristics. Disagreements were resolved through discussion and in difficult cases a third researcher was contacted for final consensus. When authors referred to other papers for more detailed information about their recruitment process, this information was used to complete the flow diagram. In addition, authors were contacted by email for additional information on recruitment items that were inexplicable or missing in their paper. When they did not reply after three weeks from the first email, they received a reminder email.

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**Figure 1.** Adopted from Gross *et al.* (2002)
6.2.4. Material

Recruitment rates (Table 1).

Intervention characteristics
We scored the type of primary intervention (cognitive behavioral, psychotherapy/counseling, psycho-education, relaxation, social support or other), the type of delivery (individual, group or couple-based), the medium of the intervention (face-to-face, by telephone, DVD/booklet/video/audio, internet, or a combination), the setting (clinical setting or at home) and the number and duration of contacts.

Trial characteristics
The type of control group (care as usual, waiting list, attention control group or active intervention), and the number of assessments and duration of follow-up was scored.

Recruitment procedures
We rated whether studies used a consecutive or a convenience sample of patients. Studies were defined as consecutive when all patients attending a clinic, getting a particular diagnosis or were otherwise eligible were approached, patients were systematically assessed for eligibility criteria, patients were recruited during a specific study period in particular clinics, or the time point of recruitment (e.g. one week after surgery) was specified. Studies were defined as convenience when the authors clearly stated that it was a convenience sample, or stated that patients were recruited by advertisement, radio commercials, flyers, internet, or a large mailing to an unknown patient population. We also scored whether studies initially screened patients for physical or psychological complaints or not.

Recruitment strategy
The way of approaching patients (in person, by mail, letter, phone or multiple approach) and the type of recruiter (physician, nurse, researcher, research assistant) was scored.

Completeness of reporting
We recorded whether studies reported complete information about their target population, and the number of patients assessed for eligibility, eligible, and randomized. The completeness of reporting was assessed by counting the number of recruitment items completely reported in each selected study. In addition, we checked whether completeness of reporting improved after introduction of the CONSORT statement in behavioral medicine at the end of 2003 (13) by distinguishing papers that were published in 2000-2005 and in 2006-2013.
Table 1. Recruitment rates definitions based on Gross et al. (2002).

<table>
<thead>
<tr>
<th>Rate</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eligibility rate</td>
<td>the ratio of number of patients eligible to number of patients assessed for eligibility * 100%</td>
</tr>
<tr>
<td>Enrollment rate</td>
<td>the ratio of number of patients randomized to number of patients eligible * 100%</td>
</tr>
<tr>
<td>Recruitment rate</td>
<td>the ratio of number of patients randomized to number of patients assessed for eligibility * 100%</td>
</tr>
</tbody>
</table>

6.2.5. Data analysis
Analyses were performed using SPSS for Windows, version 20.0. Standard descriptive statistics were generated to characterize the quality of reporting and to calculate means and standard deviations of recruitment rates. A new variable was created, distinguishing studies using a consecutive or convenience sample of patients, either with or without screening on the presence of complaints. ANOVA with post-hoc tests were used to evaluate potential significance. Recruitment rate and enrollment rate were normally distributed. For studies with a consecutive sample without screening for complaints, ANOVA with post-hoc tests were used to explore trial and intervention characteristics associated with enrollment rate. To prevent bias in our analyses, we paid special attention to studies with an unrealistic high enrollment rate of 100% \( (n=8) \), and analysed our data with and without these studies. The amount of studies with a consecutive sample with screening and a convenience sample with and without screening was too small to examine associations \( (n<10) \).

6.3 Results

6.3.1. Selection and description of studies
In initial searches, 3012 papers were identified as potentially meeting criteria. After scanning of titles and abstracts, we removed papers that did not seem to concern reports of original psychosocial interventions for adult cancer patients. The full texts of the remaining studies were rated on their fulfilment of the selection criteria. Of these, 97 studies were included in the present review.

For the primary outcome measure, 7 studies included fatigue, 9 studies pain, 15 studies distress, 12 studies depression, 6 studies anxiety, and 4 studies mood. The other studies included more than one psychological measure \( (n=39) \) or both physical and psychological measures \( (n=5) \). Sixty-two studies included a consecutive sample, 25 a convenience sample, 3 a mixed sample and 7 an unclearly defined sample. Fourteen studies used screening as a means to recruit their sample.

