The increased survival rate brings challenges for increasing the quality of life of cancer survivors. Approximately 30% of all survivors report a decrease in the quality of life due to the physical and psychological after-effects of cancer and consequent treatment [1;2] and express a need for professional support such as rehabilitation [3]. The present thesis focused on oncological rehabilitation. The study was primarily set up to examine the effects of a 15-week multidimensional rehabilitation programme on the quality of life and the degree of fatigue of cancer survivors. The aims of the study were to investigate the effect of the intensive part (i.e., the first six weeks) and the entire multidimensional rehabilitation programme on physiological functioning and on the quality of life. Another goal was to obtain more insight into patients’ appreciation of the multidimensional programme and into patients’ preferences regarding mono- and multidimensional rehabilitation programmes. Furthermore, the study aimed at obtaining more insight into variables associated with improvements in the quality of life. To this end, the correlations between sociodemographic characteristics and internal and external resources and quality of life before and after rehabilitation were explored. Because fatigue is one of most frequently-reported complaints among cancer patients, an additional goal of the study was to explore predictors of fatigue at baseline in patients referred for rehabilitation, and to examine whether or not a change in fatigue would be associated with a change in the predictors identified at baseline. Finally, as part of the thesis and within the context of a multi-centre follow-on study on oncological rehabilitation, an evidence-based physical training programme for cancer patients was developed.

This final chapter aims to discuss the results of the study in a broader context. The chapter first summarizes the main findings of the study, and overall methodological considerations are discussed. Then the clinical implications of the study are presented. Finally, theoretical reflections and future research are outlined.

**Main findings**

The multidimensional cancer rehabilitation programme, which was the theme of this study, consisted of the following four components: individual physical training, sports and games, psycho-education, and information. The study revealed that this group-wise rehabilitation programme had statistically significant and beneficial effects on various domains of cancer patients’ functioning, including improvements in physical variables, quality of life, and fatigue. Regarding physical variables, a statistically significant increase in oxygen pulse was found after six weeks of rehabilitation, reflecting genuine physiological improvements. Furthermore, a statistically significant increase in muscle strength was found in the lower extremity. With respect to quality of life, the 15-week multidimensional rehabilitation programme appeared to have beneficial and clinically relevant effects on both general and disease-specific health-related quality of life. In addition, the programme had statistically significant and clinically relevant effects on all domains of cancer-related fatigue. Patients appeared to be highly satisfied with the programme and the components, with the exception of the information component. In addition, patients seem to prefer a multidimensional programme rather than a programme with one component.
Further, the results gave insight into the processes of change. Although the rehabilitation programme had little effect on personal resources, improvements in quality of life appeared to be associated with increased self-efficacy and reductions in negative social support. Change in fatigue appeared to be predominantly associated with change in physical variables. The main predictors of fatigue and quality of life after the intervention were fatigue and quality of life at baseline.

Within the context of a national multi-centre trial, the last chapter of the present thesis focused on the development of a physical training programme based on the best available evidence. Evidence for the effectiveness of exercise on aerobic capacity, fatigue, and physical (role) functioning quality of life was found at meta-analysis level. Evidence for the beneficial effect of exercise on muscle strength was found at rct level. Aerobic exercise and progressive resistance exercise alone or combined appeared to be beneficial to cancer patients. In addition, evidence supported the notion that self-management and self-efficacy-enhancing programmes have beneficial effects on health outcomes among people suffering from various diseases, on the quality of life of cancer patients, on exercise adherence, and on later exercise behaviour. Based on these findings, a physical training programme tailored towards the patients’ individual needs and problems was developed, and consisted of aerobic exercise, progressive resistance exercise, and self-management and self-efficacy-enhancing techniques.

Methodological considerations

The results of the study should be interpreted with caution. The most important limitation of the study was the lack of a control group, which reduces the evidence for the effectiveness of the multi-dimensional programme. Furthermore, the design of the study did not provide the opportunity to compare the effects of the physical and psychological components separately. In addition, due to the response such as an over-representation of breast cancer, the results cannot be generalized to the entire cancer population. However, the group of patients covered seems to be a good reflection of clinical and daily practice, and thus the findings may be generalized to clinical practice.

