The psychosocial distress questionnaire-breast cancer

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in early-stage breast cancer patients

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Contents

Chapter 1

GENERAL INTRODUCTION

Epidemiology of breast cancer

Breast cancer is the most common form of malignancy in women worldwide [1]. In the Netherlands 13% of all women will develop breast cancer during their life span. It is estimated that 70% to 80% of all breast cancer patients is still alive after five years [2]. Breast cancer accounts for one third of all cancers in women and at diagnosis 23% of the women is younger than 55 years of age [2].

Breast cancer treatment

The number of breast cancer patients has been increasing since the late 1980s and the early 1990s [3] due to early detection and the advancement in treatment [4]. Therefore, a growing number of women lives with the severe side effects of breast cancer and its treatment. In general, breast cancer treatment is classified into local therapy (surgery, radiotherapy) and systemic therapy (chemotherapy, hormonal therapy, monoclonal anti-bodies) [5]. The mainstay of early-stage breast cancer treatment is surgery, sometimes preceded by (neo-adjuvant) chemotherapy. Surgical treatment consists of either a mastectomy, in some cases followed by local radiation therapy, or (oncoplastic) breast-conserving surgery with removal of the primary tumor, always followed by radiation therapy as part of the standard care [5]. In most cases axillary staging by means of the sentinel node procedure is performed. If the sentinel node appears to contain metastases, to date in many cases complementary lymph node dissection is performed during a second operation. The general recommendation is that the best strategy for axillary treatment per patient should be discussed during multidisciplinary consultation. In some cases axillary lymph node involvement is demonstrated by using ultrasound guided sampling. In these patients axillary lymph node dissection is performed without a preceding sentinel node procedure.

Patients who have a higher risk of breast cancer recurrence are more likely to need systemic adjuvant therapy. The risk for breast cancer recurrence is dependent on tumor size, degree of differentiation of the tumor, the presence of axillary metastasis and Her-2-Neu status. Oncologists use prognostic and predictive factors to decide which patients may benefit from adjuvant therapy. Studies have shown that adjuvant therapy improves long-term survival in breast cancer patients [6]. These therapies, aimed at destroying distant micro-metastases, consist of chemotherapy, in some cases combined with antibody agents (trastuzumab) in HER-2-Neu over expressing tumors. Moreover, hormonal therapy is prescribed for at least five years if the estrogen receptor is positive. Each type of adjuvant treatment can be used separately or in combination across time.

Psychosocial problems in breast cancer patients treated with adjuvant chemotherapy

Breast cancer diagnosis and treatment are not only associated with substantial physical complaints which interfere with daily activities [7, 8], but are also related to psychosocial problems [9-12]. Most patients experience anxiety and depressive symptoms at the time of diagnosis [12]. Although these feelings tend to decline over time [13] fear of recurrence is still regularly present at long-term follow-up. Patients also reported psychosexual problems [14-17] problems with their body image [18, 19], and problems with returning to work, sometimes resulting in financial problems [20, 21].

The prevalence of psychosocial problems among breast cancer patients is depending on the measures that are used. In general, these problems are experienced by 10% to 53% of the women shortly after diagnosis and during treatment [9, 10, 12] and affect health status (HS), i.e., impact of disease on functioning, and health-related quality of life (HRQOL), i.e., evaluation of well-being (in the physical, psychological, and social domains), in 5 to 10 years follow-up [7, 8]. Previous studies have shown that the HS and (HR)QOL of breast cancer patients who remain disease-free during 5 to 10 years of follow-up, do not differ from healthy women [17, 22, 23]. However, patients with adjuvant chemotherapy reported lower HS with regard to sexual functioning [22], physical functioning [24], and social role functioning [8]. Currently, studies focusing on the association between chemotherapy and QOL (i.e., an individual's perception of his/her position in life in the context of the culture and value systems in which he/she lives and in relation to his/her goals, expectations, standards and concerns) are lacking [25].

The importance of screening for psychosocial problems

During the course of medical treatment and follow-up, 10% to 53% of the patients with cancer experience psychosocial problems [9, 10, 12]. Unfortunately, psychosocial problems are difficult to recognize [26-28]. It is essential that patients with psychosocial problems are identified at an early stage since psychosocial problems may negatively affect therapy adherence [29], HRQOL [30] and patients' experiences of quality of care [31]. In busy daily clinical practice, psychosocial problems frequently remain unrecognized, even though they are common [26-28]. There are several reasons why psychosocial problems are not always recognized. First, recognition of psychosocial problems is often hampered by patients' belief that it is not a doctor's role to help them with their psychosocial problems [26]. Second, anxiety and depressive symptoms are associated with physical problems like fatigue, pain, sleeping problems. Health-care providers may tend to focus on these physical symptoms instead of the often underlying psychological problems [27].

Nowadays, screening for psychosocial problems in cancer patients receives much attention and is recommended by several organizations [32-35]. However, in 2006, when this study was started screening for psychosocial problems was still in its early days.

Psychosocial screening is often based on a brief self-report questionnaire. Therefore, it is a rapid method, which may help staff in busy clinics to identify patients with severe psychosocial problems and to concentrate their efforts on those who need referral for more extensive assessment. Psychosocial screening may improve communication between patients and their health-care providers [36]. Moreover, it is time saving because the information provided by screening creates the opportunity to focus on important issues [37]. In addition, Carlson and Bultz [38] showed that psychosocial care interventions have economic benefits because patients with severe psychosocial problems tend to seek more medical treatment services. When patients with severe psychosocial problems are recognized at an early stage they can be referred for an appropriate intervention, which may prevent problems from escalating and improve their (HR)QOL [32, 39, 40]. However, the randomized controlled trials (RCTs) that examined the effect of psychosocial screening on patients' HRQOL remain inconclusive [41, 42].

To our knowledge, prior to this study, the effect of psychosocial screening on HRQOL was examined in two randomized controlled trials (RCTs) [41, 42] in which patients with different types of cancer and disease stages were examined, including breast cancer patients. One study showed a positive effect on patients' HRQOL [42]. The other study found no significant effect on patients' HRQOL [41]. In addition, Detmar et al. [36] showed in a crossover randomized trial a positive effect on patient-physician communication about HRQOL issues. These studies were difficult to compare due to the heterogeneous group of patients. Moreover, psychosocial screening was performed by using different measurement tools and information was lacking about which psychosocial interventions were provided following screening.

Psychosocial screening in the Netherlands

When this study started (in 2006), there was no reliable and valid psychosocial screening instrument available in Dutch, despite the fact that the National Cancer Control Program had already stated in 2004 that psychosocial screening was important and should be incorporated in 2010 [33]. In the Netherlands, breast cancer is the most frequently diagnosed malignant disease and there are more than 13,000 new cases of breast cancer per year [43]. Women with breast cancer also face psychosocial problems that are not easily recognized [44]. It was decided to develop a breast cancer specific instrument, which provides insight in a broad range of psychosocial problems in breast cancer patients' experience during treatment and during the follow-up [45]. The availability of such an instrument provides the opportunity to screen a substantial part of the ambulant cancer population.

Within the St. Elisabeth Hospital (Tilburg, the Netherlands) a project group 'Verwijs-Wijzer' was formed in association with the Comprehensive Cancer Center South in order to examine the already existing screening instruments for psychosocial problems and verify these instruments against predetermined conditions. According to the project group a screening instrument should be (i) short, (ii) able to identify a broad range of

psychosocial problems, (iii) be comprehensive, (iv) relevant for early-stage breast cancer patients, (v) identify patients at risk for psychosocial problems, (vi) is reliable and valid, and (vii) have cut-off scores for referral and is linked to a referral system. Psychosocial problems is defined as a composite of frequently reported psychological and social problems including specific issues that are known to effect patients' (HR)QOL, and risk factors that are associated with patients' psychosocial well-being for whom referral for extended psychosocial care by a psychosocial health-care provider would be helpful. Screening for psychosocial problems differs from measuring HS (i.e., the influence of disease on physical, psychological and social functioning), HRQOL (i.e., evaluation of well-being in the physical, psychological, and social domains), and QOL (i.e., HRQOL with a wider range of domains). HS and (HR)QOL measures are developed to evaluate the benefits and harms of treatments, while screening for psychosocial problems is to detect patients at risk for or having psychosocial problems that may interfere with patients outcome on (HR)QOL.

To detect psychosocial problems in cancer patients, several screening instruments existed in 2006 including patient reported outcome QOL measurements. The most frequently used questionnaires to assess psychosocial problems were the Rotterdam Symptom Checklist (RSCL) [46], the Brief Symptom Inventory-18 (BSI-18) [47], the Hospital Anxiety and Depression Scale (HADS) [48], the European Organization for Research and Treatment of Cancer, Quality of Life Questionnaire-C30 (EORTC-QLQ-C30) [49], and the Functional Assessment of Cancer Therapy-General (FACT-G) [50]. The RSCL was developed to measure the global QOL of cancer patients and focuses on physical complaints, psychological distress, and functional activity level, while the BSI-18 measures anxiety, depressive symptoms and physical complaints. The HADS was a commonly used and validated instrument in patients with somatic diseases and only assesses anxiety and depressive symptoms [48]. The FACT-G consists of four domains (i.e., physical, emotional, social/family and functional well-being). The EORTC-QLQ-C30 has five functional scales (i.e., physical, role, cognitive, emotional, social), three symptom scales (i.e., fatigue, pain, nausea and vomiting), and one scale to measure HRQOL. The RSCL, the BSI-18 and the HADS have cut-off scores for referral and are therefore suitable for screening. However, these measurements have drawbacks. First, these instruments do not measure a broad range of psychosocial problems, such as body image, social problems, and sexual problems whereas multi-domain screening may have more benefits to discuss patients' overall well-being [51]. Second, the RSCL, BSI-18, and the HADS do not assess risk factors (i.e., lack of support, trait anxiety). Third, these measurements are not linked to a referral system for psychosocial health care. However, the EORTC-QLQ-C30 and the FACT-G measure a wide range of aspects relevant to patients' physical, psychological and social well-being. The scores are difficult to interpret, they do not have cut-off scores, and are not linked to a referral system for psychosocial care.

During the developmental phase of the Psychosocial Distress Questionnaire-Breast Cancer (PDQ-BC) the Distress Thermometer (DT) together with the Problem List (PL) was validated in the Netherlands [52]. The DT is an instrument for routine distress screening in patients treated for cancer [52]. Since 2010, the national guidelines recommend the use of

the DT and PL for psychosocial screening as part of routine clinical care in cancer settings [53]. Distress is defined as ´a multifactorial unpleasant emotional experience of a psychological, social, and/or spiritual nature that may interfere with the ability to cope effectively with cancer, its physical symptoms, and its treatment´ [32]. In the psychosocial cancer care this can be considered as an important step forward. However, the DT-PL has several drawbacks: (i) the questionnaire consists of a wide range of physical problems including problems that are irrelevant for breast cancer patients, like difficulty with speaking. Moreover, most side effects from chemotherapy (e.g., hair loss, nausea) become less relevant to discuss during follow-up, because breast cancer patients often recover within a year after treatment, except for fatigue [17]. In addition, (ii) the DT-PL does not measure risk factors for psychosocial problems. (iii) The answers provided are dichotomous (yes/no) and do not explore the extent of the psychosocial problems and are not sensitive to detect small differences in psychosocial well-being, and (iv) the outcomes are not linked to a norm-based referral system, which means that the cut-off scores do not indicate to which psychosocial care providers (social worker, psychologist or psychiatrist) patients should be referred. As a consequence, the decision to which psychosocial health-care provider a patient should be referred will depend on the expertise of the health-care providers.

In conclusion, although a number of psychosocial screening instruments exist, they have important limitations that resulted in the decision to develop a short and comprehensive multidimensional psychosocial screening instrument specific for early-stage breast cancer patients which is linked to a referral system for extended psychosocial care.

Aim of the study

This thesis is the reflection of an ongoing project initiated by a nurse practitioner in 2006 in the field of breast cancer care. In the outpatient clinic at the St. Elisabeth Hospital (Tilburg, the Netherlands) the nurse practitioner, under supervision from the physician, takes care of early-stage breast cancer patients from the initial start of chemotherapy until three months after chemotherapy.

To facilitate the communication about psychosocial problems between nurse practitioner and patients and to provide an adequate and timely referral to psychosocial care providers a screening tool for psychosocial problems was developed. At the same time this questionnaire was incorporated in the standard routine care. Patients complete the questionnaire at regular time points before they visit the nurse practitioner, who discusses the potential psychosocial problems with the patients. Subsequently, studies were initiated to evaluate the psychometric properties. Moreover, studies were performed to determine the number of patients who are referred to a psychosocial care provider and actually followed up on the advice, the course of State anxiety and Depressive symptoms and its predictors up to one year follow-up as well as the relationship between psychosocial problems with QOL.

Thus, the primary aim in the present thesis was to develop a psychometrically sound breast cancer specific screening instrument which is linked to a referral system. A cancer type specific instrument may provide a more precise insight into patients' experience during treatment and during the follow-up [45]. In addition, such a questionnaire may be more acceptable for patients to complete. The scores on the PDQ-BC provide an indication to which health-care provider the patient should be referred.

The second aim was to examine the course of anxiety and depressive symptoms and its predictors. This will provide the opportunity to identify patients at risk for psychological problems. The third aim was to examine the relationship between subscales of the PDQ-BC and QOL. This gives preliminary information about the role of psychosocial problems in relation to patients' QOL.

Participants

All early-stage breast cancer patients at the outpatient clinic of the St. Elisabeth Hospital (Tilburg, the Netherlands) scheduled for adjuvant chemotherapy were eligible for this study. In addition, patients from the Elkerliek Hospital (Helmond, the Netherlands) were also asked to participate before their surgery. Women with a psychiatric disorder and women who had insufficient knowledge of the Dutch language were excluded from participation. The data were collected from December 2006 to October 2011. All patients signed an informed consent form. Before the start of chemotherapy, the participating women completed the PDQ-BC and additional questionnaires in order to validate the PDQ-BC. After this baseline measurement the PDQ-BC patients completed the PDQ-BC at different time-points during follow-up.

Measures

PDQ-BC
The PDQ-BC consists of nine scales (35 questions in total). The questionnaire measures psychological risk factors (i.e., Trait anxiety and (lack of) Social support) and a wide range of psychosocial problems (i.e., State anxiety, Depressive symptoms, Social problems, Physical problems, Body image, Financial problems, and Sexual problems). The response options for all questions range from 1 (*not at all*) to 4 (*very much*). The time of reference is the previous week, except for the subscale Trait anxiety (which assesses how one generally feels). Trait anxiety is assessed only once, before the start of the chemotherapy. Apart from these 35 questions, the PDQ-BC has a number of questions assessing socio-demographic factors, such as marital status, age, age of children and clinical factors, such as type of surgery, type of adjuvant treatment and pre-treatment psychiatric morbidity.

HADS

The Hospital Anxiety and Depression Scale (HADS) is a self-report questionnaire with 14-items measuring levels of anxiety (HADS-A, 7 items) and depression (HADS-D, 7 items) in the medical setting [48]. The response scale is a 4-point rating scale ranging from 0 (*not at all*) to 3 (*very much*) and scores range between 0 and 21 for either anxiety or depressive symptoms. The time of reference is the previous week. The HADS has been validated in several subgroups in the Netherlands [48] and is widely used in the field of cancer [54]. In a review of Bjelland et al. [54] most factor analyses demonstrated a two-factor solution in good accordance with the HADS subscales for Anxiety (HADS-A) and Depression (HADS-D), respectively. The correlations between the two subscales varied from 0.40 to 0.74. The internal consistency was good and varied from 0.68 to 0.93 (HADS-A) and .67 to .90 (HADS-D), respectively. In most studies an optimal balance between sensitivity and specificity was achieved when caseness was defined by a score of 8 or above on both HADS-A and HADS-D [54].

Distress Thermometer

The Distress Thermometer (DT) is an instrument for routine screening of distress in patients treated for cancer [52]. The response is given on a visual analogue scale (a thermometer) from 0 (*no distress*) to 10 (*extreme distress*). Furthermore, the DT can be used together with a Problem List (PL), in order to identify the factors that are responsible for the elevated score on the DT. In this study, we used the 47-item Dutch version of the PL. This PL assesses five domains: Practical, Family/Social, Emotional, Spiritual and Physical topics. The internal consistency is good, although this multidimensional scale was not designed to function as a scale. A cut-off score ≥5 was chosen to detect patients with significant levels of distress [52]. There is no information available about the construct validity [52, 55].

CES-D

The Center for Epidemiologic Studies Depression scale (CES-D) is a 20-item self-report scale designed to measure the presence and degree of depressive symptoms. It has a 4-point response scale from 0 (*seldom or never*) to 3 (*(almost) always*). The time of reference is the previous two weeks. Scores can range from 0 to 60. Scores of ≥16 may suggest of depressive symptoms. The CES-D is a valid and reliable measure of depressive symptoms in breast cancer patients [56].

WHOQOL-100

The WHOQOL-100 is a cross-culturally developed generic multidimensional questionnaire which assesses QOL [25]. The questionnaire consists of 100 items assessing 24 facets of QOL within four domains (Physical health, Psychological health, Social relationships, Environment), General health and an Overall QOL facet. Each facet is assessed by four items which score on a 5-point Likert scale and these scores range from 4 to 20. A high score represents a good QOL, except for the facets Pain and discomfort, Negative feelings and Dependence on medication and treatments, which are negatively framed. The time

frame for the QOL items is the previous two weeks [25]. Reliability and validity are good [57-59] and sensitivity to change of the instrument is high [60]. To examine the construct validity we only used the facets Body Image and Appearance (4 items), Energy and Fatigue (4 items), Sleep and Rest (4 items), Pain and Discomfort (4 items), Social Support (4 items), Sexual Activity (4 items) and Financial Resources (4 items).

Outline of this thesis

This thesis consists of two parts. Chapter 1 is the general introduction. Part A focuses on the development and psychometric properties of the PDQ-BC and consists of three chapters. Chapter 2 describes the development of the PDQ-BC. In Chapters 3 and 4, the psychometric properties of the PDQ-BC are examined. Part B focuses on the short- and long-term (one year after treatment) psychological problems and its predictors as well as the relationship between psychosocial problems and QOL and consists of two chapters. Chapter 5 describes the course of anxiety and depressive symptoms and their predictors in breast cancer patients with adjuvant chemotherapy before the start of chemotherapy, three weeks and three months up to one year after chemotherapy. In Chapter 6, the relationship between a psychosocial screening instrument and the QOL of early stage breast cancer patients treated with adjuvant chemotherapy is examined in a pilot study. In addition, patients' QOL was compared to a healthy norm population. In Chapter 7, the main findings of the study are summarized and discussed and the reflections on limitations and strengths of the present study are provided. In addition, research and clinical implications concerning psychosocial screening are described with regard to future perspectives.

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Part A

DEVELOPMENT AND PSYCHOMETRIC PROPERTIES OF THE PDQ-BC

Chapter 2

DEVELOPMENT OF THE PSYCHOSOCIAL DISTRESS QUESTIONNAIRE-BREAST CANCER (PDQ-BC): A BREAST CANCER-SPECIFIC SCREENING INSTRUMENT FOR PSYCHOSOCIAL PROBLEMS

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Abstract

Purpose

The aim of the present study was to develop a short, easy to use psychosocial screening instrument, the Psychosocial Distress Questionnaire-Breast Cancer (PDQ-BC), and to examine the acceptability and preliminary reliability of the PDQ-BC. In addition, the referral advice to the various psychosocial care providers based on the PDQ-BC was examined to whether these referrals were justified.