6.3.2. Completeness of reporting the recruitment process
We approached 42 authors for additional information on recruitment items that were inexplicable or missing in their paper. However, only 12 authors were able to deliver us...
additional information about their number of patients assessed for eligibility \((n=5)\), being eligible \((n=3)\), randomized \((n=1)\) and their type of sample \((n=4)\) (one author delivered information on more than one missing item). Reasons for not receiving the complete information were: no reply of the authors \((n=17)\), incorrect email address of the author \((n=4)\), no longer access to the data or lost contact with the primary researcher \((n=4)\), no additional data available \((n=2)\), author in hospital or too busy \((n=3)\).

With the additional information from the 12 authors, we were able to calculate eligibility rates for 40 studies (41% of 97), enrollment rates for 75 studies (77% of 97), and recruitment rates for 43 studies (44% of 97). Nineteen studies (20% of 97) gave no information about the flow of patients through the different stages of recruitment, and only reported the number of patients randomized \((n=17)\) or unclear numbers \((n=2)\).

There was a large increase in the publication of flow diagrams after CONSORT was introduced, from 6 of 34 papers (18%) in 2000-2005 to 41 of 63 papers (65%) in 2006-2013. Completeness of reporting also improved, with 20 of 34 papers (59%) reporting the number of patients being eligible and randomized in 2000-2005 and 55 of 63 papers (87%) in 2006-2013.

Regarding completeness of reporting of recruitment procedures, 27 studies (28% of 97) did not describe the way of approaching patients, 30 studies (31% of 97) did not mention the person recruiting patients and 7 studies (7% of 97) were unclearly defined as a convenience or consecutive sample.

6.3.3. **Eligibility, enrollment, and recruitment rates**

Overall, we found a total mean eligibility rate of 65.3% \((sd 28.3, n=40)\), a mean enrollment rate of 67.1% \((sd 23.7, n=70)\) and a mean recruitment rate of 47.3% \((sd 26.4, n=43)\).

We found significantly lower mean eligibility rates for studies using a consecutive sample with screening (18.6%), compared to studies using a consecutive sample without screening (75.0%) and a convenience sample with (59.0%) and without screening (76.9%) \((F(3,36)=13.2, p<0.001)\) (Table 2).

Enrollment rates varied greatly from 17.1% to 100%. No significant differences were found in enrollment rate between the different recruitment procedures (i.e. between consecutive sampling with (69.7%) or without screening (64.6%) and convenience sampling with (70.6%) or without screening (73.6%)).

Regarding recruitment rates, studies including a consecutive sample with screening for physical or psychological complaints showed a significant lower mean recruitment rate (17.9%) than studies including a consecutive sample without screening (53.1%) and a convenience sample without screening (57.6%) \((F(3,39)=4.7, p<0.01)\).

We found 8 studies that reported an enrollment rate of 100%, meaning that all patients that were eligible were randomized and enrolled in the study. When we excluded these studies in our analysis, all mean rates became somewhat lower (a drop in
rate of 0-10%). We still found significantly lower eligibility and recruitment rates for studies including a consecutive sample with screening, compared to the other studies.

Table 2. Mean eligibility, enrollment, and recruitment rates by recruitment procedure.