The results of the study are based on the use of valid and reliable measures. Most of them appeared to have a rather good Cronbach’s alpha in the present study. However, one of the measures, the General Efficacy Scale, while initially attractive because of its global nature, may be problematic because of that same characteristic and therefore not sensitive enough to detect change in self-efficacy. As a result, behaviour specific or task specific self-efficacy ratings may be more appropriate.

An advantage in this study was the fact that the choice of a pre-post design gave no ethical problems concerning the allocation of an intervention, a control group or a waiting period, which may legitimize the choice during a pilot study. It may be assumed that the beneficial effects found may be attributed to the intervention rather than to maturation, because of the long timeline between the completion of treatment and the start of the rehabilitation programme. Another advantage of the study was that information about patients’ functioning was obtained from a medium-sized group of cancer patients referred to rehabilitation. The study provided insight into risk and resistances variables for quality of life, predictors of fatigue, and mechanisms of change in quality of life and fatigue.
General Discussion

Clinical implications

The patients in this study were referred on the presence of physical and psychological problems that appeared to be severe. The quality of life of the referred group of patients appeared to be low in relation to the normal population and to a reference group of cancer patients. Many patients reported higher scores on psychological distress than the cut-off score [4]. Moreover, the patients suffered highly from fatigue and their physical functioning appeared to be lower than predicted on the basis of age and gender. These findings underline the fact that (a) at least a part of the patients show poor adaptation to cancer or show a considerable amount of problems, and (b) this target population can be detected by the inclusion criteria used.

The results show that the rehabilitation programme under study has beneficial effects, with effect sizes ranging from ‘a small change’ to ‘a considerable change’ in the quality of life and degree of fatigue. Based on the low quality of life reported at baseline, these clinically relevant effects indicate that rehabilitation is beneficial and worthwhile for this group of patients. The findings are in line with findings of meta-analyses on the effect of psychosocial [5-7] and physical interventions [8;9], and with studies on combined interventions [10-12]. However, more research on the effectiveness of the programme is necessary, taking account of the methodological problems mentioned.

The programme appeared to be feasible for cancer survivors with various cancer diagnoses. This may also indicate that patients with several types of cancer apparently apply for rehabilitation or are referred to rehabilitation. However, an over-representation of breast cancer patients was included in the study population. Regarding disease-related variables, no effects of type of cancer, stage of disease, or time since completion of treatment were found, with the exception of change in health and pain. Regarding demographic variables, no effects of age and gender were found. Furthermore, the drop-out rate of the study was low and not related to age, gender, cancer diagnosis, time since diagnosis, and completion of treatment. Drop-out was predominantly based on cancer recurrence, and seemed not to be related to the intervention. It may therefore be concluded that the programme is applicable to a broad group of cancer patients.

The findings about patients’ preferences revealed that patients seem to prefer a multidimensional programme rather than a programme with one component. These findings may indicate that cancer survivors have a general preference for multidimensional programmes. An explanation for this may be the presence of complaints that are physical, psychological and/or social in nature. Patients may also consider ‘more’ as being ‘better’. The patients’ appreciation of the programme appeared to be high. The findings concerning patients’ preferences and appreciation imply that the programme is highly valued by the patients, which is of importance in ‘demand-driven’ working conditions. In addition, both findings plead for the implementation of the programme. However, one could argue that, when offered the choice before rehabilitation, patients may tend to label the ‘most’ as the most appropriate and, if asked after the completion of the rehabilitation course, they tend to remain satisfied with their choice, or, in other words, that a sort of ‘cognitive dissonance’ may occur [13]. Furthermore, although patients’ satisfaction is, of course, very important, it is not the same as quality of care.