Methods

Before the start of adjuvant chemotherapy, 164 (98.8%) women completed PDQ-BC as part of routine care. The PDQ-BC consists of questions about psychological risk factors (i.e., Trait anxiety and (lack of) Social support), psychological problems (i.e., State anxiety and Depressive symptoms), Social problems, Physical problems, Body image, Financial problems, Sexual problems, clinical factors (type of surgery, adjuvant treatment other than chemotherapy and psychiatric morbidity), and socio-demographic factors (marital status, age, and age of children). Confirmatory factor analysis was performed to examine the structure of the PDQ-BC. The Cronbach's alphas (for internal consistency) and Pearson's correlation coefficients (for the relationships between the PDQ-BC subscales) were calculated.

Results

The PDQ-BC appeared to be short. On average, patients indicated that they needed 5 minutes to complete the PDQ-BC. Confirmatory factor analysis supported the internal structure of the PDQ-BC (CFI=0.95 (χ^2(24)=43.3), p=.009; NNFI=0.91; RMSEA=0.073). In general, the internal consistency (Cronbach's α) was acceptable to good, except for Social Problems (α=0.42). Cronbach's alpha of the subscales Trait anxiety, State anxiety, Depressive symptoms, Body image, and Physical problems were 0.88, 0.85, 0.86, 0.79, and 0.69, respectively. Almost all PDQ-BC subscales were statistically significantly correlated with each other. The subscales Trait anxiety, State anxiety and Depressive symptoms have the highest correlations (r≥ .72; p<.01).

Conclusions

The PDQ-BC is a short and easy-to-complete screening instrument for routine use in breast cancer patient care. This instrument facilitates a greater awareness of the concerns and needs for breast cancer patients care during treatment with chemotherapy and the follow-up. The referral system seems to be good to guide allocation to the different levels of psychosocial care providers.

Keywords

Oncology, cancer, psychosocial, breast cancer, screening, psychosocial problems

Introduction

Among women, breast cancer is the most common type of malignancy worldwide [1]. Every year more than 1.2 million patients are diagnosed with breast cancer [1]. In the Netherlands, one in every eight women will be diagnosed with breast cancer during her life [2]. The prevalence rate of breast cancer has increased over the recent years as a result of earlier detection and the use of better adjuvant treatments [3]. Multimodality treatment regimens improve survival outcome but also contribute to a prolonged period of medical interventions with concurrent psychosocial problems. Patients may experience a number of psychosocial problems (i.e., a combination of psychological and social problems), notably psychological problems (i.e., anxiety, depressive symptoms) [4, 5], psychosexual functioning (i.e., impairments in sexual functioning, decreased libido, and relational problems) [5-7], body image [8, 9], physical functioning (i.e., fatigue, pain, sleep disturbance) [10, 11], social problems (i.e., household activities, job) [12] and financial problems [13]. These psychosocial problems are experienced by 10% to 50% of the breast cancer patients shortly after diagnosis and medical treatment [4, 14, 15]. Concerning the psychological problems, different studies reported prevalence rates ranging from 14% to 54% for depression [16, 17] and prevalence rates for anxiety ranging from 8.6% to 49% [5]. This variation in prevalence reflects differences in screening instruments, assessment times, definitions of anxiety and depression, and the stages of disease [18].

Studies have shown that several factors are associated with an increased risk for developing psychosocial problems, e.g., trait anxiety. Women with high scores on trait anxiety have the tendency respond to situations perceived as threatening with a rise in anxiety intensity [19, 20]. These women scored low on quality of life (QOL) [21-23] and high on fatigue [24] and psychological distress [23, 25], irrespective of diagnosis. Furthermore, lower levels of depressive symptoms and a greater sense of well-being were reported when patients experienced adequate social support, especially from family and close friends [26]. This indicates that a lack of social support could be a risk factor for depressive symptoms.

After treatment, patients frequently report a loss of sexual interest and sexual enjoyment [5]. These problems may be directly caused by the side effects of adjuvant therapies, especially chemotherapy [6] and hormonal therapy [7]. Higher degree of impairment of body image is reported in patients after mastectomy compared with patients having had breast conserving therapy [8, 9], although the impact of the type of surgery may be related to the patient's age [27].

Fatigue and pain are the most common physical side effects of treatment of breast cancer. Berger and Higginbottham [10] found that greater levels of fatigue were associated with reporting experiencing more symptoms. Moreover, breast cancer survivors who received chemotherapy may be at higher risk for severe fatigue, which has been associated with depression, pain, and sleep disturbance [10]. Finally, the first year after diagnosis, especially young women seem to suffer from psychosocial problems. One of the explanations is that younger women with breast cancer undergo more aggressive

treatment [13]. These well documented side effects can have devastating short and long term psychosocial consequences for patients.

Psychosocial problems are thought to limit the daily activities and influence the HRQOL of breast cancer patients [28, 29]. It is essential that psychosocial problems in patients are recognized at an early stage since early intervention improves outcome [30-32]. This is the main reason why it is very important to assess these problems and to try to facilitate patients to improve (HR)QOL. Thus, good oncological care needs to aim at preventing psychosocial problems by timely detection and offering help when needed. A screening instrument to reveal psychosocial problems is, therefore, important.

Nowadays, screening for psychosocial problems in cancer patients receives much attention. The Dutch National Cancer Control Programme has stated as their goal to develop a screening program for psychosocial problems in the Dutch guidelines before the year 2010 [33]. Regarding follow-up in oncology, the National Health Council strongly advocates that psychosocial care should be a regular part of follow-up [34]. To assess psychosocial problems, a number of screening instruments exist [35-38] of which most are not validated in a Dutch cancer population or only assess psychological problems (i.e., anxiety and depressive symptoms) and physical problems. Two screening instruments have been used and validated in the Netherlands. First, the Hospital Anxiety and Depression Scale (HADS) which is a 14-item scale inquiring into anxiety and depressive symptoms during the previous week. This scale has shown to be reliable and valid [39]. However, the HADS only assesses two specific psychological factors, which are depression and anxiety. Other relevant aspects have not been incorporated in this screening instrument. Second, the Distress Thermometer (DT), was developed by the American National Comprehensive Cancer Network (NCCN) [31]. It is a frequently used measure to evaluate emotional distress (i.e., social, psychological, and spiritual/religious aspects) in cancer patients. At this moment, it is the instrument of choice in the Netherlands. On a visual analogue scale (VAS), called the thermometer, patients can indicate their level of distress by indicating a number on a scale from 0 (*no distress*) to 10 (*extreme distress*). Recently, the DT is validated in a Dutch cancer population [40]. The DT has acceptable levels of sensitivity and specificity [41-43]. The DT performs best in relation to distress, but modestly with regard to anxiety and depression [44]. However, the thermometer of the DT is generic and cannot be used for specific referral to various levels of psychosocial care providers, i.e., social worker, psychologist, or psychiatrist. Apart from the thermometer, the DT contains a number of questions regarding physical, psychological, social, and spiritual/religious concerns. The answers provided are only yes/no and do not explore the extent of these problems. In addition, neither the HADS nor the DT identifies risk factors for psychological problems. Moreover, these instruments are not linked to a referral system based on norm scores for referral to the various levels of psychosocial care providers. Therefore, the project group 'Verwijs-Wijzer' of the St. Elisabeth Hospital (Tilburg, the Netherlands), in collaboration with Tilburg University, has developed the Psychosocial Distress Questionnaire-Breast Cancer (PDQ-BC). The aim of the project group was to develop a screening instrument that is multi-dimensional and assesses the most important psychosocial problems and risk factors in breast cancer patients. In this way,

this screening instrument optimizes the care providers' conversation with patients regarding all psychosocial aspects and to give cut-off scores for referral to various levels of psychosocial care providers. Therefore, the project group consisted of experts in psychosocial care, i.e., social worker, psychologist, psychiatrist, oncology nurse, nurse practitioner, and a member of the psychosocial care department of the Comprehensive Cancer Centre South.

The purpose of the PDQ-BC is to detect patients that may need psychosocial care for their psychosocial problems, not only during the treatment phase but also during follow-up. The project group defined psychosocial problems as a composite of frequently reported psychological and social problems including specific issues that are known to effect patients' (HR)QOL, and risk factors that are associated with patients' psychosocial well-being for whom referral for extended psychosocial care by a psychosocial health-care provider would be helpful. The purpose of the measurement and the definition has guided our literature search and discussions with the experts and has determined which constructs of interest are relevant and should be measured. Some patients were asked to provide input on the first draft of the PDQ-BC. Besides the frequently reported psychological concerns (i.e., anxiety and depressive symptoms) and social problems the PDQ-BC will also contain specific issues that interfere with patients' well-being, such as (long-term) physical complaints, problems with body image, sexual problems and financial problems [10, 13, 28, 45]. Because patients with a lack of support [46] and patients who having high levels on trait anxiety are at risk for more psychological distress [23] and an impaired QOL [23] the project group decided to include these risk factors in the PDQ-BC because patients with high levels on trait anxiety may benefit from psychotherapy [47]. Some common physical problems (e.g., vomiting, hair loss, arm, disabilities, lymfoedema, postmenopausal problems) were not included because extended psychosocial care is not the appropriate intervention and, in addition, these (short-term) problems are treated by a physician and are well recognized. Other problems are less common, e.g., worries about hereditary of breast cancer [48] or infertility problems accounts. Therefore, these concerns were not included in the PDQ-BC. The conceptual framework is presented in Table 1.

Based on the literature [4-16, 21, 22, 49] and discussions in the project group 'Verwijs-Wijzer', the PDQ-BC consists of nine scales assessing psychological risk factors (i.e., Trait anxiety and (lack of) Social support) and State anxiety, Depressive symptoms, Social problems, Physical problems, Body image, Financial problems, and Sexual problems. Scores on the PDQ-BC are linked to a decision tree for referral to the various levels of psychosocial care provider.

The aim of this study was to develop a short, easy-to-use psychosocial screening instrument specific for early-stage breast cancer patients (PDQ-BC) and to examine the acceptability, preliminary reliability of the PDQ-BC. In addition, this study examined whether the referral advice based on the PDQ-BC to the various psychosocial care providers was justified. It was hypothesized that almost all the subscales of the PDQ-BC correlate significantly with each other. Exceptions will be the subscales Financial problems, Social support and Sexual problems because problems in these areas are

probably absent at baseline. These subscales focus on (HR)QOL issues that may interfere with patients' psychosocial well-being during treatment phase and follow-up. Moreover, it was expected that the subscales Trait anxiety, State anxiety, and Depressive symptoms have the highest correlations with each other due to the content overlap [50-52].

Methods

Patients

Before starting the pilot study 10 early-stage breast cancer patients were interviewed during their visit to the nurse practitioner to get more insight in patients' perspective of the concept psychosocial problems. These patients were also asked if they missed relevant important aspects or items on the PDQ-BC to measure the different constructs. In addition, they were asked to judge the adequacy of the response options.

The pilot study was done from December 2006 until December 2009 at the department of medical oncology of the St. Elisabeth Hospital (Tilburg, the Netherlands). All breast cancer patients at the outpatient clinic scheduled for adjuvant chemotherapy without a history of a psychiatric disorder were eligible for this study. Patients with a psychiatric disorder often already have coaching by a care provider for psychosocial problems. It was decided that this group was excluded from this study. One hundred and sixty-six women visited the nurse practitioner before chemotherapy was started. One woman was not eligible for participation in this study due to a known psychiatric disease and one patient was excluded because she found it too difficult to complete the questionnaire. Therefore, 164 women completed the PDQ-BC. This study was approved by the local ethics committee.

Questionnaire

The PDQ-BC consists of nine subscales assessed by 35 questions, of which 31 questions were selected from existing and valid questionnaires: Center of Epidemiologic Studies Depression Scale (CES-D) [53], World Health Organization Quality of Life assessment instrument (WHOQOL-100) [54], European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Breast (EORTC QLQ BR-23) [55], and the State Trait Anxiety Inventory (STAI) [19]. A distinction was made between trait anxiety (how one generally feels; personality factor), a psychological risk factor, and state anxiety (how one feels at the moment), a psychological problem. Therefore, we needed questions assessing trait anxiety and questions assessing state anxiety, thereby increasing the number of questions that assess anxiety. The selection of the items from the scale Trait anxiety (10 questions) can be found in the article by De Vries and Van Heck [56]. This study was conducted in a sample of breast cancer patients reflecting two factors: anxiety present and anxiety absent. The short Trait version makes it possible to study the relationship between trait anxiety as a risk factor and psychosocial problems. With regard to State anxiety (six questions), an existing and already shortened instrument was used (STAI short form). This reduction from 20 to six questions has been done and validated by others

[57, 58]. This shortened instrument has good psychometric properties. It is preferable to use validated scales; therefore, we made no changes to this existing short version.

The questions concerning Depressive symptoms (seven questions), were adapted from the CES-D. The CES-D consists of a 20-item self-report scale, assessing the presence and degree of depressive symptoms [53]. The reliability and criterion validity appear to be good for the (breast) cancer population [59]. The questions on Physical (four questions), Financial (one question), and Sexual problems (one question) are derived from the Dutch version of the WHOQOL-100 [54]. The questions on Body image (two questions) were adapted from the EORTC QLQ BR-23, a reliable and valid supplementary measure of the HRQOL in breast cancer patients [55]. The CESD, WHOQOL-100 and the EORTC QLQ BR-23 were used in a prospective follow-up study concerning the role of personality factors on QOL in breast cancer patients [21, 22, 60]. The database from this study was used to perform a factor analysis (exploratory factor analysis, principle axis factoring) on each questionnaire and selecting the items with the highest factor loading. For each scale in the PDQ-BC the items with a factor loading above 0.70 were used. The only question concerning Social support was judged important by the project group for referral to the social worker because social support has shown to be a risk factor for an impaired (HR)QOL [26]. This question was developed by the group and is a combination of two existing questions into social support from the WHOQOL-100. Because the two questions made a distinction between friends and family and we did not think that this distinction was important for screening, we made a more generic question, leaving out the specific referral to family and friends. Questions about Social problems were developed by the project group because no existing questionnaires assessed the specific aspects relevant for social work, i.e., work, family and social functioning. A question on Financial problems was added by the project group based on clinical experience of the social worker that problems in this area may interfere with other psychosocial problems. We have chosen to assess this issue with a question from the WHOQOL-100 that has shown to be a good question in psychometric terms. This question is also represented in the WHOQOL-BREF [61]. Clinical practice has shown that discussing sexuality was perceived not relevant soon after diagnosis and in this stage of adjuvant treatment. At this stage of treatment, patients sometimes get irritated when they have to complete more questions about sexuality. However, patients are willing to discuss sexual issues with health professionals. Therefore, again, we have chosen one generic sexuality question from the WHOQOL-100 to address the sexuality issue. Thus, the PDQ-BC consists of nine subscales assessed by 35 questions (see Table 1, page 31), with items addressing Trait anxiety (10 questions, e.g., 'I worry too much over something that really doesn't matter'), State anxiety (six questions, e.g., 'I feel calm'), Depressive symptoms (seven questions, e.g., 'I feel depressed'), Social problems (three questions, e.g., 'There are practical problems with regard to my family as a result of the disease and treatment'), Social support (one question, 'I receive enough support from people around me'), Physical problems (four questions, e.g., 'I am satisfied with the energy that I have'), Body image (two questions, e.g., 'I find it difficult to see myself naked'), Financial problems (one question, 'I worry about money'), and Sexual problems (one question, 'I have problems with my sexual life'). The questions from the various

existing measures were formulated differently. Some questions were formulated with 'I', and other with you; and other questions were statements. Questions were reformulated in order to get a uniform format. We have chosen to let all questions start with 'I', because when we asked patients, they found this a more pleasant way of posing the questions. We also wanted a uniform response scale for the entire PDQ-BC to make it easier to complete the measure. Therefore, the response options for all questions are now ranging from 1 (*not at all*) to 4 (*very much*).

In addition, the PDQ-BC measures a number of questions concerned socio-demographic (marital status, age, and age of children) and clinical factors (type of surgery, adjuvant treatment other than chemotherapy, and pre-treatment psychiatric morbidity). Socio-demographic factors and questions on the subscale Trait anxiety only have to be completed at baseline.

Procedure

All patients who were eligible for participation were asked by the nurse practitioner to answer the questions of the PDQ-BC at their own home. During the visit with the nurse practitioner the results of screening were discussed, the scores were calculated and accompanied by an advice regarding the need for psychosocial care. This advice was based on patients' scores that were compared with predetermined cut-off values. Possible outcomes of the instrument were as follows: no referral, referral to a medical social worker, referral to a psychologist, or referral to a psychiatrist. An advice concerning a referral for psychosocial counseling was discussed with the patient by the nurse practitioner. If needed and after approval by the patient, the patient was seen by one of the psychosocial care providers, depending on the advice that originated from the scores on the various parts of the screening instrument. In case patients were referred to a psychosocial care provider, this care provider was asked to indicate whether the referral was appropriate.

The cut-off scores for Trait anxiety, State anxiety, and Depressive symptoms were derived for the cut-off scores of the original, longer questionnaires. The cut-off scores for the remaining aspects (Social problems, Financial problems and Social support) were determined during discussions within the project group. In addition, the project group also decided which cut-off scores in combination with high levels on Trait anxiety let to a referral to psychology or social work. For instance, a score slightly above the cut-off value on State anxiety (or Depressive symptoms) results in an advice for referral to social work, whereas a combination of scores above the cut-off values for both Trait anxiety and State anxiety (or Depressive symptoms) resulted in an advice to visit a psychologist. When patients have extreme high scores on Trait anxiety or Depressive symptoms, they are referred to psychiatry. For the subscales Physical problems, Sexual problems and Body image cut-off scores were not determined because these issues are discussed with the nurse practitioner and are not used for referral. These referrals scores were subsequently tested with 10 patients to see whether these scores resulted in a correct referral.

There is no sum score for the PDQ-BC. Patients are referred for extended psychosocial care based on a combination of subscale scores of the PDQ-BC (see Table 2).