<table>
<thead>
<tr>
<th></th>
<th>NO SCREENING</th>
<th>SCREENING</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Consecutive sample</td>
<td>Convenience sample</td>
</tr>
<tr>
<td><strong>Eligibility rate (sd)</strong> range</td>
<td>75.0 (16.9) *</td>
<td><strong>76.9</strong> (29.8) *</td>
</tr>
<tr>
<td></td>
<td>37.2-96.5</td>
<td>14.6-99.1</td>
</tr>
<tr>
<td></td>
<td>median</td>
<td>n=23</td>
</tr>
<tr>
<td></td>
<td>79.3</td>
<td>85.1</td>
</tr>
<tr>
<td></td>
<td>n</td>
<td>n=23</td>
</tr>
<tr>
<td><strong>Enrollment rate (sd)</strong> range</td>
<td>64.6 (25.2)</td>
<td><strong>73.6</strong> (19.8)</td>
</tr>
<tr>
<td></td>
<td>17.1-100.0</td>
<td>40.3-100.0</td>
</tr>
<tr>
<td></td>
<td>median</td>
<td>n=46</td>
</tr>
<tr>
<td></td>
<td>65.7</td>
<td>75.7</td>
</tr>
<tr>
<td></td>
<td>n</td>
<td>n=46</td>
</tr>
<tr>
<td><strong>Recruitment rate (sd)</strong> range</td>
<td>53.1 (22.2) *</td>
<td><strong>57.6</strong> (22.2) *</td>
</tr>
<tr>
<td></td>
<td>21.2-95.2</td>
<td>7.3-99.1</td>
</tr>
<tr>
<td></td>
<td>median</td>
<td>n=24</td>
</tr>
<tr>
<td></td>
<td>52.4</td>
<td>55.0</td>
</tr>
<tr>
<td></td>
<td>n</td>
<td>n=24</td>
</tr>
</tbody>
</table>

*p<0.01

**Note:** Studies with an unclearly defined (n=7) or mixed sample (n=3) were not analysed here.

6.3.4. Trial and intervention characteristics associated with enrollment rate

We examined 12 characteristics of the trial and interventions associated with enrollment rate. However, two variables (medium of the intervention, type of outcome measure) were highly skewed in their distributions and one (setting of the intervention) was too often not reported.

Studies examining the efficacy of an individual treatment showed significantly higher enrollment rates (77.4%) than studies examining a group or couples intervention (53.8%) (p<0.001) (table 3). After excluding studies reporting an enrollment rate of 100% (n=8), this difference remained significant.

Higher enrollment rates were also found for studies including an usual care control condition (73.0%), compared to studies including a waitlist, attention control or an active intervention as control condition. Yet, after excluding studies reporting an enrollment rate of 100%, this significance disappeared. The studies reporting an enrollment rate of 100% often included usual care as control group, thereby increasing the mean value in this group.

Finally, studies in which patients were approached for the study by their physician or by a nurse/researcher showed higher enrollment rates (respectively 84.9% and 69.0%) than studies using a letter, phone call, mail or a combination of
methods (45.8%) \((p<0.001)\). These associations remained significant when excluding studies with an enrollment rate of 100%.

**Table 3.** Variables related to enrollment rate (ENR) for consecutive samples without screening \((n=46)\).

<table>
<thead>
<tr>
<th>Variable</th>
<th>n</th>
<th>ENR (95% CI)</th>
<th>(F(df))</th>
<th>(r)</th>
<th>(p)-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>INTERVENTION CHARACTERISTICS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention type</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CBT</td>
<td>24</td>
<td>65.3 (55.3-75.3)</td>
<td>0.037</td>
<td>0.99</td>
<td></td>
</tr>
<tr>
<td>psychotherapy/counseling</td>
<td>6</td>
<td>61.4 (32.0-90.7)</td>
<td>3.42</td>
<td></td>
<td></td>
</tr>
<tr>
<td>psycho-education</td>
<td>6</td>
<td>64.4 (50.1-78.7)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>other</td>
<td>10</td>
<td>64.8 (40.0-89.7)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention delivery</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>individual</td>
<td>22</td>
<td>77.4 (68.9-85.9)</td>
<td>12.6</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>group/couple</td>
<td>25</td>
<td>53.8 (43.3-64.2)</td>
<td>(1.44)</td>
<td></td>
<td></td>
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<tr>
<td>Contacts</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>number</td>
<td>43</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>duration</td>
<td>37</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>TRIAL CHARACTERISTICS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>usual care</td>
<td>29</td>
<td>73.0 (64.2-81.8)</td>
<td>3.49</td>
<td>0.02  (^a)</td>
<td></td>
</tr>
<tr>
<td>attention control group</td>
<td>5</td>
<td>50.8 (20.3-81.4)</td>
<td>(3.41)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>waiting list</td>
<td>6</td>
<td>48.9 (20.0-77.7)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>active intervention</td>
<td>5</td>
<td>48.1 (22.5-73.7)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follow-up</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>number</td>
<td>46</td>
<td></td>
<td>0.05</td>
<td>0.73</td>
<td></td>
</tr>
<tr>
<td>duration (months)</td>
<td>45</td>
<td></td>
<td>0.10</td>
<td>0.52</td>
<td></td>
</tr>
<tr>
<td>Recruitment strategy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>in person physician</td>
<td>8</td>
<td>84.9 (72.5-97.2)</td>
<td>7.55</td>
<td>0.002</td>
<td></td>
</tr>
<tr>
<td>in person nurse/research.</td>
<td>15</td>
<td>69.0 (55.7-82.4)</td>
<td>(2.31)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>letter/phone/mail/mixed</td>
<td>11</td>
<td>45.8 (7.2-29.8)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) After controlling for studies with an enrollment rate of 100% this significance disappeared.