Despite the fact that the effectiveness of the programme has been examined as a whole, some findings, such as the physiological improvements and the association between...
reduction in fatigue and improvements in physical variables, indicate that the physical component (individual exercise and sports and games) seems to be a key component in cancer rehabilitation. The findings from recent meta-analyses [8;9;14;15] on the effect of aerobic exercise on aerobic capacity, fatigue, and quality of life underline the importance of physical exercise in cancer patients. The value of physical activity is also emphasized by recent cohort studies reporting that physical activity post-diagnosis has beneficial effects on cancer recurrence and survival [16;17]. Consequently, a comment entitled “Time to get moving?” [18] appeared in the Journal of Clinical Oncology in 2006, and aimed to draw attention to the protective associations of physical activity that occur post-diagnosis. Although the results of the study showed no group effects on patients’ personal resources, improvements in the quality of life were associated with increased self-efficacy. This may indicate that it would be useful and beneficial to aim future programmes at an improvement in self-efficacy. In rehabilitation, two dimensions of self-efficacy seem to be important: self-efficacy at baseline and the amount of change in self-efficacy [19]. The former has been described as a predictor of quality of life [20] and of exercise adherence [21], while the latter is mostly the result of a feeling of having mastered something and is associated with improvement in quality of life and exercise adoption. It is known that self-efficacy is enhanced through experiences of mastery [22] but it is questionable whether mastery experiences of psychological tasks (such as stress management) or physical tasks (exercises or sports) actually result in the enhancement of self-efficacy. It has been reported that the successful performance of physical tasks results in an increase in self-efficacy. Furthermore, as a consequence of an increase in task-specific self-efficacy, a general feeling of self-efficacy may occur, indicating that a person may feel more competent to perform better in daily life [22]. Finally, a change in self-efficacy may be associated with an enhancement of mood and affective responses [21] which may be the reason why people feel better after physical training. Although physical training is mainly aimed at improving cardiovascular capacity, muscle strength and daily physical functioning, these latter results may also enhance the feeling of mastery [21]. Improvements in the quality of life also appeared to be associated with reductions in negative social support. What does this mean? On the one hand, such findings may refer to an inadequate social network which may imply, in that case, that significant others such as the partner, another family member, a friend, a colleague, or employer should be involved in the programme. On the other hand, patients may also have negative perceptions about relatively ‘neutral’ events, indicating that patients themselves may profit from a cognitive training in which they learn to change negative perceptions into more neutral cognitions. Summarizing, the results of the this study indicate that a multidimensional rehabilitation programme has positive and clinically relevant effects on the quality of life and the degree of fatigue. These results induced the start of a follow-on study. This multicentre study includes a RCT on the effects of multidisciplinary rehabilitation on the quality of life compared to physical training and a waiting-list control group. A physical training programme, which was also the last subject of the present thesis, was developed for this RCT. The physical training programme was developed on the best available evidence for the positive effects of aerobic exercise and progressive muscle-resistance training on aerobic capacity, muscle strength, fatigue, and physical role functioning [8;9;14;15]. The physical training programme was integrated with self-management and self-efficacy-enhancing techniques, based on the evidence for the positive effects of self-management
programmes and self-efficacy-enhancing techniques on health outcomes in various chronic diseases, on quality of life in cancer patients, on exercise adherence, and on the adoption of a physically active lifestyle. The resulting group training programme consists of several self-management modules. It is aimed at improving physical problems and may have the following advantages: (a) tailored physical training towards focusing on the patient's established problems, and (b) provision of the training as a self-management programme that may have beneficial effects on health outcome, adherence, and a long-term physically active lifestyle. It is quite possible that an integrated physical programme of this type will have beneficial effects on quality of life, comparable to the multi-dimensional programme with four components. However, research ought to be conducted in order to examine the efficacy of the integrated programme more thoroughly.

How can rehabilitation help optimize cancer patients' functioning? This question may refer to the amount of trainability: the amount by which patients are able to reduce the discrepancy between their current and their intended physical, psychological and social functioning [23]. Some patients may be more able to train than others, probably due to the presence or absence of certain characteristics. Furthermore, trainability refers to the construct of ‘training’, which reflects ‘the systematic appliance of (...) stimuli to force the body to adapt to and recover on a higher level of functioning’. Training often refers to physical training, but it may also include training from a psychosocial view, in line with the Biopsychosocial model [24] and the notion that interventions that dovetail with each other may enhance one another. In consensus with this, the literature on exercise among cancer patients reports that exercise combined with theory-based cognitive behavioural interventions (CBT) may improve exercise adherence and adoption of exercise in the long term [25]. The underlying thoughts here include the notion that rational cognitions and self-efficacy are predictors of exercise adherence and behavioural techniques – such as the enhancement of self-efficacy and stimulation of self-management regulation – and may be needed for the adoption of a physically active lifestyle [25]. Thus, in attempting to improve physical problems relevant to cancer patients, such as aspects of exercise capacity and fatigue, aerobic exercise seems to have a positive effect and can be combined with CBT. To improve psychological problems relevant to cancer patients, such as anxiety and depression, CBT is reported to have beneficial effects [7] while physical training can also positively affect depression [26]. So, combined intervention techniques may be the most appropriate.

