Summary
Despite major advances in the detection of cancer and medical treatment, being diagnosed with cancer can trigger various negative emotions. For some patients these emotional problems remain present after the diagnostic and treatment phase. After this phase, when regular contact with health care professionals declines, psychosocial intervention may be especially relevant. In this context, an intervention RCT of Nezu et al. (2003) into the effectiveness of Problem-Solving Therapy (PST) for distressed patients showed promising results. The basic premise of PST is that when patients learn to identify and effectively cope with the problems they face, they gain an increased sense of self-efficacy, control, and confidence. According to the theory of Problem-Solving, such changes would reduce symptoms of distress and depression. In the PST intervention trial of Nezu et al. (2003), patients indeed showed improved quality of life, decreased psychological distress and depressive symptoms, as well as more effective problem-solving ability in both short- and long-term.

The main aim of this project was to replicate on the study of Nezu et al. (2003) and examine the efficacy of PST in a Dutch sample of adult cancer patients selected for heightened distress. However, during the developmental and execution phases of our project, we encountered several methodological problems, which stimulated us to discuss these topics more thoroughly in a number of papers. With our research findings, we intend to support future researchers and clinicians in the challenging task to develop and execute psychosocial intervention trials of high quality.

Routine screening for psychological distress in clinical cancer care is widely recommended in both national and international guidelines, with the purpose to early recognize and treat related psychological symptoms. In Chapter 2 of this thesis, we examined the question if screening for distress was indeed an efficient means to uncover unmet needs for psychosocial services in cancer patients. We found that distress level and need for services were moderately positively related; about half of the distressed patients reported a need for services, but also 10-20% of the non-distressed patients reported this need. Furthermore, we discovered possible gender differences in seeking services and in the type of services wanted; the majority of distressed patients already receiving services was female and more than expected patients with an unmet need was male. Taking into account the already strapped clinical resources in many oncological settings and our research findings, we concluded that relying exclusively on outcomes of screening for distress to identify patients with an unmet need for services was not so efficient as generally has been assumed.

In Chapter 3, we commented on a clinical trial of Carlson et al. (2010) into the efficacy of screening on subsequent distress in a large sample of patients with breast and lung cancer. In our commentary on the study of Carlson et al., we note that the group that was offered a chance to discuss psychosocial issues with staff irrespective of their distress
score demonstrated a larger decrease in distress than those patients who only received screening and had no access to screening results. These findings support the idea that offering patients the chance to directly discuss their needs, regardless of their screening score, might make a more substantial contribution to their wellbeing than distress screening alone.

In Chapter 4, we discussed whether implementing screening for distress was an efficient means to recruit cancer patients for a psychological intervention RCT. Screening for distress is not only recommended as part of psychosocial cancer care, it is also part of a scientific rationale. There is consistent methodological evidence that psychosocial intervention trials that do not preselect patients who report a high level of physical or psychosocial complaints often fail to demonstrate the efficacy of their intervention, because a majority of patients does not register a clinically significant effect (a floor effect). The current literature therefore strongly advocates to select patients with significant physical or psychosocial complaints, as this will increase the chance of finding a clinically significant treatment effect. In our replication study we adopted these scientific recommendations regarding screening for distress in the recruitment of patients. However, this decision led to both methodological and implementation problems. We found that, although percentages of patients with elevated distress (30-40%) were comparable to other studies, only half of these distressed patients indicated a need for services on their screening questionnaire. When we further explored this need in telephone interviews, 41% of the distressed patients reported that they had no need for psychological services, another 17% already received professional psychological services, and 13% preferred other services. Only 3.7% (n=36) of the 970 screened patients finally agreed to participate in the PST trial. Compared to the total group of distressed patients, we found that younger and more educated patients relatively more often agreed to participate in the study. The time investment in recruitment was large: 17 hours were needed to recruit one patient. We calculated that, for a sufficiently powered replication study, we should have screened 3240 patients.