Table 1. Conceptual framework of psychosocial problems and the link with the Psychosocial Distress Questionnaire-Breast

Concept	Description	Questions
Trait anxiety	A relatively stable individual differences in anxiety proneness and a personality trait (i.e., differences in the strength of the disposition to respond to situations perceived as threatening with elevations of state anxiety (Spielberger, 1970).	I feel nervous and restless. I feel calm, cool and collected. I feel that difficulties are piling up so that I cannot overcome them. I worry too much over something that really doesn't matter. I am bothered by disturbing thoughts. I feel secure. I feel at ease. I have a steady mood. There are thoughts that bother me. I get in a state of tension or turmoil as I think over my recent concerns and interests.
State anxiety	A transitory psychobiological emotional state or condition that is characterized by subjective, consciously experienced thoughts and feelings relating to tension and apprehension, nervousness, and worry that vary in intensity and fluctuate over time (Spielberger, 1970).	I feel calm. I feel tense. I feel upset. I am relaxed. I feel content I am worried.
Depressive symptoms	Symptoms associated with persistent feeling of sadness and keep one from functioning well or from feeling good, which can lead to a variety of emotional physical and physical problems.	I was bothered by things that usually don't bother me. I felt that I could not shake off the blues even with the help from my friends or family. I had trouble keeping my mind on what I was doing. I feel depressed. I felt that everything I did was an effort. I felt fearful. I felt sad.
Body image	How one felt about their own body appearance.	I felt physically less attractive as a result of my disease or treatment. I find it difficult to see myself naked.
Financial problems	The level of stress about one's financial status.	I worry about money.
Sexual problems	The level of problems with one's sexual life.	I have problems with my sexual life.
Physical problems	The level of physical problems (fatigue, sleep, pain) that interfere with psychosocial well-being.	I am satisfied with the energy that I have. I have difficulties with sleeping. I have pain complaints. Pain prevents me from doing what I need to do.
Social support	The extent to which one feels supported by family, friends or other significant others in time of need.	I receive enough support from people around me.
Social problems	Limitations in ability to carry out activities in social role function (managing in the home, employment and recreation).	There are practical problems with regard to my family as a result of the disease and treatment. My medical condition and treatment have impaired my social functioning. Due to the disease and treatment there are problems with my employer.

Table 2. Referral system according the Psychosocial Distress Questionnaire-Breast Cancer

Medical social work	Psychology	Psychiatry
State anxiety between ≥14 and ≤15[1]	State anxiety score ≥16 and ≤23	24
Trait anxiety ≥21	Trait anxiety ≥21 and State anxiety ≥14[1] and or Depressive symptoms ≥13[2]	
Depressive symptoms ≥13 and ≤19[2]	Depressive symptoms ≥20 and ≤27	28
Financial problems ≥3		
Social support = 4 (reverse score)		
Social problems ≥9		

[1] At least 2 scores at 3 of 4 after (reverse) score; [2] At least 3 scores at 3 or 4 after (reverse) score

Statistical procedure

For each of the six scales of the PDQ-BC that consists of more than one item, an exploratory factor analysis (method PCA) was performed to examine whether each scale constitutes one factor. A confirmatory factor analysis (CFA) was conducted to test whether the a priori structure of the PDQ-BC is suited to a population with breast cancer patients [62]. The hypothesized model is presented in Figure 1. Goodness of fit was verified by the following fit indices: the Comparative Fit Index (CFI), the Non-Normed Fit Index (NNFI), and the Root Mean Square Error of Approximation (RMSEA). The models have a satisfactory to good fit when: CFI and NNFI is at least 0.90 and RMSEA is 0.06 or smaller [63]. Internal consistency was examined with Cronbach's alpha in the total population. Depending on the number of questions in a (sub)scale, Cronbach's alpha should be at least 0.70 in case of four items or more [64, 65]. Pearson's correlation coefficients for the relationships between the PDQ-BC subscales were calculated. Statistical Package for the Social Sciences (SPSS) 17.0 was used for all calculations, except for the CFA, these data were processed by AMOS [66].
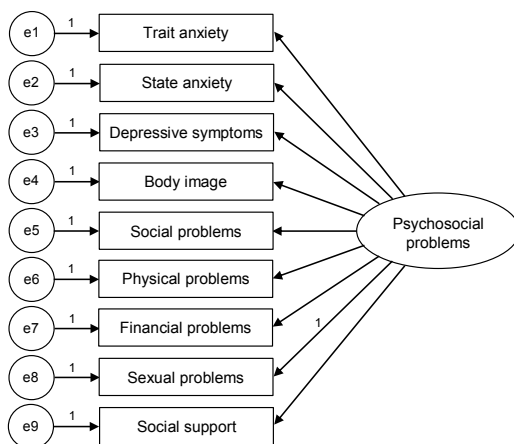
Figure 1. The hypothesized model

Results

Socio-demographic and clinical characteristics of the participants are shown in Table 3.

Table 3. Socio-demographic and clinical characteristics of the participants (*N*=164)

Characteristics	
Age	50.3 ± 8.9 (range 29-69)
Living with partner: (yes/no)	138 (84.1) / 26 (15.9)
Kids at home: (yes/no)	85 (51.8) / 79 (48.2)
Previously diagnosed with breast cancer: (yes/no)	6 (3.7) / 158 (96.3)
Previous psychosocial treatment: (yes/no)	33 (20.1) / 131 (79.9)
Type of surgery:	
Breast conserving therapy	47 (28.7)
Mastectomy	116 (70.7)
No surgical treatment (due to neo-adjuvant chemotherapy)	1 (0.6)
Axillary dissection: (yes/no)	113 (68.9) / 51 (31.1)

Mean ± standard deviation are presented for age, percentages are between brackets, except for age

Internal structure
Correlations between the subscales are shown in Table 4. All correlations were statistically significant, except the correlations of (i) Social support with Physical problems and Body image and (ii) Financial problems with Sexual problems and Social support. The subscales Trait anxiety, State anxiety, and Depressive symptoms have the highest correlations with each other (*r*'s between .70 and .80).

In general, the results of the principle components analyses supported the one factor structure of each scale. With the exception of the scale Trait anxiety, which had two factors (one method factor consisting of all recoded items), all scales showed to consist of one factor using the Eigenvalue >1 criterion, a criterion known to quickly overestimates the number of factors. The structure of the PDQ-BC was examined with confirmatory factor analysis. The model without allowing for any correlated error terms had a CFI of 0.87, a NNFI of 0.821 and a RMSEA of 0.116 (χ^2(27)=82.19) To reach a better fit, the model required two correlations of two error terms (Social problems with Financial problems; Social problems with Physical problems) to reach a CFI of 0.93 (χ^2(25)=54.3, *p*=.001; NNFI= 0.88; RMSEA=0.088). This fit further improved by adding another correlation between two error terms (Body image with Problems with sexual life) to reach a CFI of 0.95 (χ^2(24)=43.3, *p*=.009; NNFI=0.91; RMSEA=.073).

Reliability
The Cronbach's alphas of the subscales Trait anxiety, State anxiety, Depressive symptoms, Body image, Social problems, and Physical problems were 0.88, 0.85, 0.86, 0.79, 0.42, and 0.69, respectively.

Table 4. Correlations between the subscales of the PDQ-BC

	Trait anxiety	State anxiety	Depressive symptoms	Social problems	Physical problems	Body image	Social support	Financial problems
State anxiety	0.72							
Depressive symptoms	0.72	0.79						
Social problems	0.29	0.30	0.41					
Physical problems	0.42	0.45	0.49	0.41				
Body image	0.28	0.39	0.40	0.27	0.32			
Social support	-0.28	-0.20[a]	-0.16[a]	-0.20[a]	**-0.07**	**-0.04**		
Financial problems	0.20[a]	0.20[a]	0.21	0.34	0.28	0.24	**-0.08**	
Sexual problems	0.35	0.26	0.32	0.35	0.19[a]	0.30	-0.29	**0.14**

Correlations are significant at p<.01 (2-tailed tested), except for the [a] correlations (significant at $p<.05$; 2-tailed tested); numbers in bold are not significant correlated.

Referral

Figure 2 shows the percentage of patients receiving a referral advice. The scores of 77 patients (47%) indicated a referral for psychosocial counselling (i.e., 29 to medical social work and 48 to medical psychology). Of the latter group, five patients already had psychosocial therapy in a mental care setting outside the hospital. Twenty-nine patients (17.7%) agreed to be referred for social counselling, five to a medical social worker, 19 to a medical psychologist, and five to a professional outside the hospital. Two patients with a referral advice to medical psychology preferred medical social work. Two patients with a referral to a psychologist preferred medical social work. Also two patients with a referral for medical psychologist were referred to a psychiatrist before they had any contact with a psychologist. Thus, of all participants, 14.6% was actually referred for psychosocial counselling within the hospital. Forty-eight (29.3%) with an advice for referral did not want to be referred because they did not (yet) had experienced the need. Based on the discussions in the multidisciplinary meeting between health-care professionals, it was concluded that all referrals based on the PDQ-BC were correctly made.
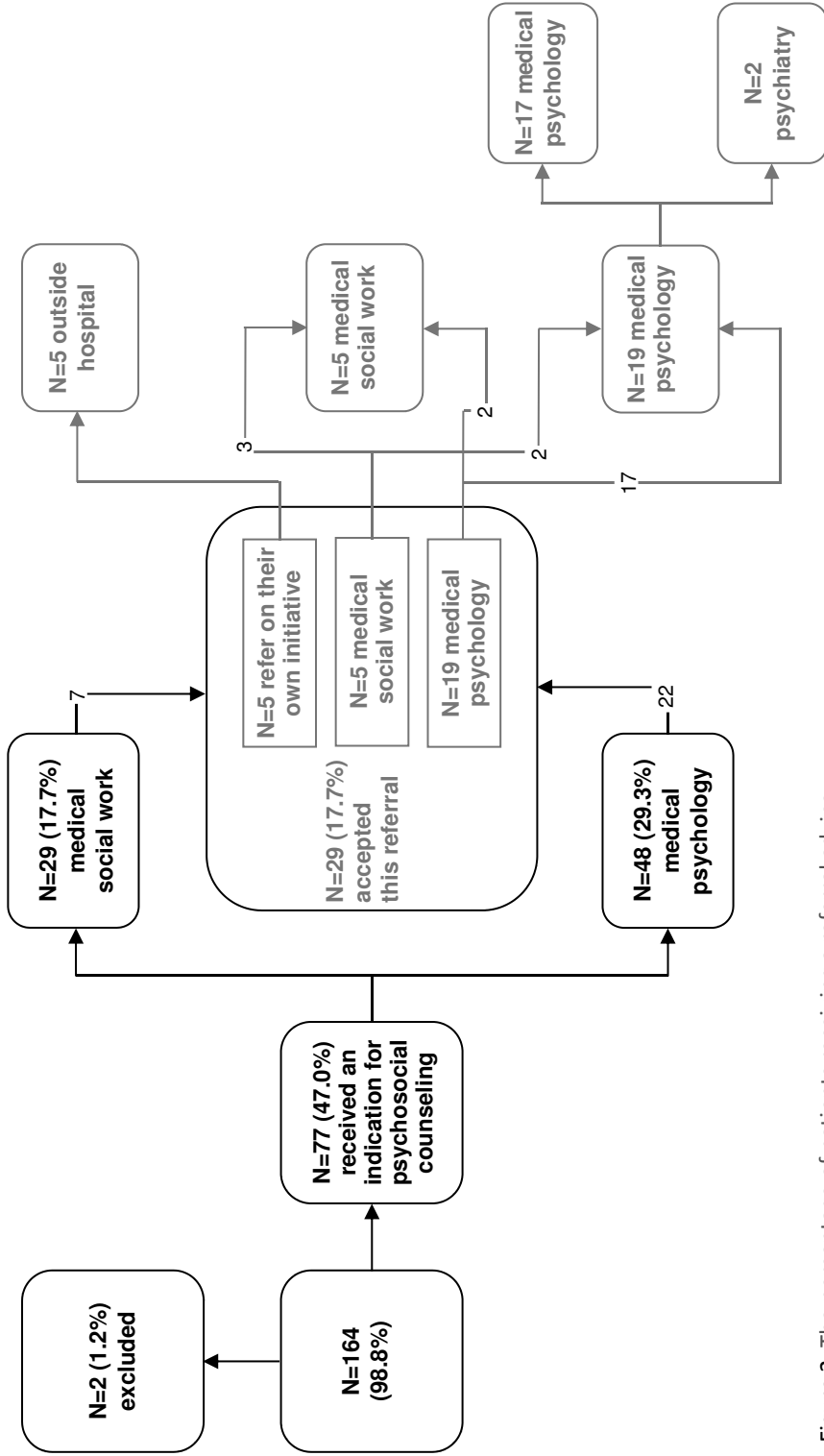
Figure 2. The percentage of patients receiving a referral advice, according to the Psychosocial Distress Questionnaire-Breast Cancer

Acceptability of the PDQ-BC

One hundred and sixty-four patients completed the PDQ-BC. Only one patient was unable to fill in the screening instrument due to limited mental capacities. On average, patients indicated that they needed 5 minutes range to complete the PDQ-BC. Patients indicated that the PDQ-BC was easy to complete and the questions were perceived as relevant. They did not find it burdensome to complete the instrument, but found it normal that these topics were discussed.

Discussion

The aim of this study was to develop a short, easy to use psychosocial screening instrument specific for breast cancer patients (PDQ-BC) and to examine the acceptability, and preliminary reliability of the PDQ-BC. In addition, this study examined whether the referral advice based on the PDQ-BC to the various psychosocial care providers was justified.

Apart from these primary goals, there are several benefits to develop a short and comprehensive, yet easy screening tool. First, about 10% to 50% of the women with breast cancer suffer from psychosocial problems [4, 14-16]. The recent national guidelines state that psychosocial care for cancer patients is obligatory and screening measures should be implemented as part of the regular care of cancer patients [37]. As such, patients with extended psychosocial problems can be identified and professional psychosocial support can be offered. Secondly, a brief questionnaire will be easy to incorporate into the regular care because it takes little time to complete and to score the results. Thus, a short screening tool can be completed several times during treatment and during the follow-up program without additional burden to patients and health professionals, making implementation more probable. Another screening instrument used in the Netherlands is the Distress Thermometer (DT). There are several differences between both measures. One difference is that the PDQ-BC is tailored for breast cancer patients, thereby not including problems that are irrelevant for patients, such as difficulty with speaking as a physical dysfunction. The cut-off scores of the PDQ-BC concern specific aspects. Thus, the PDQ-BC provides cut-off scores for all nine scales. Moreover, the PDQ-BC has a differentiated outcome measure and not dichotomous (yes/no) assesses the extent to which patients experience problems instead of a more undifferentiated yes/no response. Based on this information, the PDQ-BC results in a clear cut-off value for referral to the various specific psychosocial care providers.

Patients indicated that the PDQ-BC was easy to complete and the questions were perceived as relevant. They did not find it burdensome to complete the instrument. Only one patient was unable to complete the screening instrument due to limited mental capacities.

The nurse practitioner experienced that the PDQ-BC was a good tool to systematically discuss a range of relevant psychosocial problems. In this way, no problem areas were neglected and the nurse practitioner could spend attention solely on those

areas in which patients experienced problem(s), which makes the discussion of these problems more patient-tailored and, thus, more efficient. The instrument facilitates a greater awareness of the concerns and needs for breast cancer patients during treatment and regular follow-up. Based on this experience, our findings underline the acceptability and usefulness of the PDQ-BC in clinical practice.

The PDQ-BC appears to have a good internal consistency. The internal consistency of a scale is considered good when it is above 0.70 [64, 65]. Following this, the internal consistency of the most subscales was good. However, the subscale social problems had a much lower Cronbach's alpha. There are two probable reasons why the alpha of the scale Social problem is low. First, all scales with less than four questions will have an instable and often too low alpha. This is caused by the way an alpha is calculated. Second, the low alpha for Social problems may be caused by the fact that each item was designed to tap into a different aspect of social problems (i.e., practical problems concerning family, practical problems with regard to work, my medical situation/ treatment has impaired me in my social functioning) which makes a high alpha less likely. This provides a broad picture of patients' social problems. In addition, structural equation modelling showed that the structure of the PDQ-BC had a good fit.

As was hypothesized almost all PDQ-BC subscales were significantly correlated with each other. The subscales Trait anxiety, State anxiety and Depressive symptoms had the highest correlation coefficients. As was expected, Financial problems had a low correlation with Sexual problems and Social support correlated low with Body image, Financial problems and Physical problems.

Regarding the referral indications according the PDQ0-BC this study showed that 77 patients (47%) from the 164 patients have an indication for counselling, of whom 24 patients (31%) were actually referred. This prevalence of psychosocial problems was comparable to that reported in previous studies [4, 14-16]. In line with previous studies, we also found that not all patients with an increased level of these problems agreed to the suggested referral. This study showed similar rates of declination as compared to other studies [40, 67].

Five patients had a referral indication for medical social work, and 19 patients for psychology. Besides the care from the treating physician and nurse practitioner, most of the other patients refused referral except for five patients who preferred care from a social care provider outside the hospital. More patients were referred to a psychologist than a social worker. An explanation could be that the PDQ-BC assesses risk factors for psychosocial problems. That is, an increased level of Trait anxiety in combination with an increased level of State anxiety or Depressive symptoms on the PDQ-BC is an indication for referral to a medical psychologist. Patients high on trait anxiety have a tendency to respond with a rise in anxiety in stressful situations and are at risk of experiencing, for instance, more psychological distress [23, 25] and a low QOL [21, 22, 25]. These patients may benefit from psychotherapy [47]. According to the health professionals, patients were correctly referred to medical social work or medical psychology.

It is conceivable that during the phase of treatment the need for psychosocial support changes and as a result the rate of patients who seek referral. Therefore, it is

necessary to examine the referral information for psychosocial care across time. We do not yet have information on test-retest reliability. Future studies will need to focus on examining these features of the PDQ-BC as well as the sensitivity and specificity.

In conclusion, the PDQ-BC is developed with special attention to specific issues relevant for early-stage breast cancer patients. It seems to be a useful instrument for selecting and referring those breast cancer patients who experience psychosocial problems and also seek to be referred. Patients who refrain from psychosocial care are monitored. The PDQ-BC is an easy to complete questionnaire and its psychometric properties are promising.

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Chapter 3

THE PSYCHOSOCIAL DISTRESS QUESTIONNAIRE-BREAST CANCER (PDQ-BC) IS A USEFUL INSTRUMENT TO SCREEN PSYCHOSOCIAL PROBLEMS

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Abstract

Purpose
Recently, the Psychosocial Distress Questionnaire-Breast Cancer (PDQ-BC), a screening instrument specific for patients with early-stage breast cancer, was developed. The aim of this study was to examine the floor and ceiling effects, reliability and the construct validity of the PDQ-BC subscales Depressive symptoms, Social Support, Sexual Problems and Financial Problems.

Methods
Before patients (*N*=123) received adjuvant chemotherapy they completed the PDQ-BC, the Center for Epidemiologic Studies Depression Scale (CES-D) and the facets Social support, Sexual activity, and Financial resources of the World Health Organization Quality of Life assessment instrument (WHOQOL-100). Descriptive statistics were used to describe the floor and ceiling effects for the PDQ-BC subscales. Cronbach's alphas were used to provide information on the internal consistency of the PDQ-BC subscales. Pearson's correlation coefficients and item-total correlations were calculated between the PDQ-BC subscales. To evaluate the construct validity a priori stated hypotheses were tested using Pearson's correlation coefficients.

Results
Floor effects were present in the PDQ-BC subscales Social problems, Body image, Financial problems and Sexual problems, whereas ceiling effects were only found in the Social support subscale. The Cronbach's alpha coefficients of the subscales Trait anxiety, State anxiety, Depressive symptoms, Body image, and Physical problems ranged from 0.70 to 0.87. Social problems had a low consistency (0.39). Almost all PDQ-BC subscales were statistically significantly correlated with each other. Corrected item-total correlations confirmed the PDQ-BC structure. The PDQ-BC subscale Depressive symptoms correlated *r*= .80 (*p*<.01) with the CES-D. The PDQ-BC subscales Social support and Financial problems were correlated with the corresponding WHOQOL-100 facets Social support and Financial resources (*r*= .55 and *r*= -.68, *p*'s<.01, respectively). The PDQ-BC subscale Sexual problems had a moderate correlation with the related facet Sexual activity (WHOQOL-100; *r*= -.31; *p*<.01). Lower correlations were found between the PDQ-BC subscales and (scales of) questionnaires that were expected to be unrelated.