Furthermore, rehabilitation techniques seem to be most beneficial and effective if they are provided in a way that patients themselves are able to reduce the discrepancy between current and intended functioning. This implies, for example, that problems and goals will be defined in collaboration with the individual patient [27]. Furthermore, rehabilitation seems to be most beneficial and effective if the physical and psychosocial techniques are provided in a tailor-made manner, which means applied individually and according to the individual’s needs. For physical training, this implies a programme that is tailored to individual physical problems, which are defined using maximum bicycle ergometry, for example, while the improvement of these problems can be reached using a plan based on this same ergometry. For the psychosocial component, tailor-made may imply that the CBT is defined as ‘exploration and change of individual and irrational perceptions, enhancement of self-management, including individual goal setting, self-monitoring, and self-reaction,'
or the appliance of self-efficacy enhancing techniques’. Tailor-made does not imply, however, that the interventions are only geared to individuals; a tailor-made approach can also be used within a group-programme. The additional advantages of a group programme may be the opportunity to enhance self-efficacy through the processes of modelling, and the possibility to affect social support [28].

**Implementation?**

Based on the above-mentioned results of the intervention study and on literature, a wholehearted ‘Yes’ would be the appropriate answer to the question as to whether rehabilitation may be beneficial to cancer patients. The response to the question as to whether oncological rehabilitation should be implemented also seems to be ‘Yes’. The question as to whether rehabilitation for cancer patients should be multidimensional in its nature also seems to require a positive answer. However, the methodological considerations of the present study do not make it possible to answer the question as to whether or not the programme should be implemented as a multidimensional programme including four components. Nevertheless, cancer rehabilitation programmes should be comprehensive and ought to address the multidimensional needs of the cancer patients during recovery [29].

From a normative and social perspective, however, it seems to be legitimate to say that it is a good initiative to implement the four-component multidimensional programme as a part of regular care for cancer patients. Definitively: the need for rehabilitation exists, patients are satisfied with the programme, and the programme seems to be feasible, beneficial, and to have clinically relevant effects. In the meantime, it is necessary to conduct more and good clinical research on the topic of oncological rehabilitation.

Further research on the effects of a physical training programme that is tailor-made and integrated with attention to illness perception and self-management ought to clarify whether this type of programme would be equally effective as a programme with four components. This seems to be interesting because of the aspect of cost-effectiveness. Until now (spring of 2007) the programme with four components has not been compensated by the basic health insurance policies in the Netherlands. The physical self-management programme developed could be more interesting to the health insurance companies. Beside the content of the programmes, however, the growing number of patients referred to rehabilitation demands open access to structural care provision.

When implementing oncological rehabilitation, attention should be paid to the referral of patients. The present inclusion and exclusion criteria for the programme seem to be appropriate, selecting a population of patients with persistent physical and psychosocial complaints after the completion of cancer treatment; thus, those who are most likely to need it are selected. However, our experience shows that there is a discrepancy between the percentage of patients that need rehabilitation (25-30%) [3] and the percentage of patients that are actually referred to rehabilitation. The impression exists that about 10% of the patients are currently referred to rehabilitation. Thus, referral seems to lag behind the need, whereas an adequate system of referral is essential for the cancer rehabilitation programme. Cancer rehabilitation seems an area that will continue to grow as medical professionals realize the necessity for post-cancer treatment intervention to improve the quality of life.

Furthermore, the question may be raised as to whether the figure of 25% is a good estimation of the number of patients that need rehabilitation, taking into account the
literature reporting a higher number of patients suffering from physical problems. For example, Chapter 6 reports that the number of cancer patients suffering from fatigue varies from 61% to 99%. Based on these figures, the 25% mentioned may be an underestimation of the need for rehabilitation. In contrast, not every person with problems actually needs support.