Other main problems to execute our study were lack of time of nurses and oncologists to actually distribute the screening questionnaire (only 25% of the potential participants received a screening questionnaire), concurring questionnaire research, and unwillingness of staff to participate in the distribution of the questionnaire. These findings led to the conclusion that the implementation of routine screening for distress in regular clinical cancer care proved to be an inefficient means to recruit patients, in this case for an RCT concerning PST. In our opinion, from a methodological point of view, a multicenter approach is indispensable to screen a sufficient amount of potential participants for an adequately powered intervention RCT. Additional important issues are commitment and practical possibilities of participating care professionals and funded staff assistance at each participating site.
The earlier mentioned intervention RCT of Nezu et al. (2003) showed promising results on various outcome measures in both short- and long-term. One of the main aims of the current project was to replicate this RCT, in order to assess the generalizability of the PST intervention to the Dutch healthcare setting. In Chapter 5, we reflect on the methodological and implementation problems we encountered. We adopted the design of Nezu et al. (2003) by screening a mixed sample of cancer patients for distress, and using a waitlist control condition in our intervention study. Based on methodological recommendations and literature concerning the course of distress of cancer patients, we also made some changes in the design: we used a *consecutive* instead of a *convenience* sample, we recruited patients after completion of medical treatment instead of during treatment, and we provided no financial compensation for participation. As already mentioned in Chapter 4, only 36 patients were randomized, 18 into the PST-intervention and 18 into the waitlist control condition. Considering the treatment integrity of the intervention, it appeared that only half of the intervention condition (n=9) received PST as planned. The low retention was mainly due to the methodological decision for a moderate distress level as inclusion criterion; some patients recovered earlier than foreseen in the protocol. Other patients had difficulty with adherence to the protocol, or dropped out because of being randomized to the waiting list control condition. Differences in the Netherlands and in the USA between the psychosocial healthcare system and between the general wellbeing may have contributed to the problems we encountered. In the Netherlands psychosocial services are relatively easy accessible and to some extent financed by the Dutch healthcare system, which may have been a reason for patients dropping out and one of the main reasons for the low recruitment rate of the present study. Many patients experienced sufficient social support from family and friends, or the availability of professional psychosocial support nearby.

We recommend that future intervention studies a.) incorporate a flexible number of treatment sessions in their design to be able to pay attention to the personal needs of patients, and b.) take the quality, accessibility and structure of the healthcare context in which the RCT is to be implemented into account in order to develop feasible and relevant trials.

As we did not succeed in recruiting a sufficient number of patients into an RCT for an adequately powered trial, we decided to undertake a systematic review concerning other studies in this domain. In Chapter 6, we describe the results of our systematic review, focusing on the completeness of reporting of the recruitment process of patients. In many of the included RCTs (n=97) we found incomplete and unclear reporting of the recruitment process. After contacting several authors for inexplicable or missing information in their papers, we were able to calculate *eligibility*, *enrollment* and *recruitment rates* for respectively 41%, 77% and 44% of the studies. For 20% of the studies we could not calculate these rates: they only reported the number of patients randomized.
Eligibility rate  the number of patients eligible/ the number of patients assessed for eligibility * 100%

Enrollment rate  the number of patients randomized/ the number of patients eligible * 100%

Recruitment rate  the number of patients randomized / the number of patients assessed for eligibility * 100%

Studies including a consecutive sample and convenience sample without the use of screening showed the highest percentages of eligible and randomized patients. As expected, we found much lower percentages of eligible and randomized patients for studies that included a consecutive group of patients and additionally used screening for heightened physical or psychological complaints. Higher enrolment rates were found in studies examining an individual instead of a group or couples intervention, and when patients were approached by a physician, nurse or researcher instead of more impersonal media. Our findings showed that the reporting of recruitment data needs much more attention in future publications. An understanding of the recruitment method and the amount of patients recruited in an intervention trial is not only essential for the validity and generalizability of potential results, but also to get insight in the likely uptake of interventions when they become disseminated and implemented in routine care. This is only possible when researchers are provided with clear definitions and guidelines about the ratios to report and additional space in their papers to report this process.

In conclusion, we learned from this replication study concerning Problem-Solving Therapy (Nezu et al., 2003) that an earlier intervention trial proven to be effective and successful is not without any question generalizable to another healthcare context. Many of our research findings raised doubts about methods to be used, as well as the state of the art concerning screening and the RCT-design as ‘gold standard’ in psychosocial intervention research. First, we raised critical questions about the efficiency of screening for distress to detect unmet needs in cancer patients, and to recruit a sufficiently powered sample of patients for an intervention study. Second, we discussed several methodological problems we encountered in our attempt to replicate the trial of Nezu et al. (2003). It was an anticlimax to find out that, in the years following the start of our replication study, several meta-analyses excluded this trial as an extreme outlier, as the authors came to the conclusion that the trial reported unrealistically high effect sizes for their primary outcome measure, namely distress. Third, we established incomplete and unclear reporting of the recruitment process in many of the psychosocial intervention RCTs for cancer patients we reviewed. This suggests that there may be a lot of bias in research findings concerning the feasibility and maybe the effectiveness of psychosocial interventions as well. We hope that the current thesis increases insight in the possibilities and pitfalls in the execution of a psychosocial intervention study. It is a
challenging task to recruit and retain a sufficient number of patients in an intervention study. Crucial in this task is to tailor the intervention to the healthcare context of the country in question and to the *individual* needs of the patient. Finally, to assess and improve the quality of psycho-oncological care, it is important that researchers clearly describe their design, the intervention process and their research findings. This transparency will clarify which aspects are to be taken into account in the understanding and the implementation of eventual trial findings. With this thesis we tried to make a contribution to that.