Conclusions
The PDQ-BC has expected floor and ceiling effects for particular subscales and sufficient internal consistency. Furthermore, the construct validity on the PDQ-BC subscales Depressive symptoms, Social support, and Financial problems was confirmed. However the hypothesis for the subscale Sexual problems could not be confirmed. This study indicates that the PDQ-BC subscales examined in this study can be used to screen for psychosocial problems in patients with early-stage breast cancer as part of routine care.

Keywords
Oncology, cancer, psychosocial problems, breast cancer, screening, psychometrics

Introduction

Every year more than 1.2 million patients are diagnosed with breast cancer [1]. In the Netherlands, one in every eight women will be diagnosed with breast cancer during her life [2, 3]. Multimodality treatment regimes improve survival outcome [4], but also contribute to a prolonged period of medical interventions with concurrent psychosocial problems (i.e., a combination of psychological and social problems) [5].

Apart from presence of physical disability caused by the side effects of treatment, Health Related Quality of Life (HRQOL) can be impaired [6] by the presence of anxiety, depression, body image problems, sexual problems, and financial problems. These psychosocial problems are experienced by 10% to 50% of patients with early-stage breast cancer shortly after diagnosis and medical treatment [7-10]. It is known that these problems are difficult to recognize, even though they are common. There are several reasons to explain why social problems often go unrecognized by oncology professionals. First, patients are often reluctant to inform their health-care providers about their suffering [7]. They often believe it is not a doctor's role to help with their emotional concerns [8]. Second, it is quite conceivable that anxiety and depression may mimic physical symptoms, whereby health-care providers tend to focus more on these physical symptoms of treatment [9]. It has become increasingly important to focus on and to recognize these different psychosocial problems in patients since early psychological intervention improves outcome [10-12]. This objective is increasingly seen as part of comprehensive oncological care [13], which is reflected in the Dutch guidelines [14, 15], and in the international guidelines to develop a screening program for psychosocial problems [10, 16]. Screening for psychosocial problems requires a reliable, valid questionnaire that identifies the variety and severity of these psychosocial problems specific for patients with early stage breast cancer. In general, cancer-specific distress questionnaires give a more precise insight into patients' experience. These instruments are more clinically relevant, because they more clearly pinpoint (psychosocial) treatment consequences [17, 18].

Recently, the multi-dimensional Psychosocial Distress Questionnaire-Breast Cancer (PDQ-BC) was developed [19]. The PDQ-BC differs from the other instruments in that it assesses psychological risk factors and a range of psychosocial problems and issues that are known to effect (HR)QOL specifically relevant in patients with early-stage breast cancer. In addition, it appears to be a useful instrument for selecting and referring those patients who experience psychosocial problems and request to be referred to the different kind of psychosocial care providers (e.g., medical psychologist, medical social worker, and psychiatrist).

Preliminary analyses have shown that the internal consistency was acceptable. Structural equation modeling showed that the structure of the PDQ-BC has a good fit [19].

The aim of the present study was to further examine the following psychometric properties of the PDQ-BC: floor and ceiling effects, reliability, and construct validity of the PDQ-BC subscales Social support, Sexual problems, Financial problems, and Depressive symptoms.

Methods

Participants

Patients with early-stage breast cancer who visited the outpatient clinics of the St. Elisabeth Hospital (Tilburg, the Netherlands) and the Elkerliek Hospital (Helmond, the Netherlands) between June 2008 and March 2010 were asked to participate in the present study. All patients gave written informed consent. The Elkerliek Hospital only included patients in 2009. Eligible patients needed to be able to read in Dutch. Patients with a psychiatric disorder were excluded because they often already have coaching by a care provider for psychosocial problems. Patients completed the PDQ-BC, Center for Epidemiologic Studies Depression Scale (CES-D), and the three selected facets of the World Health Organization Quality of Life assessment instrument (WHOQOL-100) before start of chemotherapy (St. Elisabeth Hospital). In the Elkerliek Hospital, patients completed the questionnaires before surgical treatment.

Three patients were excluded due to inability to speak Dutch, and two patients refused to participate because they felt too much emotional distress to take time to administer the questionnaire. This study was approved by the local ethics committees of both hospitals.

Instruments

The PDQ-BC is a multi-dimensional screening instrument, that consists of nine scales using 35 questions assessing psychological risk factors (i.e., Trait anxiety and (lack of) Social support) and State anxiety, Depressive symptoms, Social problems, Physical problems, Body image, Financial problems, and Sexual problems. All questions have a 4-point rating scale ranging from 1 (*not at all*) to 4 (*very much*). High subscale scores indicate more psychosocial problems, except for Social Support for which higher scores indicate fewer problems [19]. The subscales Social support, Financial problems, and Sexual problems each consist of one generic question. The questions in the subscales Social support and Financial problems provide the information needed to determine whether or not patients should be referred to a social worker. Moreover, the subscale Sexual problems only consists of one item because patients perceive discussing sexual problems during treatment as irrelevant and sometimes get irritated.

The CES-D is a 20-item self-report scale designed to measure the presence and degree of depressive symptoms. It has a 4-point response scale from 0 (*seldom or never*) to 3 (*(almost) always*). Scores can range from 0 to 60; scores ≥16 are indicative of depressive symptoms. The CES-D was established as a valid and reliable measure of depressive symptoms in patients with breast cancer [20, 21]. The CES-D was found to have good internal consistency, with Cronbach's alpha coefficients exceeding 0.85, as well as adequate test–retest reliability [20].

The WHOQOL-100 is a cross-culturally developed generic multi-dimensional questionnaire that consists of 100 items assessing 24 facets of QOL within four domains (Physical health, Psychological health, Social relationships, Environment) and a general evaluative facet (i.e., Overall QOL and General health) [22]. The response scales are 5-

point scales, and scores on each facet and domain can range from 4 to 20. A high score represents a good QOL, except for the facets Pain and discomfort, Negative feelings, and Dependence on medication and treatments, which are negatively framed. The time frame of reference is the previous two weeks. Reliability and validity are good [22-24], and sensitivity of the instrument is high [25]. In the present study, we only used the facets Social support, Sexual activity and Financial resources.

Socio-demographic variables
Patients were asked to answer a number of questions concerning socio-demographic factors (marital status, age, age of children) and clinical factors (type of surgery, adjuvant treatment, pre-treatment psychiatric morbidity).

Statistical procedure
Descriptive statistics (frequencies, means, standard deviations, ranges, and percentages) were generated to characterize the study population in terms of socio-demographic aspects.

Floor and ceiling effects of the PDQ-BC were defined as the percentage of participants who reported the lowest score (1) or highest score (4), respectively, on each of the nine subscales. Floor and ceiling effects were considered to be present if more than 15% of the patients had either the lowest possible score (floor effect) or the highest (ceiling effect) possible score on the PDQ-BC subscales [26]. When floor effects are present, this indicates that only a limited number of patients have these specific psychosocial problems at all. A ceiling effect is exactly the opposite. This information is important for two reasons. First, if (nearly) all patients obtain the lowest possible score (floor effect), the question does not discriminate between patients and is therefore a useless question that not provide information on the population. The same is true when (nearly) all patients endorse the highest possible score (ceiling effect). Second, floor and ceiling effects may indicate that the instrument may have limitations regarding detecting deterioration or improvement, respectively, over time in longitudinal assessment. Concerning floor effects it was hypothesized that for the subscale Social problems, Body image, Financial problems and Sexual problems in the phase of active treatment patients are less concerned about these issues. Moreover, the floor effect for Financial problems is expected due to the income protection insurance in the Netherlands.

A ceiling effect for the subscale Social support was expected because almost all patients receive a lot of support and attention between diagnosis and end of treatment.

To examine the relationships between the PDQ-BC subscales, corrected item-total correlations and Pearson's product-moment correlations were used. It was expected that almost all the subscales of the PDQ-BC correlate significantly with each other. However, exceptions will be for the subscales Financial problems, Social support and Sexual problems, because problems in this area are probably absent before start of chemotherapy. The questions on these subscales focus on frequently reported (HR)QOL issues [27-30] that may interfere with patients' psychosocial well-being during treatment phase and follow up and were added to the PDQ-BC based on the literature and clinical

experience of the project group. Moreover, it was expected that the subscales Trait anxiety, State anxiety, and Depressive symptoms have the highest correlations with each other due to the content overlap [31-33].

Internal consistency was examined using Cronbach's alpha coefficients. Cronbach's alpha coefficients should be at least 0.70 in case of four items or more [34, 35].

Construct validity is the degree in which a measurement is related to other constructs that are theoretically predicted to correlate with it [34]. In absence of a gold standard the hypotheses testing approach was chosen to evaluate the construct validity. A priori hypotheses were formulated based on the assumption that the correlations between the PDQ-BC subscales and similar questionnaires should be high ($r \geq .50$) whereas correlations between the PDQ-BC subscales with dissimilar questionnaires should be lower [36]. Cohen [37] also differentiates the lower correlations in moderate ($r= .30$ to $.49$) and small correlations ($r= .10$ to $.29$). Construct validity was tested using Pearson's product–moment correlation coefficients. The following eight hypotheses were formulated regarding the expected correlations between the PDQ-BC subscales Depressive symptoms, Social support, Sexual problems, and Financial problems, on the one hand, and the CES-D and the related facets of the WHOQOL-100, on the other hand:

1. The score on the PDQ-BC subscale Depressive symptoms correlates with the score on the CES-D with $r> .50$.
2. The scores on the PDQ-BC subscale Social support correlates with the score on Social support (WHOQOL-100) with $r> .50$.
3. The scores on the PDQ-BC subscale Sexual problems correlates with the score on Sexual activity (WHOQOL-100) with $r> .50$.
4. The scores on the PDQ-BC subscale Financial problems correlates with the score on Financial resources (WHOQOL-100) with $r> .50$.
5. The scores on the PDQ-BC subscale Trait anxiety correlates with the score on the CES-D with $r> .50$.
6. The scores on the PDQ-BC subscale State anxiety correlates with the score on the CES-D with $r> .50$.
7. The scores on the PDQ-BC subscales Social problems, Physical problems, Body image, Social support, Financial problems and Sexual problems correlate with the score on the CESD with $r< .50$.
8. R's of the PDQ-BC subscales Depressive symptoms – CES-D, Social Support – Social support (WHOQOL-100), Financial problems – Financial resources (WHOQOL-100) and Sexual problems – Sexual activity (WHOQOL-100) are higher compared with the correlations of the PDQ-BC subscales Depressive symptoms, Social support, Financial problems with dissimilar facets of the WHOQOL-100.

The Statistical Package for the Social Sciences (SPSS) 17.0 was used for all calculations.

Results

Socio-demographic and clinical characteristics of the participants are shown in Table 1. The total sample comprises of 123 patients with early-stage breast cancer. Most patients had already received surgical treatment.

Information on floor and ceiling effects as well as missing data is shown in Table 2. Floor effects were present in the subscales Financial problems and Social problems, Body image and Sexual problems. Only the subscale Social support had a ceiling effect. The highest percentage of missing data was only 1.6% for the subscale Depressive symptoms.

The internal relations between the PDQ-BC and the corrected item–total correlations are shown in Table 3. Almost all subscales of the PDQ-BC were significantly correlated with each other. There are a few exceptions. Sexual problems was not related to Social support and Social support was not related to Social problems, Physical problems and Body image. Moreover, Social problems was not related to State anxiety and Financial problems was not related to Trait anxiety, State anxiety, Depressive symptoms, Body image and Social support. The corrected item–total correlations showed that all scales were related with the total concept psychosocial problems.

Construct validity

Seven of the eight a priori stated hypotheses were confirmed. As expected, the PDQ-BC subscales Social support and Financial problems had high correlations with the similar facets of the WHOQOL-100 and the PDQ-BC subscale Depressive symptoms had a high correlation with the CES-D. In addition, the PDQ-BC subscale Depressive symptoms and the corrected CES-D score (i.e., minus the questions from the PDQ-BC) had a correlation of r= .77. The subscale Sexual problems (PDQ-BC) had a moderate correlation with the related facet Sexual activity (WHOQOL-100). Lower correlations were found between PDQ-BC subscales, and the unrelated aspects of the other questionnaires. For instance, low correlations were found between the PDQ-BC subscale Sexual problems and the WHOQOL-100 facet Financial resources. With the exception of the PDQ-BC subscales Trait anxiety and State anxiety that had a high correlation with the CES-D. Moderate correlations were found between the facet Social support (WHOQOL-100) and Financial problems (PDQ-BC) and between Physical problems (PDQ-BC) and the CES-D.

Internal consistency

Cronbach's alpha coefficients of the subscales Trait anxiety, State anxiety, Depressive symptoms, Body image, Social problems and Physical problems were 0.87, 0.85, 0.83, 0.75, 0.39 and 0.70, respectively.

Table 1. Socio-demographic and clinical characteristics of the participants (*N*=123)

Characteristics	
Age	50.8 ± 10.2 (range 29-73)
Living with partner: (yes/no)	107 (87.0) / 16 (13.0)
Children at home: (yes/no/missing)	56 (45.5) / 48 (39.0) / 19 (15.4)
Previously diagnosed with breast cancer: (yes/no)	3 (2.4) / 120 (97.6)
Previous psychosocial treatment: (yes/no/missing)	24 (19.5) / 94 (76.4) / 5 (4.1)
Type of surgery / planned surgery:	
Breast conserving therapy	30 (24.4) / 14 (11.4)
Mastectomy	68 (55.3) / 11 (8.9)
Axillary dissection: (yes/no)	70 (56.9) / 53 (43.1)

Mean ± standard deviation are presented for age, percentages are between brackets, except for age

Table 2. Floor and ceiling effects on the subscales of the PDQ-BC

	Min. score	Max. score	Mean	SD	Missing values (%)	Floor %	Ceiling %
Trait anxiety	10	35	19.72	5.34	0.0	1.6	0.8
State anxiety	6	22	12.72	3.44	0.0	2.4	0.8
Depressive symptoms	7	25	11.78	3.55	2 (1.6)	7.3	0.8
Social problems	3	10	4.75	1.75	1 (0.8)	29.5	0.8
Physical problems	4	15	7.68	2.46	1 (0.8)	6.5	1.6
Body image	2	8	3.10	1.37	1 (0.8)	45.5	0.8
Financial problems	1	4	1.41	0.72	1 (0.8)	69.9	2.4
Sexual problems	1	4	1.41	0.70	1 (0.8)	67.5	3.3
Social support	1	4	3.75	0.51	0.0	3.3	78.0

Min= minimum score; Max= maximum score; SD= standard deviation; Floor= floor effects; Ceiling= ceiling effects; PDQ-BC= Psychosocial Distress Questionnaire-Breast Cancer

Table 3. Correlations between the subscales of the PDQ-BC

	Trait anxiety	State anxiety	Depressive symptoms	Social problems	Physical problems	Body image	Social Support	Financial problems
State anxiety	0.75							
Depressive symptoms	0.74	0.76						
Social problems	0.21	**0.17**	0.28					
Physical problems	0.32	0.40	0.45	0.49				
Body image	0.22	0.27	0.28	0.32	0.38			
Social support	-0.26	-0.28	-0.17	**-0.10**	**-0.10**	**-0.01**		
Financial problems	**0.14**	**0.08**	**0.09**	0.42	0.20	**0.07**	-0.14	
Sexual problems	0.32	0.26	0.27	0.26	0.35	0.34	**-0.15**	0.23
Corrected Item-Total Correlation	0.70	0.76	0.79	0.36	0.51	0.37	-0.25	0.18

All correlations are significant at *p*<.05 (2-tailed tested), except the numbers in bold
PDQ-BC= Psychosocial Distress Questionnaire-Breast Cancer

Table 4. Pearson's correlation coefficients between the PDQ-BC and CES-D and Facets of the WHOQOL-100

	Facet 14 WHOQOL Social support	Facet 15 WHOQOL Sexual activity	Facet 18 WHOQOL Financial resources	CES-D
Trait anxiety	-0.18			0.72
State anxiety		-0.25		0.76
Depressive symptoms				**0.80**
Social problems	-0.22	-0.25	-0.30	0.25
Physical problems		-0.23		0.44
Body image		-0.22		0.28
Social support	**0.55**	0.28	0.33	-0.25
Financial problems	-0.38		**-0.68**	
Sexual problems	-0.18	**-0.31**	-0.18	0.24

All correlations are significant at *p*<.05 (2-tailed tested); Numbers in bold indicate the expected high correlations (*p*<.01). PDQ-BC= Psychosocial Distress Questionnaire-Breast Cancer; WHOQOL= World Health Organization Quality of Life assessment instrument; CES-D= Center for Epidemiologic Studies Depression Scale

Discussion

The PDQ-BC was developed in order to structurally assess psychosocial problems of patients with early-stage breast cancer during treatment and during follow-up, and to identify patients having psychosocial problems. This is necessary to be able to offer these patients special enhanced psychological care by psychosocial care providers to improve patients' (HR)QOL as quickly as possible. The PDQ-BC differs from the existing screening instruments because it is cancer-specific, and although it has a limited number of questions, it assesses the most important (risk factors of) psychosocial problems [19]. Moreover, it is linked to a referral system based on norm scores for referral to the various levels of psychosocial care providers, which is very useful in the daily clinical practice.

The objective of this study was to further examine the floor and ceiling effects, reliability, and the construct validity of the PDQ-BC. The PDQ-BC consists of nine subscales of psychosocial problems. In this study, the construct validity of four subscales (i.e., Social support, Sexual problems, Financial problems and Depressive symptoms) was examined. The other subscales, Physical problems, Body image and Social problems, have not yet been examined on the construct validity. This part was not performed in the present study because we did not want to increase patients' burden any further by completing more questions. The subscales Trait anxiety [38] and State anxiety [39] already have been validated in other studies. As a consequence, it will not be necessary to further examine the construct validity of these subscales.

As hypothesized we found floor effects for the subscales Social problems, Body image and Sexual problems and a ceiling effect for the subscale Social support. This indicates that these problems do not exist before the start of chemotherapy. However, several studies have shown that these problems are frequently reported during follow-up

[30, 40-44]. Therefore, it is important to include these aspects in the PDQ-BC, since this instrument is developed to examine psychosocial problems during treatment and follow-up and give the opportunity to look more detailed and at more points in time whether women have psychosocial problems. Furthermore, it is worth noting that the scales Financial problems, Sexual problems, and Social support are represented by a single item, which means that these scales have less variability in responses and, therefore, floor or ceiling effects are larger than in the other subscales.

   With regard to the relations between the subscales, we expected that almost all subscales were significantly correlated with each other. This is a confirmation of the good fit of the questionnaire structure found in our previous study using confirmatory factor analysis [19]. However, in line with our previous study [19] there were exceptions for the subscales Physical problems, Financial problems, Social support, Sexual problems and Body image. These subscales were added because these problems may interfere with patients' psychosocial well-being during treatment phase and in the follow-up [6, 41, 45, 46]. In this study, the PDQ-BC appears to have a good internal consistency, except for the subscale Social problems. These results were expected and consistent with the preliminary results from our previous study [19]. Probably reasons for this low coefficient are that this subscale has less than four questions and that each item of the subscale concerns a different aspect of social problems (work, family and social activities) to provide a broad picture of patients' social problems.