The way in which the cardiac rehabilitation is embedded in regular care could be taken into greater consideration when reviewing oncological rehabilitation. A distinctive feature of cardiac rehabilitation is the extent to which screening and selection are embedded in the process of referring patients to cardiac rehabilitation. Prior to cardiac rehabilitation, all patients who have undergone myocardial infarcts or bypass surgery are screened during hospitalization, just before discharge. Based on the extent and the nature of the problems, patients are selected for various forms of rehabilitation, such as a short programme for patients with physical problems or a lengthier programme for patients with both physical and psychological problems, and finally, a complex rehabilitation programme for those patients with severe physical and/or psychological problems. The screening prior to cardiac rehabilitation during the hospitalization period could serve as an example for oncological rehabilitation. The Comprehensive Cancer Centre North Netherlands has recently started a screening project in which the problems of cancer patients can be explored using a distress thermometer. On this basis, patients can be referred for support such as social work or rehabilitation.

If a cancer rehabilitation programme is implemented, it is important that the intervention is provided and implemented as intended. To ensure the integrity of the treatment, it is necessary that the designer of the programme delivers a good manual [30] with clear specifications of the content and procedures of the programme [31]. Besides this, it is recommended that therapists have affinity with the manner of working and should receive special training in physiology, psychology, and oncology. In addition, in chronic diseases such as cancer, it is quite possible that the approaches taken will be increasingly aimed at self-management. This may imply that the interventions change from therapist-oriented (i.e., the therapist prescribes the intervention while the patients follow these instructions) to patient-oriented, where the role of the therapist shifts from health-care provider to ‘coach’ [32]. A patient-oriented intervention is characterized by the patients’ active participation, taking personal responsibility and changing their lifestyle. Therapists supervise the self-management process by setting goals in collaboration with the patient, for example, guiding his or her actions (such as physical training), and initiating processes of self-reflection (providing feedback). During the pilot study of the integrated physical self-management programme, we observed that therapists relapsed into their usual roles and preferences, which is a threat to the integrity of the treatment [33]. Finally, to ensure the integrity of the treatment, patients should also understand and commit themselves to the self-management approach by assuming responsibility and displaying active participation. Providing good information and an estimation of expectations and goal-setting may contribute to this end.

**Theoretical reflections**

At the start of the study, the International Classification of Functioning, Disability and Health (ICF) model was taken as a starting point, as it is useful for the classification of problems. The problems of cancer patients can be adequately reported in terms of function, activities and participation, especially from a rehabilitation perspective. However, despite
the usefulness of this model to classify problems, it may be less useful as a framework for guiding research aiming to understand relationships between physical and psychological problems, to capture the adaptation process, and to develop supportive interventions.

Other frameworks such as the Biopsychosocial model [34] may be more useful for understanding associations between physical and psychosocial problems and for developing interventions. The Biopsychosocial model may also be useful as an entry point, and also indicates the interdependence between the various dimensions, which seems to be useful in the rehabilitation of cancer patients. This interdependence includes the situation that physical problems may also result in psychosocial problems and vice versa, and that, besides physical effects, physical interventions may have psychosocial effects, and that psychosocial interventions may have a conditional effect on physical problems. Additionally – and importantly – interventions that fit together may also enhance one another. In the present thesis on cancer rehabilitation in patients who were referred on the basis of the presence of combined physical and psychosocial problems, the Biopsychosocial model functioned as (1) a framework for problems and for the development of the multidimensional programme with four components, and as (2) a theoretical fundament in the integrated physical self-management programme in which a deliberate choice was made in favour of physical and psychosocial intervention techniques that would enhance one another.

In addition, the Self-regulatory model [35] and the Common Sense model of Leventhal [36] may provide better guidance in understanding the process of adaptation to changes in life. Furthermore, the Self-regulatory model may provide more tools to develop behavioural interventions such as self-management programmes, whereas the Common Sense model may be helpful in developing cognitive interventions. Self-regulation theory focuses on the ways in which individuals direct and monitor their activities and emotions in order to attain their goals [37]. Self-management covers the six phases of goal setting, monitoring, comparing, decision making, taking action, and self-reaction that may also determine the development of future programmes, in addition to providing insight. Leventhal’s Common Sense model [36] illustrates that patients’ perceptions about their disease may affect their coping with the disease and their final functioning [38]. It appears that perceptions of illness can be changed therapeutically [39], and may serve as predictors for the attendance during cardiac rehabilitation [40].