### 6.4 Discussion

While some previous studies already discussed aspects of the completeness of reporting the recruitment process of clinical trials (8-10,14), the completeness of reporting of psychosocial RCTs for cancer patients has not previously been systematically reviewed. We found incomplete and unclear reporting of the recruitment process in many of the studies reviewed. Only 41%-77% of the papers reported sufficient information to calculate recruitment rates, and 20% only reported the number of patients randomized, giving no insight in the acceptability and likely uptake of the intervention, neither to which target population the findings can be generalized. In addition, about 30% of the studies provided insufficient information about the way of approaching patients and the person recruiting patients. Our total mean eligibility and enrollment rates (resp. 65% and 67%) were comparable to those found by Moyer et al. (resp. 65% and 73%)(11). The highest eligibility and recruitment rates were found for studies with a consecutive
sample without screening or a convenience sample without screening, with lower eligibility and recruitment rates for studies that screened a consecutive group of patients on physical or psychological complaints. Higher enrollment rates were found in studies examining an individual instead of a group or couples intervention and when patients were approached by their physician, nurse or researcher instead of using more impersonal media.

Although we found a large increase in the publication of flow diagrams after the introduction of the CONSORT statement in behavioral medicine (13), even in many publications including a flow diagram information about the number of patients assessed for eligibility and eligible remained absent. Moyer et al. also found that less than half of the psychosocial intervention studies for cancer patients reported the number of patients approached to participate (11). Giving a closer look to the CONSORT checklist of items to be included in the reporting of a randomized clinical trial (5-7), we found that important items for external validity, such as the target population, counts of the patient recruitment process before randomization and the method of recruitment are not clearly prescribed. This was also noted by others (15). As a result of the absence of these guidelines, complete and adequate reporting of these items may lack guidance or may be seen as less important by researchers.

We found considerable lower mean eligibility (18.6%) and recruitment (17.9%) rates for studies that relied upon screening on symptoms of a consecutive sample of patients, than for studies that did not rely upon screening. It makes sense that requiring patients to have elevated levels of symptoms in order to be eligible will lead to a relatively low percentage of approached patients to meet this criterion and thus a low eligibility rate. In addition to this reasoning, it shows that many patients screened and reporting high levels of complaints, actually report no need for psychosocial services and interest to participate, which has been observed by others as well (16-18). However, screening is currently recommended as a means to include a more targeted sample of patients (19), as including only patients with a high level of complaints will increase the chance of finding a clinically significant treatment effect. As screening a consecutive sample of patients is found to be a very time-consuming undertaking (20), an alternative is to recruit a convenience sample of patients and screen them after they have shown interest in participation. Selecting patients in this way may take less effort and will probably result in a patient sample more in need for and willing to participate in an intervention trial.