   According to Terwee et al. [34] 75% of the predefined hypotheses should be confirmed. In this study all a priori formulated hypotheses were confirmed (88%), except the hypothesis for the subscale Sexual problems. This subscale had a moderate correlation with the facet Sexual activity (WHOQOL-100) instead of the expected high correlation. In this study the construct validity could not be confirmed for the subscale Sexual problems. There may be several explanations for this finding. For instance, the fact that the subscale only has one item or that the subscale taps into different sexual problems or asks for intensity instead of frequency when compared with the WHOQOL-100 facet Sexual activity. Regardless of the reason for not finding the expected high association, the question concerns problems with sex. We know this from clinical experience. Therefore, one can use this subscale/question in daily practice to facilitate communication about Sexual problems. The usefulness of the subscale for research purposes is less evident.

   In accordance with expectations, the subscale Depressive symptoms had the highest correlation with the CES-D. This was also the case for the correlation when the overlap in items was removed. Moreover, Trait anxiety and State anxiety were highly correlated with the CES-D. The high correlations between the anxiety subscales and the subscale Depressive symptoms were in line with other studies due to concept and assessment overlap [31, 32, 33]. The subscale Physical problems had a moderate correlation with the CES-D, probably caused by content overlap, especially in fatigue [33]. In general, the PDQ-BC has a good divergent validity.

   We could not examine test-retest reliability because a stable period without stressful events (e.g., chemotherapy) is needed. Therefore, further study is needed to examine

these properties of the PDQ-BC. Moreover, the construct validity of the PDQ-BC subscales Physical problems, Body image and Social problems still needs to be examined.

In conclusion, the PDQ-BC has good psychometric properties for measuring depressive symptoms, social support, financial and sexual problems in patients with early-stage breast cancer. Screening these patients with the PDQ-BC will contribute to an appropriate management of psychosocial problems as an integral part of total care for women with breast cancer. The PDQ-BC is a short, self-administered screening instrument that appears to be valid and reliable. Therefore, it can be used to screen psychosocial problems in patients with early-stage breast cancer as part of routine care [19] to prevent psychosocial problems by timely detection and offering help when needed during treatment and follow-up, finally to try to facilitate patients to improve (HR)QOL.

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Chapter 4

RELIABILITY AND VALIDITY OF THE PSYCHOSOCIAL DISTRESS QUESTIONNAIRE-BREAST CANCER (PDQ-BC)

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Abstract

Purpose

The aim of this study was to evaluate the test-retest reliability, construct validity, and sensitivity and specificity of the Psychosocial Distress Questionnaire-Breast Cancer (PDQ-BC) and to compare its referrals with the Distress Thermometer (DT).

Methods

This study was conducted in two groups of patients with early-stage breast cancer scheduled for adjuvant chemotherapy in St. Elisabeth Hospital (Tilburg, the Netherlands). Group 1 (*N*=54) consisted of a stable group of breast cancer patients who had completed their treatment at least three years ago. In March 2011 they completed the PDQ-BC twice within one week interval to examine the test-retest reliability using the intra class correlation coefficients (ICC).

The construct validity of the PDQ-BC subscales Body image, Physical problems, Social problems, and Depressive symptoms was tested in group 2 (*N*=80). Before the start of adjuvant chemotherapy patients completed the PDQ-BC, and as comparator measurements the Hospital Anxiety Depression Scale (HADS-D) and the Distress Thermometer accompanied by the Problem List (DT-PL) between January 2010 and September 2011. Some of these patients (*N*=55) also completed the related facets of the World Health Organization Quality of Life assessment instrument (WHOQOL-100). Pearson's correlation coefficients were calculated to examine the construct validity.

Sensitivity and specificity values of the PDQ-BC subscales State anxiety and Depressive symptoms were calculated based on the HADS-A and HADS-D criteria (threshold ≥8) for identifying positive cases. A Chi-square test was performed in which the number of referrals according to the PDQ-BC and the DT was compared.

Results

The ICC ranged from 0.79 to 0.95. The PDQ-BC subscale Body image correlated *r*= .50 (*p*<.01) with the facet Body Image and Appearance (WHOQOL-100), Social problems (PDQ-BC) correlated *r*= .54 with the Practical domain (DT-PL; *p*<.01). The PDQ-BC subscale Physical problems correlated *r*≥ -.48 (*p*<.01) with the related facets of the domain Physical health (WHQOL-100) and correlated *r*= .72 (*p*<.01) with the domain Physical (DT-PL). The PDQ-BC subscale Depressive symptoms had a moderate correlation with the HADS-D (*r*= .47; *p*<.01). Lower correlations were found between the PDQ-BC subscales and questionnaires that were expected to be unrelated. The PDQ-BC subscale Body image correlated *r*= -.03 with the facet Energy and Fatigue (WHOQOL-100), *r*= -.02 with the facet Sleep and Rest (WHOQOL-100), and *r*= .16 with the facet Pain and Discomfort (WHOQOL-100). The PDQ-BC subscales Physical problems and Social problems correlated *r*= -.27 and *r*= -.07, respectively, with the WHOQOL-100 facet Body Image and Appearance. The subscales State anxiety and Depressive symptoms (PDQ-BC) had a sensitivity of 87.5% and 78.6%, respectively, and a specificity of 81.1% and 73.0%, respectively, compared to the

HADS. Less patients had a referral advice according to the PDQ-BC (N=36; 46.8%) compared with the DT (N=47; 61.1%) (χ^2(1)=14.1, p<.001).

Conclusions

The PDQ-BC shows good construct validity and test-retest reliability. The construct validity of the PDQ-BC subscales Social problems, Physical problems, Body image, and Depressive symptoms was confirmed. However, the subscale Physical problems had a slightly lower correlation with the facet Energy and fatigue (WHOQOL-100) than hypothesized. The PDQ-BC has a satisfactory sensitivity and specificity of the subscales State Anxiety and Depressive symptoms.

Keywords

Oncology, cancer, psychosocial, breast cancer, screening, psychosocial problems

Introduction

Studies in early-stage breast cancer have shown that 10% to 50% of patients experience psychosocial problems during treatment and in the follow-up [1-5]. These psychosocial problems include anxiety [6], depressive symptoms [7], impairments in sexual functioning [6, 8], body image [9-11], physical functioning [12, 13], social issues [14], and financial problems [15]. Even though these problems are quite common, they remain difficult to recognize [2]. Patients are often reluctant to inform their health-care providers about their suffering [3] and they believe it is not a doctor's role to help with their emotional concerns [2]. Moreover, patients normalize their feelings and in addition it is quite conceivable that anxiety and depression may mimic physical symptoms, whereby health-care providers tend to focus more on these physical symptoms of treatment [16].

In a meta-analysis Osborn et al. [17] reported that recognizing anxiety and depressive symptoms is essential, as cognitive behavioral therapy has been shown to reduce depressive symptoms and anxiety and improve quality of life (QOL). Associated with this finding, several organizations, such as the National Health Council [18] and the National Comprehensive Cancer Network [4] strongly advocate that patients who are in need of a psychosocial intervention should be identified early on. This implies that screening should be implemented in the health-care process [4].

Conceptual basis of the scale

Although different psychosocial screening instruments exist [19, 20], these instruments are all generic and not cancer type–specific. For instance, the Hospital Anxiety Depression Scale (HADS), a frequently used psychosocial screening instrument, only assesses anxiety and depression [21]. Problems that often occur in breast cancer patients such as body image, a lack of support, social problems, and sexual problems are not assessed. In contrast, the Distress Thermometer (DT) and the accompanying Problem List (PL), another frequently used screening instrument in the Netherlands, assesses psychosocial problems and a wide range of physical problems, including problems that are irrelevant for breast cancer patients, such as difficulty with speaking. In general physical problems become less relevant during the follow-up, because breast cancer patients often recover from the physical complaints within a year after treatment, except for fatigue [22, 23]. Thus, a specific psychosocial questionnaire is recommended because it provides a more precise insight into patients' experience during treatment and the follow-up [24]. In addition, it makes such a questionnaire more acceptable for patients to complete.

To assess psychosocial problems and risk factors specifically relevant for patients with early-stage breast cancer, a project group has developed the Psychosocial Distress Questionnaire-Breast Cancer (PDQ-BC) [25, 26]. Experts in psychosocial care, (social worker, psychologist, psychiatrist, oncology nurse, nurse practitioner, Comprehensive Cancer Centre South psychosocial care member) participate in this project group.

Description of the Psychosocial Distress Questionnaire-Breast Cancer

Based on a literature search by the project group and the experiences of ten patients (face validity) [25], the PDQ-BC consists of nine scales with 35 questions. There are two scales assessing psychological risk factors: Trait anxiety (10 questions) and (lack of) Social support (1 question); and seven scales assessing psychosocial consequences of diagnosis and treatment of early-stage breast cancer: State anxiety (6 questions), Depressive symptoms (7 questions), Social problems (3 questions), Physical problems (4 questions), Body image (2 questions), Financial problems (1 question), and Sexual problems (1 question). The response options for all questions range from 1 (*not at all*) to 4 (*very much*). Except for the personality characteristic Trait anxiety (assessing how one generally feels), the time frame of reference is the previous week. In addition to the PDQ-BC, the questionnaire set comprised items on socio-demographic (marital status, age, age of children) and clinical factors (type of surgery, adjuvant treatment other than chemotherapy, pre-treatment psychiatric morbidity). To refer patients to either a social worker, psychologist, or psychiatrist, a combination of the cut-off scores for each subscales has been established.

The internal consistencies of the PDQ-BC subscales ranged from 0.70 to 0.87. Social problems demonstrated a low consistency (.39 to .42) [25, 26]. Structural equation modelling, a way to test whether the scales can be perceived as separate scales despite the fact that they are correlated, was examined in a sample of 80 patients. It showed that the structure of the PDQ-BC had a good fit

(CFI=0.95 (χ^2(24)=43.3, *p*=0.009; NNFI=0.91; RMSEA=0.073) [25]. In a previous study the construct validity of the PDQ-BC subscales Social support, Sexual problems, Depressive symptoms, and Financial problems was confirmed [26]. The subscales Trait anxiety [27] and State anxiety [28] have been shortened and validated by others.

The present study focuses on (i) the test-retest reliability of the PDQ-BC (ii) the construct validity of the PDQ-BC subscales Body image, Physical problems, and Social problems and Depressive symptoms (iii) the sensitivity and specificity of the subscales State anxiety and Depressive symptoms (PDQ-BC) compared to the HADS-A (anxiety) and HADS-D (depressive symptoms) for identifying psychological problems and, (iv) the referral rate of the PDQ-BC to psychosocial health-care professionals compared with the referral rate of a generic measure (the Distress Thermometer (DT).

Methods

Samples
Two groups of women with early-stage breast cancer participated in this study. The first group (Group 1, *N*=64), was used to examine the test-retest reliability of the PDQ-BC and consisted of disease-free breast cancer patients who had completed their treatment with adjuvant chemotherapy between February 2007 and January 2009 at the St. Elisabeth Hospital (Tilburg, the Netherlands). In March 2011, this group of patients was sent a

package that included an information letter about the study, an informed consent form, a prepaid return envelope, and the PDQ-BC. The patients were instructed to return the completed package in one week's time. After one week the PDQ-BC and a pre-paid return envelope were again sent to the patients with the request to complete and return the questionnaire as soon as possible. The purpose of a second group (Group 2, *N*=90) was to evaluate the construct validity. This group consisted of women with early-stage breast cancer who visited the outpatient clinic of the St. Elisabeth Hospital (Tilburg, the Netherlands) between January 2010 and September 2011. They were asked to participate in this study prior to the start of their chemotherapy. All patients in Group 2 completed the PDQ-BC, the HADS and the DT, and the accompanying Problem List (PL). Some members of Group 2 (*N*=55) also participated in a multicenter, prospective longitudinal study related to objective and subjective cognitive functioning after cytostatic treatment and the effect on their QOL [29-31]. These 55 patients also completed several facets of the WHOQOL-100: Body Image, Energy and Fatigue, Sleep and Rest, and Pain and Discomfort that are used to examine construct validity.

All patients of both groups gave written informed consent. Eligible patients needed to be able to read and comprehend Dutch language. Patients with a psychiatric disorder were excluded because they had often already been counselled by a care provider for psychosocial problems or were referred to a psychiatrist because of a psychiatric disorder. This study was approved by the medical ethics committee of the St. Elisabeth Hospital.

Socio-demographic variables

All patients (Group 1 and 2) answered a number of questions concerning socio-demographic factors (age, living alone or with partner, age of children) and/or clinical factors (type of surgery, adjuvant treatment, pre-treatment psychiatric morbidity).

Measures

The flow chart of the questionnaires is presented in Figure 1. As comparable measurements to the PDQ-BC subscales the DT, the WHOQOL-100 and the HADS were completed.

The DT is a validated generic instrument for routine screening of distress in patients treated for cancer [32]. The response scale is a visual analogue scale (a thermometer) from 0 (*no distress*) to 10 (*extreme distress*). Respondents circle the number that best describes how distressed they have been in the past week. Furthermore, the DT can be accompanied by a 47-item Problem List (PL). This PL can be used to identify those factors responsible for the elevated DT score. This PL assesses five domains: Practical, Family/Social, Emotional, Spiritual, and Physical. Respondents indicate whether or not any of the items listed has been a problem in the past week. The internal consistency of the total scale is good, however, the Cronbach's alphas of the practical and spiritual domains were not acceptable [32]. A cut-off score ≥5 for the DT is indicative of significant levels of distress in patients [32].

The WHOQOL-100 is a cross-culturally developed generic multidimensional questionnaire that consists of 100 items assessing 24 facets of QOL within four domains

(Physical health, Psychological health, Social relationships, Environment) and a general evaluative component such as Overall QOL and General health [33-35]. The response scales are 5-point scales. Scores on each facet and domain can range from 4 to 20. A high score represents a good QOL, with the time frame of reference being the previous two weeks. Reliability and validity are good as evidence [33-35] and sensitivity to change of the instrument is high [36]. A change in score of 1 on the WHOQOL-100 is proposed as the minimal clinically important difference for women with early-stage breast cancer [37]. In the current study, we only used the facets Body Image and Appearance (4 items), Energy and Fatigue (4 items), Sleep and Rest (4 items), and Pain and Discomfort (4 items). These facets belong to the WHOQOL-100 domains Physical health and Psychological health.

The Hospital Anxiety and Depression Scale (HADS) is a generic questionnaire with 14-items measuring levels of anxiety (HADS-A, 7 items) and depression (HADS-D, 7 items). The response scale is a 4-point rating scale ranging from 0 (*not at all*) to 3 (*very much*). The time frame of reference is the previous week. The HADS has been validated in cancer patients and is widely used in the field of cancer [38]. Furthermore, it has been validated in several subgroups in the Netherlands [39]. Zigmond and Snaith [21] recommended for anxiety (HADS-A) and depression (HADS-D) a cut-off of ≥8 for possible cases. In a review of Bjelland et al. [38] the sensitivity and the specificity with a cut-off score of ≥8 for anxiety (HADS-A) and depressive symptoms (HADS-D) were in general within the range of 0.70 to 0.90.
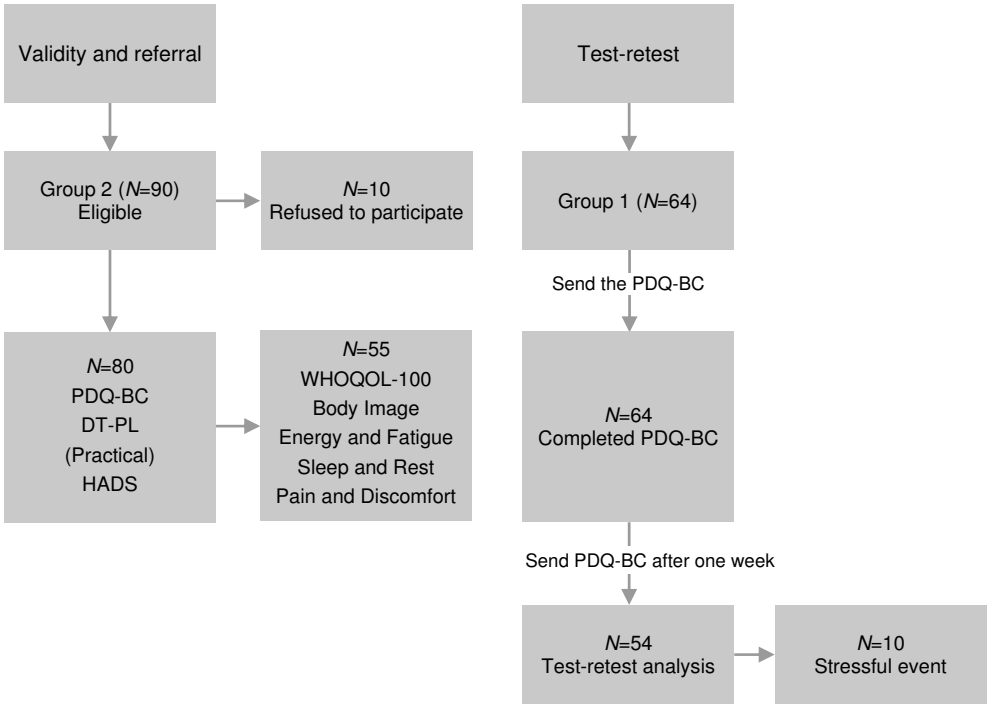

Figure 1. Flow chart questionnaires

Approaches to reliability and validity
Test-retest (Group 1, N=64)
To establish test-retest reliability (the consistency of the instrument measured on two occasions), it is necessary that no changes occurred between the two time points of assessments. Thus, the period between the two time points should be kept short. Therefore, we chose a time interval of one week. Moreover, patients should not experience any stressful events concerning their problems between the two time points which could influence the assessment. A stressful event was defined as any event that the patient considered stressful. Such an event could influence the answers of patients at the second time point. Patients were asked to answer the following question: ´Did you experience a stressful event during the last week?´ Patients who experienced stressful events could distort the consistency assessment and therefore, were deleted from the analyses. The test-retest reliability was examined by using the Intraclass Correlation Coefficient (ICC$_{consistency}$, two-way mixed model) [40, 41]. ICC above .70 is considered to be good [42].

Internal consistency (Group 1, N=54)
The internal consistency was examined using Cronbach's alpha coefficients. Cronbach's alpha coefficients should be at least .70 in case of four items or more [42, 43].