To capture the physical adaptation process and to develop a physical training intervention, a study of physiology and of the model of Wasserman [41] may be helpful. This model illustrates that patients’ exercise capacity may be reduced due to various reasons, which also seem relevant in cancer rehabilitation. Through the appropriate application of physiological training principles, a number of causes of reduced exercise capacity, such as loss of oxygen uptake or muscle strength, for example, may be treated adequately.

Finally, Bandura’s Social Cognitive theory [22] provides a framework with the main construct of self-efficacy that mediates physical and psychological health. In addition, the construct appears to be predictive for quality of life and for exercise adherence, while change in self-efficacy is associated with the adoption of exercise in the longer term. Because self-efficacy originates from four sources – mastery experiences, verbal persuasion, modelling and physiological arousal – it seems to be very applicable to integrate the construct in physical interventions.
In sum, the above-mentioned models can play a role in oncological rehabilitation programmes because they provide insight into associations and provide a foundation for interventions. The Biopsychosocial system perspective provides a basis for the understanding of associations between physical and psychosocial problems and their consequent interventions in cancer patients. The Self-regulation model [35], the Common Sense model [36] and the Social-Cognitive theory [22] may be of importance for the development of future interventions aimed at behavioural change, such as the adoption of a physically active lifestyle. This assumption is made on the knowledge that cognitive preparation precedes behavioural change [42] and that phases of self-regulation (such as goal setting) and self-efficacy-enhancing techniques may be easily incorporated in an intervention, and may therefore be valuable for oncological rehabilitation programmes.

**Future research**

Future research should examine the effects of the multidimensional programme more thoroughly, and should also be aimed at the examination of the effects of the various components. Therefore, a RCT should examine the effects on the quality of life, using a full factorial design which means a multidimensional programme (psycho-education and physical training), a physical programme, a psycho-educational programme, and a (waiting) list control group.

Further research is required in order to explore the association between physical training, illness perception and self-efficacy and the effectiveness on proactive coping, exercise adherence, self-management skills and a physically active lifestyle in cancer patients. In addition, future research could also examine the effects of the integrated physical self-management programme on the quality of life and on fatigue, in comparison to a control group and a placebo group. Besides the effect on the quality of life, it would be interesting to conduct more research on the effects of the programme on the resumption of work.

Although the multidimensional programme was feasible for various types of cancer, the number of patients with cancer types other than breast cancer was low per diagnosis group. Therefore, future research should include more patients with various types of cancer and should investigate whether or not different programmes would be effective for patients with different types of cancer.

Furthermore, the study showed that fatigue and quality of life after the rehabilitation programme were mainly associated with fatigue and quality of life at the baseline. This suggests that it could be more beneficial if problems could be prevented and/or that it would be interesting to examine the effect of screening and of early intervention. Further research may be aimed at the examination of the effects of only physical or combined rehabilitation performed at an earlier stage of the disease, such as during cancer treatment. Until now, no RCTs to measure the effects of physical training during chemotherapy or radiotherapy have been conducted in the Netherlands. However, a number of foreign studies show that ‘aerobic exercise’ during cancer treatment may prevent physical deterioration [43-45]. In line with this, the effects of pre-surgery exercise on exercise capacity, muscle strength, fatigue and post-surgery complications can be examined in some types of cancer.

More research should be done on the intensity of physical training. The current impression is that the intensity of physical training may vary between 60 to 80% of the maximum heart rate in patients without co-morbidity and with an objective reduction of...
exercise capacity. However, it has been reported that over-intensity of physical training may have negative effects on fatigue and on quality of life [46]. This is supported by a meta-analysis [21] that concluded that moderate intensity in healthy subjects may be more effective in enhancing psychological well-being than high intensity. Because moderate intensity is also recommended for its beneficial effect on physical health, this implies that a high intensity is not necessary to promote physical and psychological health, but further research in cancer patients seems to be warranted. In addition, more research should be devoted to the safety of increased physical activity, especially among groups of survivors in which cardiotoxicity is frequently reported.

Finally, further research should pay more attention to the role of social support in cancer rehabilitation. The finding that the experience of negative social support has both a concurrent and prospective negative effect on quality of life, and that change of negative social support is associated with improvements in quality of life should be involved in the development of screening measures, future interventions, and consequent research.
Reference List


General Discussion