Biomedical trials in general (21,22) and cancer clinical trials (23,24) in particular also report trouble recruiting patients (25). In these trials, the presence of a placebo or no treatment group showed to be associated with lower recruitment and enrollment rates (26-28). For psychosocial interventions, we did not find this association. It can be reasoned that the chance to be randomized to care as usual is seen less as a barrier to participate in psychosocial intervention research than in a clinical trial were there is a more urgent need for treatment. We did find a higher enrollment rate in trials examining
an individual treatment instead of a group- or couples-based program, which supports findings from previous research (29). The substantially higher mean enrollment rates for studies with a physician as recruiter show that recruitment by a person valued or regarded as authority by the patient may give a strong impulse on recruitment rates. A review into the recruitment and willingness of cancer patients to participate in clinical trials also found that the relationship with the physician played an important role in patients’ choice whether or not to participate (28). On the other hand, the higher enrollment rates might also be explained by the physician already preselecting patients, and considering which patients would be willing to participate in the intervention study.

During the review process, we found that recruitment information was often described in an ambiguous way. Some authors for example, reported the number of patients being referred to the study by a physician or who already consented to be screened for study participation as the full sample ‘approached’ (30,31). Even more questionable, 8 studies reported randomizing 100% of eligible patients. We gave particular attention to these studies. In some of them, insufficient details were provided to determine how investigators could claim that all patients were interested in enrolling in the intervention trial. In other studies, it was apparent that the point from which recruitment was calculated was after loss or exclusion of any uninterested or ineligible patients. Also in some studies, eligibility criteria included patients’ willingness to participate and being randomized or to provide informed consent. Yet, when eligible patients declining to participate are defined as ineligible, this leads to a large overestimation of the acceptability of the intervention. To prevent similar bias in recruitment rates in reports of other clinical trials, these findings call for more explicit standards in reporting the recruitment process.

6.4.1. Limitations

To begin with, it is possible that, although we conducted an extensive search by a professional documentalist, some reports were not included because of difficulty of identifying them or language limitations. Also, we restricted our search to interventions including more than one contact with a therapist. Single session interventions with homework exercises, audio/dvd or internet use were thereby excluded. Including these interventions might have affected the recruitment rates found. Furthermore, in our analysis of intervention and trial characteristics related to enrollment rate, we had to combine categories for some characteristics. Thereby, interesting information was lost, especially concerning the types of interventions and the intervention delivery. In addition, we approached several authors for additional information on recruitment items that were unclear in their paper, but only few responded. A drawback of this low response was that this led to the inclusion of a number of poorly reported studies, of which some raised questions about the calculated recruitment and enrollment rates. Finally, a question that could succeed from our present review study is whether studies that are more successful in recruiting a powered and adequately selected patient sample
also provide stronger evidence of efficacy. As this was beyond the purpose of our review, further research is needed to address this question.

### 6.4.2. Recommendations

As we found that many publications lacked information about their recruitment procedures and recruitment rates, we recommend additionally prescribing the number of patients assessed for eligibility and the method of recruitment as required items in the CONSORT checklist (table 4). Awareness of the importance of these counts should stimulate investigators to attempt to record them during the recruitment phase of their trial.

Calculations of recruitment rate depend on determining what the overall denominator of recruitment is. We recognize that reporting the number of patients assessed for eligibility may be a challenge for cancer trials using the internet as a recruitment strategy (32), or using a combination of methods to identify patients, such as pre-screening of patient registries, consecutively assessing patients in a clinic, and using flyers and referrals of physicians. In that case, it would be better to describe the number of patients assessed and recruited with each method to give insight in the different rates of recruitment for each method. In addition, we suggest to refine the CONSORT flow diagram (figure 3). The revised flow diagram should provide more guidance for the reporting of eligibility counts and criteria for screening on the presence of complaints, which remain absent in the current CONSORT version. For studies that include patients based on high complaints, we propose to distinguish between screening criteria and other inclusion criteria. In some studies, patients are screened twice on the presence of complaints, e.g. first with a short screening instrument to identify patients who are eligible on the main inclusion criteria (e.g. depressive symptoms), and then with a more comprehensive diagnostic instrument to identify patients with a specific diagnosis (e.g. Major Depressive Disorder) and fulfilling other inclusion and exclusion criteria. For these studies, we included a second box ‘excluded’ on the left side of the flow diagram. Reporting the screening criteria separately will deliver more insight in the percentage of patients with high physical or psychological complaints for whom the intervention is supposed to be effective. In addition, we recommend to report more details of the number of patients excluded and their reasons, as this will provide insight in the selection process and, in turn, facilitate evaluation of external validity and clinical relevance of the trial.
Table 4. Proposed additions (in bold) to the ‘CONSORT 2010 checklist of information to include when reporting a randomized trial’ (Moher et al., 2010).