Construct validity (Group 2, N=80)
Construct validity is the degree in which a measurement is related to other constructs that are theoretically predicted to correlate with it [44]. The hypotheses testing approach was chosen to evaluate the construct validity of the PDQ-BC subscales in absence of a gold standard [45]. A priori hypotheses were formulated based on the assumption that the correlations between the PDQ-BC subscales and similar questionnaires should be high ($r \geq .50$) whereas correlations between the PDQ-BC subscales with dissimilar questionnaires should be lower. Cohen [40] also differentiates the lower correlations in moderate ($r = .30$ to .49) and small correlations ($r = .10$ to .29). Construct validity was tested using Pearson's product–moment correlation coefficients. The following six hypotheses were a priori formulated regarding the expected correlations between the subscales (i) Body image (PDQ-BC) and the facet Body Image and Appearance (WHOQOL-100) (ii) Physical problems (PDQ-BC) and the domain Physical (DT-PL) and the facets Energy and Fatigue, Sleep and Rest, Pain and Discomfort (WHOQOL-100) (iii) Social problems (PDQ-BC) and the domain Practical (DT-PL) and, (iv) Depressive symptoms (PDQ-BC) and the HADS-D:

1. The score on the subscale Body image (PDQ-BC) correlates strong with the score on the facet Body Image and Appearance (WHOQOL-100) with $r > .50$.
2. The scores on the subscale Physical problems (PDQ-BC) correlates strong with the scores on the Physical domain (DT-PL) and the scores on the facets Energy and Fatigue, Sleep and Rest and Pain and Discomfort (WHOQOL-100) with $r > .50$.

3. The score on the subscale Social problems (PDQ-BC) correlates with the score on the domain Practical (DT-PL) with $r > .50$.
4. The score on the subscale Depressive symptoms (PDQ-BC) correlates moderate with the score on the HADS-D with $r < .50$ because the questions on the subscale Depressive symptoms (PDQ-BC) were adapted from the CES-D. The CES-D focuses on depressed affect [46] while the emphasis in the HADS-D is more on anhedonia [47]. Therefore, a moderate and not a high correlation is expected.
5. The scores on the subscale Social problems and Physical problems (PDQ-BC) correlate low with the facet Body Image and Appearance (WHOQOL-100) with $r < .29$.
6. The score on the subscale and Body image (PDQ-BC) correlates low with the facets Energy and Fatigue, Sleep and Rest, Pain and Discomfort (WHOQOL-100) with $r < .29$.

Sensitivity and specificity (Group 2, N=80)
Sensitivity refers to the proportion of patients with anxiety and or depressive symptoms identified by the HADS-A (≥ 8) and HADS-D (≥ 8) that are correctly identified as cases by the PDQ-BC subscales State anxiety (≥ 14) and Depressive symptoms (≥ 13). Specificity refers to the proportion of patients without psychological problems as identified by these subscales on the PDQ-BC that correctly identified as patients without anxiety and depressive symptoms [48, 49].

The sensitivity was calculated by the number of true positives divided by the number of true positives plus the number of false negatives. The specificity was calculated by the number of true negatives divided by the number of true negatives plus the number of false positives [48, 49].

Referral (Group 2, N=80)
A Chi-square test was used to examine the relationship between patients who scored ≥ 5 on the DT (i.e., presence of elevated distress) and the referral advice of the PDQ-BC before start of chemotherapy (Time-1).

The Statistical Package for the Social Sciences (SPSS) 19.0 was used for all calculations [50].

Results

Participants
All patients met the inclusion criteria (Group 1 and Group 2). As shown in Figure 1, in Group 1 (*N*=64) no patients refused to participate. They were asked to complete the PDQ-BC within one week interval. Of these patients 10 patients reported a stressful event in this week, excluding them for the test-retest analyses resulting in a group of 54 assessable patients. In Group 2 (*N*=90) 10 patients refused to participate because they felt it would cause them too much emotional distress to take time to complete the questionnaire resulting in a group of 80 assessable patients. The clinical characteristics of Group 1 (*N*=54) and Group 2 (*N*=80) are presented in Table 1.

Table 1. Baseline socio-demographic and clinical characteristics of the participants

Characteristics	Group 1 (*N*=54)	Group 2 (*N*=80)
Age	51.4 ± 8.0 (34-68)	51.3 ± 8.6 (29-71)
Living with partner: (yes/no)	39 (72.2) / 15 (27.8)	69 (86.3) / 11 (13.8)
Children at home: (yes/no)	17 (31.5) / 36 (66.7)	16 (20.0) / 64 (80.0)
Previously diagnosed with breast cancer: (yes/no)	2 (3.6)	0 (0.0)
Previous psychosocial treatment: (yes/no)	15 (27.8) / 39 (72.2)	23 (28.8) / 55 (68.8)
Type of surgery:		
Breast conserving therapy	16 (29.6)	40 (50.0)
Mastectomy	38 (70.4)	40 (50.0)
No surgical treatment (due to neo-adjuvant chemotherapy)	0 (0.0)	1 (1.3)

Mean ± standard deviation are presented for age, percentages are between brackets, except for age

Reliability assessments

Internal consistency (Group 1, N=54)
Cronbach's alpha coefficients (see Table 2) ranged from 0.91 (State anxiety) to 0.97 (Financial problems, Social support).

Test-retest reliability (Group 1, N=54)
Patients returned the questionnaires within 9.8 ± 5.9 days. In total, ten patients reported a personal or work stressor in the period between the two assessment times. Therefore, they were excluded from the test-retest reliability analyses. The response rate was 100% because patients were reminded by the nurse practitioner by telephone call. Overall, the values of the ICC of the selected items ranged from .83 (State anxiety) to .94 (Financial problems; see Table 2).

Table 2. Test-retest reliability and internal consistency for the PDQ-BC (Group 1, *N*=54)

Subscales of the PDQ-BC	ICC	95% CI	Cronbach's alpha
State anxiety	0.83	0.72-0.90	0.91
Depressive symptoms	0.86	0.77-0.92	0.93
Social problems	0.90	0.83-0.94	0.95
Physical problems	0.91	0.85-0.95	0.95
Body image	0.85	0.75-0.91	0.92
Financial problems	0.94	0.89-0.96	0.97
Sexual problems	0.93	0.88-0.96	0.96
Social support	0.94	0.89-0.96	0.97

PDQ-BC= Psychosocial Distress Questionnaire-Breast cancer; CI= Confidence Interval; ICC= Single Measure Intraclass Correlation Coefficient

Validity assessments

Construct validity (Group 2, N=80)
Table 3 shows that five out of the six predefined hypotheses about the correlations were confirmed. The correlation between the PDQ-BC subscale Physical problems and the facet Energy and Fatigue (WHOQOL-100) had a slightly lower correlation than hypothesized.

Table 3. Pearson's correlation coefficients between the PDQ-BC and related constructs

| | **PDQ-BC** | | | |
	Social problems **(N=80)**	**Physical problems** **(N=55)**	**Body image** **(N=55)**	**Depressive symptoms** **(N=80)**
DT Problem List				
Practical	0.54[a]	0.51[a]	0.59[a]	0.36[a]
Social and family	0.44[a]	0.45[a]	0.55[a]	0.43[a]
Emotional	0.54[a]	0.60[a]	0.53[a]	0.74[a]
Religious spiritual	0.32[a]	0.40[a]	0.48[a]	0.46[a]
Physical	0.56[a]	0.72[a]	0.57[a]	0.63[a]
WHOQOL-100				
Energy and Fatigue	-0.30[b]	-0.48[a]	-0.03	-0.28[b]
Sleep and Rest	-0.19	-0.51[a]	-0.02	-0.47[a]
Body Image and Appearance	-0.07	-0.27	-0.50[a]	-0.14
Pain and Discomfort	0.21	0.52[a]	0.16	0.46[a]
HADS-D	0.37[a]	0.44[a]	0.42[a]	0.47[a]

[a] Correlations are significant at $p<.01$ (2-tailed tested); [b] Correlations are significant at $p<.05$ (2-tailed tested); PDQ-BC= Psychosocial Distress Questionnaire-Breast Cancer; DT Problem List= Distress Thermometer Problem List; WHOQOL-100= the World Health Organization Quality of Life instrument; HADS-D= the Hospital Anxiety and Depression Scale-Depression scale

Sensitivity and specificity (Group 2, N=80)
Taking the HADS-A and HADS-D (threshold ≥8) as a criterion for identifying anxiety and depressive symptoms, the PDQ-BC subscale State anxiety and the PDQ-BC subscale Depressive symptoms adequately detected anxiety and depressive symptoms, with a sensitivity of 87.5% and 78.6% and a specificity of 81.1% and 73.0%, respectively. The ROC curve predicting Depressive symptoms (PDQ-BC) according to the HADS-D (≥8) showed an area under the curve of 0.80 (standard error, 0.07; 95% confidence interval, 0.65-0.94; $p<.001$). For the PDQ-BC subscale State anxiety and HADS-A the ROC curve showed an area under the curve of 0.89 (standard error, 0.05; 95% confidence interval, 0.80-0.98; $p<.001$). Decreasing or increasing the cut-off score of the PDQ-BC subscale Depressive symptoms with one point results in a sensitivity of 85.7%-50.0% and a specificity of 68%-84.1%, respectively. Decreasing or increasing the cut-off score of the PDQ-BC subscale

State anxiety with one point results in sensitivity of 85.7%-77.4%, and a specificity of 79.2%-88.7%, respectively. The PDQ-BC subscale State anxiety (≥14) provided a positive predicted value (PPV) of 68% and a negative predicted value (NPV) of 93%. The PDQ-BC subscale Depressive symptoms (≥13) provided a PPV of 39% and a NPV of 94%.

Referral (Group 2, N=80)
Three patients had a score on the PL but did not complete the DT thermometer. Therefore, the comparison between the PDQ-BC and the DT concerning referral consisted of 77 patients (*N*=77).

Figure 2 compares the referral advice of the PDQ-BC against the DT. When comparing patients who scored ≥5 on the DT with the referral advice of the PDQ-BC, it appeared that, although the referral of 40.3% of the patients was consistent between both measures, in general the referral was significantly different ($\chi^2(1)$= 14.1, *p*<.001). According to the PDQ-BC, the scores of 36 patients (46.8%) indicated a referral for psychosocial counseling, while 47 patients (61.1%) had a referral advice according the DT. Five patients (13.9%) with a referral advice on the PDQ-BC, agreed to be referred for counseling and two patients (5.6%) had already psychosocial care outside the clinic at Time-1. Twenty-nine patients (80.6 %) with an advice (PDQ-BC) for referral, did not want to be referred for counseling at that moment. Although they recognized their problems, they wanted to try to resolve them on their own. Of these 29 patients, eight patients (27.6%) asked for a referral within a year after treatment with chemotherapy. Moreover, five patients (6.5%) had a referral advice according the PDQ-BC while the DT did not suggested referral. Of these five patients, three patients (0.6%) have been referred because of their psychosocial problems after they completed the chemotherapy treatment. In addition, 16 patients (20.8%) had a referral based on the DT, while the PDQ-BC suggested that referral was not needed. Of these 16 patients, three patients (18.8%) were referred to health-care professionals a few weeks later during the chemotherapy treatment period. Two patients were treated by a psychologist, one patient because of acute psychological decompensation, the other patient experienced a divorce during her cancer the treatment. In addition, one patient contacted with a social worker, since she was fatigued and had to raise a son with Attention Deficit Hyperactivity Disorder (ADHD). Thus, 16 of all 80 patients (20.8%) were actually referred for psychosocial counselling within the hospital.
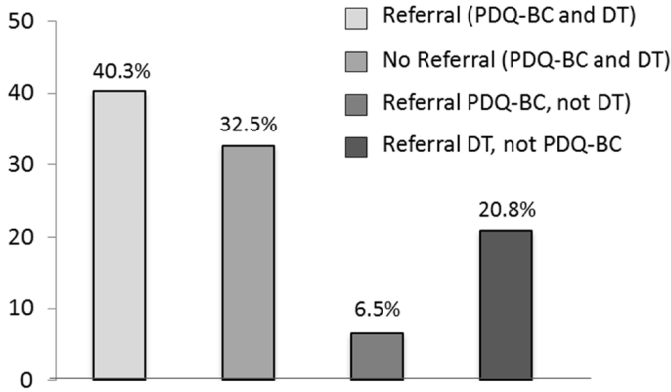
Figure 2. Referral advice according to the PDQ-BC and DT (*N*=77); PDQ-BC= Psychosocial Distress Questionnaire-Breast Cancer; DT= Distress Thermometer

Discussion

Screening for distress is recommended to identify those patients who are in need for psychosocial help [4, 18]. Several studies demonstrated that increased distress is reflected in a poor HRQOL [14, 51, 52]. Early intervention may be lifesaving since a depressive mood is associated with poor compliance with chemotherapy [53, 54].

The 35-item PDQ-BC is a short, self-administered screening instrument specifically for patients with early-stage breast cancer that can be easily used to screen psychosocial problems as part of routine care [25, 26]. Moreover, the PDQ-BC assesses all aspects relevant for early-breast cancer patients in nine subscales assessing psychological risk factors (2 subscales) and a wide range of psychosocial problems (7 subscales). In addition the PDQ-BC has a referral system based on norm scores for referral to the various levels of psychosocial care such as social worker, psychologist, and psychiatrist [25, 26].

A screening instrument to reveal psychosocial problems is important since several meta-analyses have demonstrated the efficacy of psychosocial counselling in reducing distress [55-57]. In addition, Carlson et al. [58] demonstrated that psychosocial interventions can reduce health-care costs in breast cancer patients. Thus, psychosocial counselling may also have an economic benefit.

In line with previous studies, the PDQ-BC showed to have a good internal consistency in women with breast cancer who are treated with adjuvant chemotherapy. Overall, the test-retest reliability was very good for all the subscales of the PDQ-BC. According to Terwee et al. [43] 75% of the predefined hypotheses should be confirmed. In this study five out of six predefined hypotheses are confirmed (83%). In accordance with our expectations the subscale Depressive symptoms (PDQ-BC) had a moderate correlation with the HADS-D. Furthermore, the construct validity of the PDQ-BC subscales Body image, Social problems, Physical problems, and Depressive symptoms, on the one hand, and the facets of the WHOQOL-100 and DT-PL, on the other hand, was confirmed except

for the relationship between the PDQ-BC subscale Physical problems with the WHOQOL-100 facet Energy and Fatigue that had a slightly lower correlation (difference 0.48 versus 0.51) than hypothesized.

The ability of an instrument to powerfully select only those patients with high levels of psychosocial problems (sensitivity) and not refer patients without psychosocial problems (specificity) is important because the aim is to offer help when needed and prevent the needless use of generally scarce psychosocial care. Because no gold standard exists to calculate the sensitivity and specificity of the PDQ-BC, it was decided to investigate the sensitivity and specificity of the subscales Depressive symptoms and State anxiety (PDQ-BC). For these subscales, the HADS-A and HADS-D was used as a criterion because of their wide-spread use and the long-term experience with these tests to assess depression and anxiety in cancer patients. Results showed a high accuracy for identifying patients with anxiety (87.5%) and depressive symptoms (78.6%) as well as to rule out patients without these conditions (specificity, 81.1% and 73.0%, respectively).

In this study, 46.8% of the patients had a referral advice according to the PDQ-BC. This percentage is in accordance with percentages found in existing studies on psychosocial problems [32, 59]. The referral advice according the DT was 61.1%. This difference in percentage of referral between both instruments may be due to the fact that the problem list of the DT also incorporates physical complaints (vomiting, nausea, and diarrhea) that are solely caused by treatment toxicity and are not associated with psychosocial problems. The fact that these physical complaints are part of the PL may trigger patients to weigh these complaints in the DT score.

In our study, a few weeks after completion of the screening instruments there were three patients that needed to be referred by the nurse to a social worker/psychologist. It turned out that these patients had a high score on the DT but not on the PDQ-BC. These three patients had severe and acute psychosocial problems. Because these patients regularly visit a nurse at multiple points during chemotherapy treatment, the acute problems were recognized by the nurse. Therefore, it is expected that these visits also have a monitoring role and these visits complement the screening instrument in identifying psychosocial problems in between.

Our population only consisted of Caucasian early-stage breast cancer patients. In order for the findings to be more generalizable, a larger study with a diverse population should be conducted.

In conclusion, this study showed that the PDQ-BC has good test-retest reliability and a satisfactory construct validity for the subscales Body image, Social problems, Physical problems, and Depressive symptoms. This is in line with the already known good internal consistency and construct validity of the other subscales [25, 26]. Moreover, the PDQ-BC has a satisfactory sensitivity and specificity for the subscales State anxiety and Depressive symptoms. The PDQ-BC can be regarded as a useful instrument for selecting and referring those patients with breast cancer who experience psychosocial problems. Moreover, this questionnaire facilitates the communication about patients' concerns and potential needs for early-stage breast cancer patients´ care during treatment with chemotherapy and the follow-up.

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Part B

SHORT- AND LONG-TERM PSYCHOLOGICAL
PROBLEMS AND ITS PREDICTORS

Chapter 5

PREDICTORS AND THE COURSE OF STATE ANXIETY AND DEPRESSIVE SYMPTOMS IN BREAST CANCER PATIENTS WITH ADJUVANT CHEMOTHERAPY TREATMENT: A ONE-YEAR LONGITUDINAL STUDY

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Abstract

Purpose
To examine the course and predictors of State anxiety and Depressive symptoms in women with early-stage breast cancer up to one year after chemotherapy.

Methods
Patients (*N*=182) completed the Psychosocial Distress Questionnaire- Breast Cancer (PDQ-BC) before the start of adjuvant chemotherapy, three weeks, three months, and one year after completion of chemotherapy. Linear mixed-effects models with a specified covariance pattern model were used to examine the course and predictors of State anxiety and Depressive symptoms.

Results
Overall, State anxiety and Depressive symptoms declined over time (*p*<.001). Concerning State anxiety and Depressive symptoms patients with high Trait anxiety scores showed a larger decline over time than patients with low scores on Trait anxiety, while patients without a partner did not show this decline. Moreover, patients with more Physical problems (between-subjects) had more Depressive symptoms over time compared to patients with less Physical problems. Concerning State anxiety main effects were found for Physical problems (within- and between subjects), Social support (within- and between subjects), and radiotherapy. Concerning depressive symptoms main effects for Depressive symptoms were found for hormonal therapy, radiotherapy, and Social support (within subjects), and Physical problems (within subjects).

Conclusions
The levels of State anxiety and Depressive symptoms declined over time. Patients without a partner, having more Physical problems, high scores on Trait anxiety, a lack of support and radiotherapy are at risk for higher levels of State anxiety and depressive symptoms. Hormonal therapy is a risk factor for higher levels of depressive symptoms.

Keywords
Oncology, cancer, breast cancer, anxiety, depressive symptoms

Purpose

Being diagnosed with breast cancer may cause psychological distress, i.e., anxiety and/or depressive symptoms [1-4]. The prevalence rates in these studies differ substantially due to the study design (i.e., descriptive, one-point data), treatment (lumpectomy versus mastectomy, chemotherapy, and/or radiotherapy). Therefore, the results of the different studies are often hard to compare because of the variety of divergent definitions and measures of the constructs. In spite of these discrepancies, the corresponding prevalence of anxiety and depressive symptoms is twice as high as in the general female population [1]. Twenty to 50% of the women with early stage breast cancer have anxiety or depressive symptoms or both at diagnosis during the first year after diagnosis. Burgess [1] showed that the prevalence of anxiety and depression was highest at time of diagnosis when 30% of the patients with early-stage breast cancer experienced anxiety and depressive symptoms. The prevalence declines to 15% one year after diagnosis [1]. Other studies also showed that anxiety and depressive symptoms improve over time [1, 3], however, fear of recurrence is still regularly present at long-term follow-up [5].

Several factors such as poor family relationship and functioning [6], maladaptive problem solving and conflict solving [6], and presence of pain, and fatigue [6] are associated with an increased risk for developing anxiety and depressive symptoms. Concerning anxiety, high scores on trait anxiety prior to diagnosis [7, 8] and patients with a younger age experience more anxiety at long-term follow-up [1, 9]. With regard to depressive symptoms, studies showed that patient factors, such as stressful life events [10], less optimism [10], sleep disturbance [10], ambivalence concerning the expression of negative emotions [10], poorer social functioning [10] as previous psychological treatment [1], a lack of support [1, 11], pain [3], fatigue [3], and trait anxiety [7, 12, 13] are more important than socio-demographic factors and clinical factors [1]. Pain [14], fatigue [15], and sleep disturbance [16] often co-occur with anxiety and depressive symptoms in symptom clusters [16-18]. Since it is clinically relevant to be able to determine which patients are at risk for developing anxiety and depressive symptoms during follow-up and to understand the course of psychological problems, this prospective study examined the course of anxiety and depressive symptoms in patients with breast cancer before the start of (neo-) adjuvant chemotherapy up to one year after chemotherapy. The second aim was to study the socio-demographic factors (partner status, age, children at home <12 year), the clinical factors (radiotherapy, hormonal therapy, type of surgery), and the patient factors (Trait anxiety, previous psychological treatment, Social support, Physical problems) to identify if these factors are predictors for State anxiety and/or Depressive symptoms before the start of adjuvant chemotherapy and during the year after chemotherapy.

Methods

Participants

All 197 patients with early stage breast cancer who visited the outpatient clinic of the department of medical oncology of the St. Elisabeth Hospital (Tilburg, the Netherlands) were asked to participate in the present study before start of (neo-)adjuvant chemotherapy. The patients consisted of two groups. The first group (*N*=17) completed the Psychosocial Distress Questionnaire-Breast Cancer (PDQ-BC) from June 2008 until January 2009 at three time points: before the start of (neo-)adjuvant chemotherapy (Time-1), three weeks (Time-2) and three months (Time-3) after chemotherapy. The second group (*N*=165) completed the PDQ-BC also one year after treatment (Time-4) from October 2008 until September 2012. All patients gave written informed consent. Eligible patients needed to be able to read in Dutch. In addition, patients with a psychiatric disorder were excluded. The medical ethics committees of the St. Elisabeth hospital approved this study.

Instruments

The PDQ-BC consists of nine scales with 35 questions assessing psychological risk factors (i.e., Trait anxiety and (lack of) Social support) and psychosocial problems (i.e., State anxiety, Depressive symptoms, Physical problems, Social problems, Body image, Financial problems, and Sexual problems). The response options for all questions range from 1 (*not at all*) to 4 (*very much*). The time frame of reference is the previous week, except for the personality characteristic Trait anxiety (i.e., assessing how one generally feels) is only assessed once, at Time-1. In addition, socio-demographic, clinical factors and patient factors are part of the PDQ-BC on a one page information sheet. The psychometric properties of the PDQ-BC are good [19, 20]. The subscales State anxiety [21] and Trait anxiety [22] were validated by others.

Statistical procedure

Descriptive statistics concerning socio-demographic, clinical, and personal are presented. Independent t-test and Chi-square tests were used to examine the potential differences on baseline socio-demographic and clinical variables for participants and non-participants, completers and persons with missing values on a time point (non-completers), and Group 1 and Group 2.

Linear mixed-effects models with a specified covariance pattern model were used to examine the course of State anxiety and Depressive symptoms [23]. The purpose of these models is identical to repeated measures (M)ANOVA and can be seen as a linear regression analysis that takes the correlational structure of the repeated measures into account [23]. However, an important difference is that in repeated measures (M)ANOVA subjects with any missing observation are omitted from the analysis whereas mixed-effects models uses all available time points of a person [23]. As such, mixed-effects models are more efficient and more robust concerning missing data [23]. Time was analyzed as a categorical predictor with four levels (cf. Time-1, Time-2, Time-3, and

Time-4). The fixed-effects parameters of the models were estimated with maximum likelihood. After inspecting the log likelihood ratio test, Akaike Information Criterion, and Bayesian Information Criterion with restricted maximum likelihood the compound symmetry error covariance matrix was found most appropriate.

Socio-demographic variables, clinical variables, and Trait anxiety were analyzed as time-invariant predictors. Social support and Physical problems were measured on each of the four time points and are analyzed as time-varying predictors [23, 24]. The effect of time-varying predictors was split into two effects: the between-subjects effects (e.g., the degree to which the individual's average Social support is related to their average Sate anxiety level) the within-subjects effects (e.g., the degree to which variation in an individual's support over time is associated with a change in their State anxiety scores).

The interactions of time with all predictors were tested in a model including all interactions. In order to correctly interpret all model parameters, all predictors (except time) have been grand-mean centered [23, 25]. For simplicity, the final models only contain significant interactions. To identify a parsimonious model, a backward selection method was used (p<.05). Q-Q plots of residuals were checked to test the assumption of normality for both final models. For significant interaction effects, post-hoc simple effects were performed. In secondary analyses linear mixed-effects models were rerun excluding patients with neo-adjuvant chemotherapy in order to examine the effect of neo-adjuvant treatment on the course of levels of State anxiety and Depressive symptoms. All analyses were performed in the Statistical Package for Social Sciences (SPSS) 19.0 using a significance level of α=.05.

Results

Group 1 consisted of 17 patients and all the patients were eligible and consented to participate. Of the 180 patients (Group 2), three patients were excluded due to inability to speak Dutch and 12 patients declined participation because they felt too much emotional distress to take time to complete the questionnaire. Thus, at baseline (Time-1), 182 women completed the PDQ-BC. Group 1 consisted of 17 patients and Group 2 of 165 patients. The socio-demographics and clinical factors of Group 1 and 2 are presented in Table 1. There were no differences in socio-demographic factors between Group 1 and Group 2, completers and non-completers as well as participants and non-participants. Table 2 shows the number of cases at each time point that participated in the study.

Table 1. Baseline socio-demographic and clinical characteristics of the participants

Characteristics	Group 1 (*N*=17)	Group 2 (*N*=165)	Total Group (*N*=182)
Age	51.06 ± 7.9 (40-65)	50.4 ± 9.2 (29-71)	50.6 ± 9.1 (29-71)
Living with partner: (yes/no)	14 (82.4) / 3 (17.6)	144 (86.37) / 22 (13.3)	157 (86.3) / 25 (13.7)
Children at home: (yes/no)	10 (58.8) / 7 (41.2)	61 (37.0) / 104 (63.0)	71 (39.0) / 111 (61.0)
Previous psychological treatment: (yes/no)	3 (17.6) / 14 (82.4)	40 (24.1) / 125 (75.8)	43 (23.6) / 139 (76.4)
Surgical treatment			
Breast conserving therapy	6 (35.3)	63 (38.2)	69 (37.9)
Mastectomy	11 (64.7)	102 (61.8)	113 (62.1)
Radiotherapy: (yes/no)	8 (47.1) / 9 (52.9)	82 (49.7) / 83 (50.3)	93 (51.1) / 89 (48.9)
Hormonal therapy: (yes/no)	11 (64.7) / 6 (35.3)	129 (72.1) / 46 (27.9)	130 (71.4) / 52 (28.6
Neo-adjuvant chemotherapy: (yes/no)	0 (0.0) / 17 (100.0)	6 (3.6) / 159 (96.4)	6 (3.3) / 176 (96.7)

Mean ± standard deviation are presented for age, percentages are between brackets, except for age

Table 2. Response patterns and the number of patients on each time point that participated in the study (total) and that were used in the analyses for State anxiety and Depressive symptoms

Number of patients who completed	T1	T2	T3	T4	Total	State Anxiety	Depressive symptoms
All four time points	x	x	x	x	98	91	87
The first three time points	x	x	x		41	35	38
Three time points except Time-3	x	x		x	5	7	7
Three time points except Time-2	x		x	x	7	8	9
The first two time points	x	x			11	12	13
Two time points except Time-2 and Time-4	x		x		4	4	3
Two time points except Time-2 and Time-3	x			x	2	2	4
Time-2 and Time-3		x	x		0	0	1
Time-1	x				14	14	12
Time-2		x			0	1	0
Total	182	155	150	112	182		
Total State anxiety	174	147	138	108		175	
Total Depressive symptoms	172	145	138	107			173

T1= before start chemotherapy; T2= three weeks after chemotherapy; T3= three months after chemotherapy; T4= one year after chemotherapy

Course and predictors of State anxiety

Overall, the estimated marginal means (EMM) for time showed that State anxiety at Time-1 was 12.6 and decreased 2 points to 10.9 at Time-2, then increased a little to 11.0 at Time-3, and finally showed a decrease of 0.6 points to an EMM of 10.4 at Time-4 (p<.001; see Figure 1).

The interaction effects of partner (p=.029) and Trait anxiety (p<.001) with time were significant (Table 3). Patients living without and with a partner had similar State anxiety scores on Time-1 (EMM of 12.3 and 12.6, respectively) and both had a similar decrease from Time-1 to Time-2 (EMM of 10.3 and 11.0, respectively; Figure 1a). From Time-2 to Time-4 patients without a partner showed an increasing trend whereas the patients with a partner showed a decreasing trend. At Time-4 the difference between patients without partner (EMM=11.5) and with partner (EMM=10.2) was largest but still not significant (p=.055, Table 3). Patients with higher scores on Trait anxiety had overall higher State anxiety levels compared to patients with a mean or low Trait anxiety score. This difference was largest on Time-1 and became smaller over time (Figure 1b). The effect of Trait anxiety with time was significant on all time points (p's<.001 for Time-1 to Time-3 and p=.001 for Time-4; see Table 3).

The main effects of radiotherapy and the between- and within-subjects effects of Social support and Physical problems were significant (see Table 3). More specifically, patients without radiotherapy scored on average 0.7 points lower (p=.022) on State anxiety than patients with radiotherapy. Patients that on average experienced less Social support had on average higher scores on State anxiety (between-subjects effect β= -.61, p=.029). Moreover, patients that showed change in Social support on a time point also showed change in State anxiety. That is, Social support is related to lower State anxiety (within-subjects effect β= -.60, p=.007). Patients that on average experienced more Physical problems had on average higher scores on State anxiety (between-subjects effect β= 0.56, p<.001). Furthermore, patients with more Physical problems than average on a time point became also more anxious (within-subjects effect β= .47, p<.001). Whether or not patients received neo-adjuvant treatment did not have effect on the course and levels of State anxiety.

Course and predictors of Depressive symptoms

Overall, EMM for time showed that the depressive symptoms at Time-1 was 11.9 and decreased to 11.6, 11.0, and 10.6 at Time-2, Time-3, to Time-4, respectively (p<.001; see Figure 2).

The interaction effects of partner (p=.025), Trait anxiety (p<.001), and Physical problems (between-subjects effect, p=.044) were significant (Table 3). Patients living without and with partner had similar Depressive symptoms scores on Time-1 (EMM of 11.7 and 11.9, respectively). From Time-1 to Time-4 patients without a partner showed an increasing trend whereas the patients with a partner showed a similar decreasing trend. Only at Time-4 the difference between patients without partner (EMM=12.3) and with partner (EMM=10.3) was significant (β= -2.08, p=.003). Patients with higher Trait anxiety had overall more Depressive symptoms on all time points. This difference was largest on

Time-1 (β= .34, *p*<.001) and became smaller across time (β= .15, *p*=.001 at Time-4; Figure 2b). Patients with on average more Physical problems (between-subjects effect) reported on average more depressive symptoms on all time points (all *p*'s<.001). This difference was smallest at Time-1 (β= .42) and largest on Time-2 (β= .77).

The main effects of radiotherapy, hormonal therapy, and the within-subjects effects of Social support and Physical problems were significant over time (see Table 3). Patients without radiotherapy or without hormonal therapy had fewer Depressive symptoms than patients with radiotherapy (β= .85, *p*=.005) or hormonal therapy (β= .84, *p*=.004). Patients that showed an increase in Social support compared to their own average Social support on a time point reported less Depressive symptoms (within-subjects effect β= -.52, *p*=.026). Change in Physical problems was associated with change in Depressive symptoms (within-subjects effect; β= .56, *p*<.001). Whether or not patient received neo-adjuvant treatment, did not have effect on the course and levels of Depressive symptoms.

Figure 1. Probing of the two interaction effects for State anxiety: a) interaction between time and partner; b) interaction between time and Trait anxiety
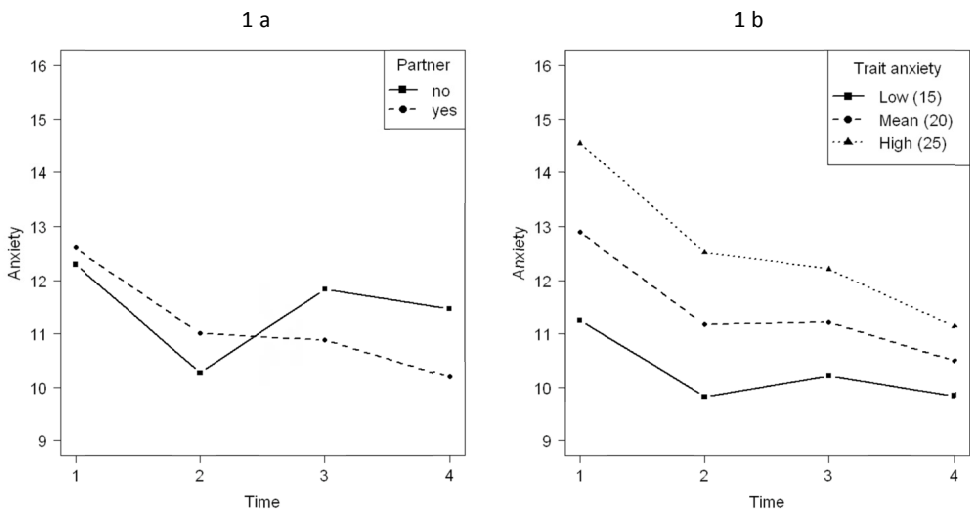
	Time-1	Time-2	Time-3	Time 4
Overall mean	12.6	10.9	11.0	10.4
Partner (no)	12.3	10.3	11.8	11.5
Partner (yes)	12.6	11.0	10.9	10.2
Trait anxiety (low = 15)	11.3	9.8	10.2	9.8
Trait anxiety (mean = 20)	12.9	11.2	11.2	10.5
Trait anxiety (high = 25)	14.6	12.5	12.2	11.1

Time-1= before start chemotherapy; Time-2= three weeks after chemotherapy; Time-3= three months after chemotherapy; Time-4= one year after chemotherapy

(a) (b) (c)
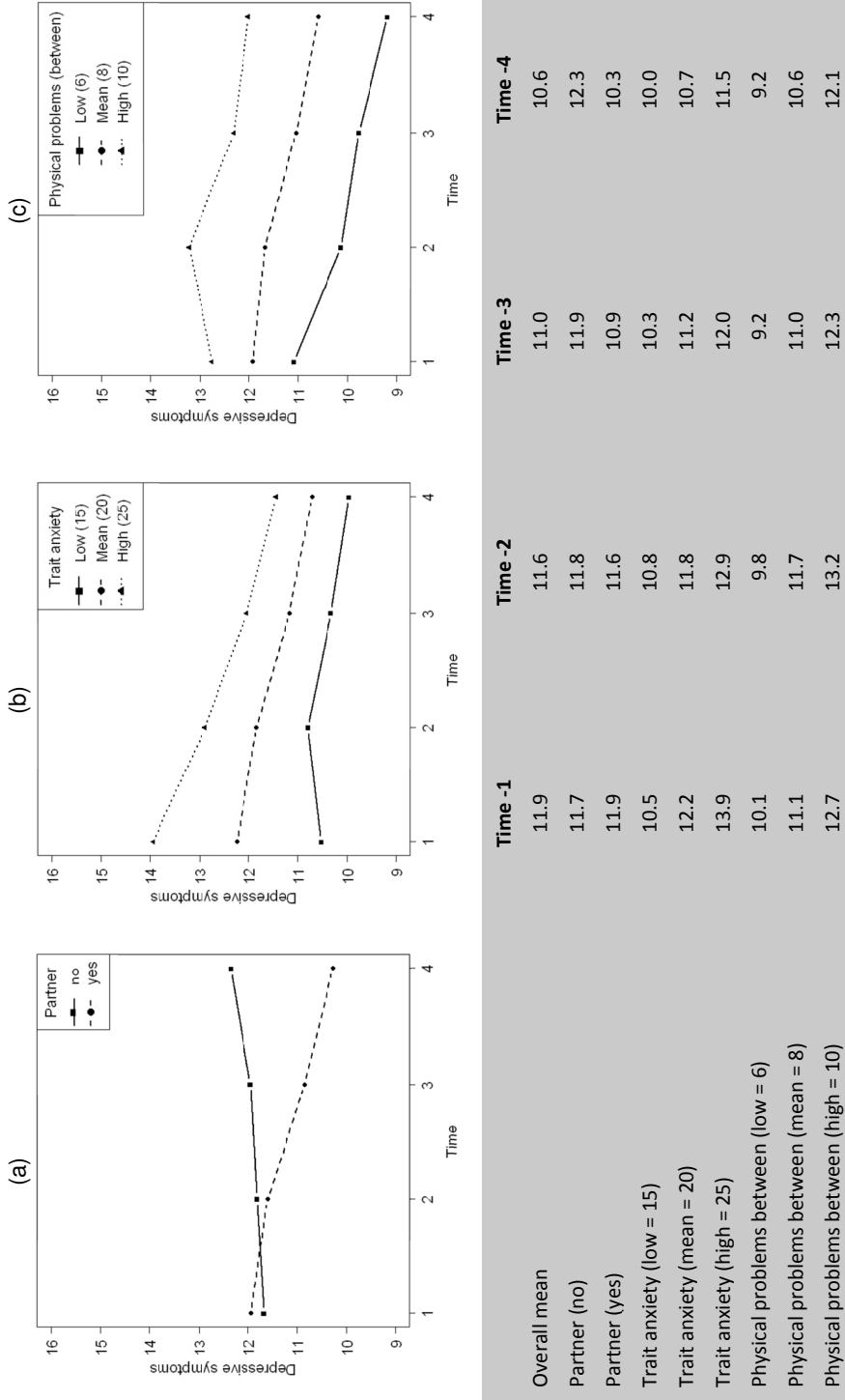
Figure 2. Probing of the three interaction effects for Depressive symptoms; a) interaction between time and partner; b) interaction between time and Trait anxiety; c) interaction between time and Physical problems between-subjects effects

	Time -1	Time -2	Time -3	Time -4
Overall mean	11.9	11.6	11.0	10.6
Partner (no)	11.7	11.8	11.9	12.3
Partner (yes)	11.9	11.6	10.9	10.3
Trait anxiety (low = 15)	10.5	10.8	10.3	10.0
Trait anxiety (mean = 20)	12.2	11.8	11.2	10.7
Trait anxiety (high = 25)	13.9	12.9	12.0	11.5
Physical problems between (low = 6)	10.1	9.8	9.2	9.2
Physical problems between (mean = 8)	11.1	11.7	11.0	10.6
Physical problems between (high = 10)	12.7	13.2	12.3	12.1