<table>
<thead>
<tr>
<th>Item No</th>
<th>Checklist item</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methods Participants 4a</td>
<td>Eligibility criteria for participants</td>
</tr>
<tr>
<td></td>
<td>Settings and locations where the data were collected</td>
</tr>
<tr>
<td></td>
<td>Method of recruitment</td>
</tr>
<tr>
<td></td>
<td>Recruitment strategy (e.g. use of medical records/databases, referral sources, flyers, advertisements, phone calls, email, letters, screening methods)</td>
</tr>
<tr>
<td></td>
<td>Recruiter (e.g. physician, researcher, research assistant, nurse, volunteer)</td>
</tr>
<tr>
<td></td>
<td>Setting of recruitment (e.g. hospital, clinic, in- or outpatient unit, other setting)</td>
</tr>
<tr>
<td></td>
<td>Type of study sample (e.g. consecutive, convenience, other sample)</td>
</tr>
<tr>
<td>Results Participant flow 13a</td>
<td>For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analyzed for the primary outcome</td>
</tr>
<tr>
<td></td>
<td>Number of patients assessed for eligibility or reasons why this number is unknown</td>
</tr>
<tr>
<td></td>
<td>Number of patients eligible or reasons why this number is unknown</td>
</tr>
<tr>
<td></td>
<td>Reasons for patients to be excluded before randomization (e.g. did not meet inclusion criteria or screening criteria, declined to participate, declined to be assessed)</td>
</tr>
</tbody>
</table>

6.4.3. Conclusions

This review showed that the reporting of recruitment data requires additional attention in future psychosocial intervention studies. This is only possible when researchers are aware of the importance of reporting details of the recruitment procedures and are provided with clear definitions and additional space in literature to report this process. Estimates of eligibility, enrollment, and recruitment rates based on what is currently available in literature may be unrealistic and lead to failures to meet recruitment goals and compromised designs as investigators attempt to cope with lower than expected recruitment goals. An understanding of how patients were recruited is essential to evaluate the target population to which findings can be generalized. In turn, this information is important for both replication studies and for effectiveness studies, giving insight in the likely uptake of interventions when they become disseminated and implemented in routine care. With the current call for more attention to the integration of psychosocial care into practice this is crucial information (3,4).

Funding

This work was supported by a grant from the Dutch Cancer Society (RUG-2007-3805) and a grant from the Dutch Cancer Society’s National Cancer Control Campaign.
Figure 3. Suggestions for a revised CONSORT Flow Diagram.

**Screening on complaints**

- Excluded \( n= \)
  - Did not meet 1st screening criteria (give reasons) \( n= \)

- Excluded \( n= \) (optional)
  - Did not meet 2nd screening criteria (give reasons) \( n= \)

**Enrollment**

- Assessed for eligibility
  - Excluded \( n= \)
    - Did not meet inclusion criteria (give reasons) \( n= \)
    - Other reasons (give reasons) \( n= \)

- Eligible \( n= \)
  - Excluded \( n= \)
    - Declined to participate (give reasons) \( n= \)
    - Other reasons (give reasons) \( n= \)

- Randomized \( n= \)

**Allocation**

- Allocated to intervention \( n= \)
  - Received allocated intervention \( n= \)
  - Did not receive allocated intervention (give reasons) \( n= \)

- Excluded from analysis (give reasons) \( n= \)

- Analysed \( n= \)
  - Excluded from analysis (give reasons) \( n= \)

- Analysis

- Follow-Up
  - Lost to follow-up (give reasons) \( n= \)
    - Discontinued intervention (give reasons) \( n= \)

- Lost to follow-up (give reasons) \( n= \)
  - Discontinued intervention (give reasons) \( n= \)
References


8. Rothwell PM. External validity of randomised controlled trials: "to whom do the results of this trial apply?". Lancet. 2005;365(9453):82-93.


Appendix 1. Papers included in the review.


Chapter 6