Table 3. Estimates of fixed effects for State anxiety and Depressive symptoms

Predictor[a]	State anxiety			95% Confidence Interval		Depressive symptoms			95% Confidence Interval	
	B	SE	Sig.	Lower Bound	Upper Bound	B	SE	Sig.	Lower Bound	Upper bound
Time[b]			**<.001**					**<.001**		
Time-1 (intercept)	12.57	0.19	**<.001**	12.21	12.94	11.89	0.19	**<.001**	11.52	12.27
Time-2 – Time-1	-1.67	0.24	**<.001**	-2.14	-1.19	-0.26	0.25	.299	-0.76	0.23
Time-3 – Time-1	-1.55	0.26	**<.001**	-2.06	-1.05	-0.89	0.26	**.001**	-1.41	-0.37
Time-4 – Time-1	-2.21	0.28	**<.001**	-2.77	-1.66	-1.34	0.29	**<.001**	-1.91	-0.76
Children at home	-0.17	0.30	.577	-0.76	0.42	-0.29	0.30	.335	-0.89	0.31
Radiotherapy	0.67	0.29	**.022**	0.10	1.25	0.85	0.30	**.005**	0.26	1.43
Hormonal therapy	0.42	0.28	.137	-0.13	0.97	0.84	0.28	**.004**	0.27	1.40
Previous psychosocial treatment	0.16	0.30	.592	-0.43	0.75	0.22	0.30	.476	-0.38	0.82
Type of surgery (Ref=BCT)	0.19	0.29	.528	-0.39	0.76	-0.06	0.30	.851	-0.65	0.54
Age	-0.01	0.02	.432	-0.04	0.02	-0.02	0.02	.345	-0.05	0.02
Social support: between	-0.61	0.28	**.029**	-1.16	-0.06	0.10	0.28	.718	-0.45	0.66
Social support: within	-0.60	0.22	**.007**	-1.04	-0.17	-0.52	0.23	**.026**	-0.98	-0.06
Physical problems: between	0.56	0.07	**<.001**	0.43	0.60					
Physical problems: within	0.47	0.06	**<.001**	0.35	0.60	0.56	0.07	**<.001**	0.43	0.69

REF= reference category; BCT=breast conserving therapy

Predictor[a]	State anxiety					Depressive symptoms				
				95% Confidence Interval					95% Confidence Interval	
	B	SE	Sig.	Lower Bound	Upper Bound	B	SE	Sig.	Lower Bound	Upper bound
Interaction effects										
Partner*Time[b]			**0.029**					**.025**		
Partner at Time-1	0.32	0.55	.564	-0.76	1.39	0.25	0.56	.652	-0.85	1.36
Partner at Time-2[c]	0.73	0.61	.227	-0.46	1.93	-0.20	0.64	.750	-1.45	1.05
Partner at Time-3[c]	-0.95	0.64	.137	-2.21	0.30	-1.09	0.68	.108	-2.43	0.24
Partner at Time-4[c]	-1.28	0.67	.055	-2.59	0.03	-2.08	0.69	**.003**	-3.43	-0.72
Trait anxiety*Time[b]			**<.001**					**<.001**		
Trait anxiety at Time-1	0.33	0.03	**<.001**	0.26	0.40	0.34	0.04	**<.001**	0.27	0.41
Trait anxiety at Time-2[c]	0.27	0.04	**<.001**	0.20	0.34	0.21	0.04	**<.001**	0.13	0.29
Trait anxiety at Time-3[c]	0.20	0.04	**<.001**	0.12	0.27	0.17	0.04	**<.001**	0.09	0.25
Trait anxiety at Time-4[c]	0.13	0.04	**.001**	0.05	0.21	0.15	0.04	**.001**	0.06	0.24
Physical problems between*Time[b]								**.044**		
PP-b at Time-1						0.42	0.10	**<.001**	0.22	0.61
PP-b at Time-2[c]						0.77	0.11	**<.001**	0.55	0.99
PP-b at Time-3[c]						0.63	0.11	**<.001**	0.41	0.85
PP-b at Time-4[c]						0.70	0.12	**<.001**	0.47	0.94

[a] All predictors (except Time) are grand-mean centered; [b] Analysis of Variance (ANOVA) type III test; [c] Post-hoc test of simple effects

Statistically significant results ($p < 0.05$) are shown in bold.

Ref = reference category, BCT = breast conserving therapy; PP-b=physical problems (between-subjects)

Discussion

The aims of this prospective study were to examine the course of State anxiety and Depressive symptoms in women with early stage breast cancer before the start of (neo)-adjuvant chemotherapy up to one year after chemotherapy. In addition, this study describes the socio-demographic, clinical, and patient factors as predictors of State anxiety and depressive symptoms.

Overall, the levels of State anxiety and Depressive symptoms decreased significantly over time, which is in line with previous studies in women with breast cancer [1].

Concerning the socio-demographic factors (partner status, age, children at home <12 years) patients without a partner are at risk for being or becoming more anxious over time. This finding is in line with the study of Tuinman et al. [26]. They showed that the relationship of younger and middle age patients is independently related to high distress [26]. Age and having children at home were not significantly related to anxiety and depressive symptoms. This is in contrast with previous studies which showed that younger age was associated with more anxiety [1, 9] and depressive symptoms [1, 27] in long-term follow up. Due to the study design (i.e., participants, instruments, time points in follow-up, definitions of younger patients) are these results difficult to compare with the current study and therefore no explanation could be found for these unexpected finding.

Regarding the clinical factors, patients treated with radiotherapy had higher scores on State anxiety and had more Depressive symptoms. This is in line with a review of Stiegelis et al. [28] that showed that cancer patients in general may experience anxiety and depressive symptoms prior, during and after radiotherapy. In our study, it has to be taken into account that radiotherapy started four weeks after ending chemotherapy (between Time-2 and Time-3) whereas the scores on State anxiety and Depressive symptoms already were high at Time-1, i.e., before the start of adjuvant chemotherapy (Time-1). Thus, patients with radiotherapy were already more anxious and had more depressive symptoms before radiotherapy started. Patients with hormonal therapy had already more Depressive symptoms, but did not have elevated levels of State anxiety. Although menopausal symptoms are positively associated with depressive symptoms [29], in this study hormonal therapy started after chemotherapy. Thus, at baseline patients were not yet menopausal induced by chemotherapy or hormonal therapy. The fact that patients scheduled for hormonal therapy had more depressive symptoms could indicate that they are already reluctant to start this kind of treatment. Physical problems were a predictor of State anxiety and Depressive symptoms over time. Patients who experienced more Physical problems had more Depressive symptoms and this difference was most pronounced at Time-2 to Time-4. At this time point patients suffered from many physical complaints that were caused by the chemotherapy. This is also the moment that the appointments with the doctor and nurse practitioner decrease. This possibly added a focus on physical problems that resulted in feelings of uncertainty and feeling alone. Concerning patient factors, patients with higher scores on Trait anxiety have higher levels on State anxiety and Depressive symptoms across time compared to patients with a mean or low level on Trait anxiety. This is in accordance with previous studies that found that

patients with cancer and high scores on Trait anxiety are more anxious [7, 8] and report more depressive symptoms [7, 12]. The reason that the largest difference was found at Time-1 may be patients' uncertainty about the side effects of chemotherapy. Therefore, these patients with high scores on Trait anxiety have to be identified early in time and offered psychosocial counselling. In contrast with previous studies [1, 10], previous psychological treatment did not predict State anxiety and Depressive symptoms over time. It may be that patients had received psychosocial counselling for other reasons than anxiety or depressive symptoms. However, we did not record this information. The finding that patients with a lack of Social support are more anxious and have more depressive symptoms is in line with the study of Burgess et al. [1]. They showed that a lack of intimate confiding relationship was associated with anxiety and depressive symptoms. Studies on depressive symptoms among breast cancer patients showed that depressive symptoms were associated with poor social support [2, 30].

This study has some strengths and limitations. A limitation of this study is that our population consisted of Dutch native early stage breast cancer patients. In order to generalize our findings to other ethnicities and different stages of breast cancer a study with a more diverse study population should be conducted. This study did not examine the psychological state of patients in the transition phase from active treatment to picking up their lives .There is a need for research on psychosocial wellbeing among breast cancer patients in the six and nine months follow-up. Moreover, studies have to be conducted to develop an appropriate psychosocial care plan for patients at risk for psychological problems.

Several strengths of this study should be acknowledged. First, in this prospective longitudinal study the data were analyzed with linear mixed models which is a more sophisticated statistical method because of the advantage of dealing with missing data. As such, there was less drop-out although patients did not complete the questionnaire at all four time points. Second, this study identifies longitudinal predictors not only predictors assessed at baseline, i.e., before start of chemotherapy.

In conclusion, highest levels of State anxiety and Depressive symptoms were registered before start of chemotherapy and declined in the first year after chemotherapy. In addition, this study showed that patients without a partner, radiotherapy, having high scores on Trait anxiety, experience more Physical problems and a lack of Social support are at risk for State anxiety and Depressive symptoms. Moreover, patients with hormonal therapy are at risk for depressive symptoms. This kind of information is useful for health-care providers, since it helps them to identify patients who are at risk for high scores of State anxiety and Depressive symptoms as well as helping them and offer them special attention to their complaints.

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Chapter 6

PREDICTORS OF QUALITY OF LIFE IN PATIENTS WITH EARLY-STAGE BREAST CANCER TREATED WITH CHEMOTHERAPY: A PILOT STUDY OF THE RELATIONSHIP BETWEEN PSYCHOSOCIAL SCREENING AND QUALITY OF LIFE

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Abstract

Purpose
The aim of this pilot study was to examine the relationship between a psychosocial screening instrument and the quality of life (QOL) of early-stage breast cancer patients treated with adjuvant chemotherapy. Another aim was to examine the QOL before the start of adjuvant chemotherapy (Time-1) and three months after finishing chemotherapy (Time-2) and to compare these scores to a healthy norm population.

Methods
Patients completed the Psychosocial Distress Questionnaire-Breast Cancer (PDQ-BC) and the World Health Organization Quality of Life assessment instrument (WHOQOL-100) before start and three months after chemotherapy. Multiple linear regression analyses identified PDQ-BC factors that predicted patients' QOL. One sample t-tests were used to compare the patients' QOL scores with the norm population.

Results
Patients with more Physical problems, Depressive symptoms, having problems with their Body image and patients' factors (i.e., younger patients, having no partner) predicted lower scores on different QOL domains at Time-2. Compared to the norm scores, the study group had significantly lower scores on the General QOL facet (p=.019; Time-1). Moreover, significantly lower scores were found on the domain Physical health at both time points (p<.001) and higher scores on the domain Social relationships at Time-1 (p<.001) and Time-2 (p<.002).

Conclusions
Psychosocial screening provides information about patients who are at risk for an impaired QOL shortly after finishing chemotherapy. Before the start and shortly after the end of chemotherapy the experience of patients' QOL is lower on Physical health and higher on Social relationships compared to the normal population.

Keywords
Breast cancer, predictors, psychosocial problems, quality of life, chemotherapy

Introduction

Worldwide the incidence of breast cancer is increasing [1] and it has become the most common malignancy in women in the Netherlands [2]. The advancements in adjuvant treatment have contributed to an increasing number of women who live with the long-term side effects of treatment [3]. Most patients with early-stage breast cancer undergo surgical treatment and/or radiotherapy, taxane-based chemotherapy, hormonal therapy and sometimes treatment with monoclonal anti-bodies (trastuzumab) [4]. Studies have shown that these treatment modalities are associated with a prolonged period of medical interventions with concurrent psychosocial problems [5-8]. These psychosocial problems are experienced by 10 to 53% of the breast cancer patients shortly after diagnosis and adjuvant chemotherapy [6, 7]. However, the prevalence of these psychosocial problems is depending on the method, measures and time point of assessment [9, 10].

Studies showed that the HRQOL (i.e., evaluation of well-being in the physical, psychological, and social domains) of breast cancer patients who remained disease-free is comparable to healthy women [11-13] except for patients with adjuvant chemotherapy they reported persistent physical problems one year after treatment [11]. In addition, patients described worsened physical functioning and poorer sexual functioning many years after ending chemotherapy [14].

Nowadays, screening for psychosocial problems is recommended by several organizations [15, 16] to prevent problems from escalating and psychosocial interventions has been suggested to improve patients HRQOL [15, 17, 18]. However, Mitchell [19] concluded in his recent review that the effect of psychosocial screening on HRQOL is controversial. In this review, the effect of psychosocial screening on HRQOL was examined in seven randomized controlled trials (RCTs) in which patients with different types of cancer and disease stages were examined including breast cancer patients [20-26]. In the study of Velikova et al. [20], patients in the intervention (with feedback) and attention-control (screening alone) group showed a better HRQOL compared to the control group (no screening). Furthermore, the use of HRQOL data (feedback) positively influences the physician-patient communication and improved some patients' HRQOL and emotional functioning [20]. Only three studies were conducted among breast cancer patients [21, 22, 24] of these studies one showed benefit of psychosocial screening on HRQOL in the intervention group compared to the control group [22]. In this study patients received only feedback from their clinician when they scored low on HRQOL, which resulted in an improvement of HRQOL [22]. Thus, in the review of Mitchell [19] two out of seven RCTs showed that psychosocial screening had a positive effect on HRQOL [20, 22]. The other five studies [21, 23-26] showed no effect on HRQOL. Moreover, Detmar et al. [27] showed in a crossover randomized trial a positive effect of more frequently discussed HRQOL issues, this intervention facilitated patient-physician communication. The studies on the effect of psychosocial screening on HRQOL are difficult to compare due to the heterogeneous group of cancer patients with different stages of disease and treatment, different time points of screening and psychosocial interventions. Moreover, psychosocial screening was performed by using different measurements tools.

Studies on the association between chemotherapy and QOL [28] (i.e., an individual's perception of his/her position in life in the context of the culture and value systems in which he/she lives and in relation to his/her goals, expectations, standards and concerns) are lacking [28]. To the best of our knowledge, previous studies on the relationship of predictors contributed to the different domains on QOL which are assessed with a screening measure for psychosocial problems were not performed. It is plausible that psychosocial problems (i.e., a combination of psychological and social problems) contribute differently to the different QOL domains across treatment and in the follow-up in women with early stage breast cancer. Knowledge about the predictors on QOL helps to identify patients who are at risk as well as helping them and offering them special attention for their concerns by close monitoring by the nurse practitioner.

The first aim of this pilot study was to identify which factors assessed with a screening instrument for psychosocial problems in early stage breast cancer patients predict patients' QOL shortly after chemotherapy. The second aim was to examine these patients' QOL before the start of adjuvant chemotherapy (Time-1) and three months after finishing chemotherapy (Time-2) and compare these scores with a norm population.

Methods

Participants

All patients visiting the outpatient clinic of the St. Elisabeth hospital (Tilburg, the Netherlands) from January 2009 until August 2011 were asked to participate in the current study and in a related multicenter, prospective longitudinal study examining the objective and subjective cognitive functioning after cytostatic treatment and its effect on QOL. The nurse practitioner informed the patients about both studies during their first appointment before start of adjuvant chemotherapy treatment. Eligible patients needed to be able to read and comprehend Dutch. Patients with a psychiatric disorder were excluded because they had often already been counselled by a care provider for psychosocial problems or were referred to a psychiatrist because of a psychiatric disorder. When patients agreed to participate, they completed the PDQ-BC and the WHOQOL-100 before start of chemotherapy (Time-1) and three months after chemotherapy (Time-2). All patients signed informed consent. This study was approved by the ethics committee of the St. Elisabeth Hospital.

Instruments

The PDQ-BC consists of nine scales with 35 questions assessing psychological risk factors (i.e., Trait anxiety and (lack of) Social support) and psychosocial problems (i.e., State anxiety, Depressive symptoms, Physical problems, Social problems, Body image, Financial problems, and Sexual problems). The response options for all questions range from 1 (*not at all*) to 4 (*very much*). In addition, socio-demographic, clinical factors and patient factors are part of the PDQ-BC on a one page information sheet. The time frame of reference is the previous week, except for the personality characteristic Trait anxiety (i.e., assessing

how one generally feels) is only assessed once, at Time-1. The psychometric properties of the PDQ-BC are good [29, 30]. The subscales State anxiety [31] and Trait anxiety [32] were validated by others. For the short Trait anxiety scale a cut-off score of >20 was identified as a risk factor. To select patients with high levels of State anxiety (≥14) and Depressive symptoms (≥13) the PDQ-BC has shown to have a satisfactory sensitivity (87.5% and 78.6%, respectively) and specificity (81.1% and 73.0%, respectively). The cut-off scores for the aspects Social problems (>8), Social support (4, reverse score) and Financial (>2) were determined by the project group [33] and further based on a small pilot study. For the subscales Physical problems, Sexual problems and Body image cut off scores were not used because these outcome scores are discussed with the nurse practitioner and are not used for referral.

The WHOQOL-100 is a cross-culturally developed generic multidimensional questionnaire that consists of 100 items assessing 24 facets of QOL within four domains (Physical health, Psychological health, Social relationships, Environment) and one general facet called Overall QOL and General health [28]. Each facet and domain is assessed by four items with a 5-point Likert scale. Scores on the domains range from 4 to 20. High scores represent a good QOL. The time of reference is the previous two weeks. Reliability and validity are good [28] and sensitivity of the instrument is high [34]. The norm population are healthy women <70 years [35].

Statistical analysis

In order to preserve statistical power, univariate linear regression analyses were used to select the factors for the multivariate linear regression analyses (MRA). The dependent variables in the univariate regression analyses were the WHOQOL-100 domains Physical health, Psychological health, Social relationships, Environment and the facet Overall QOL and General health. Independent variables were demographic factors (i.e., age, having a partner yes/no, kids living at home yes/no), patient factors (i.e., previous psychological treatment yes/no, clinical factors (type of surgery, radiotherapy, hormonal therapy) and the PDQ-BC subscales Trait anxiety (>20), State anxiety (≥14), Depressive symptoms (≥13), Social support (4, reverse score), Social problems (>8), Financial problems (>2) and Physical problems, Body image, Sexual problems (continuous data).

Subsequently, the significant predictors were used as independent variables in the MRA (method: forward) that was performed to identify those factors that best predicted patients' QOL at Time-2. To compare the scores of the different WHOQOL-100 domains on QOL (Physical health, Psychological health, Social relationships, Environment and the Overall QOL and General health facet with the scores of the norm population one sample t-tests were used.

All analyses were performed with the Statistical Package for Social Sciences (SPSS) version 19.0.

Results

All patients (*N*=53) were women with a mean age of 52 years (SD=10.3). Twenty-eight percent of the patients underwent previous psychological treatment. At Time-1, 34% scored above the cut-off score on the subscale Trait anxiety, 32% scored high on State anxiety, and 28% scored high on Depressive symptoms. Socio-demographic and clinical characteristics of the participants are shown in Table 1.

Table 1. Baseline socio-demographic, patient and clinical characteristics of the participants (*N*=53)

Characteristics	
Age	52.0 ± 10.3 (range 29-69)
Living with partner: (yes/no)	47 (88.7) / 6 (11.3)
Kids living at home: (yes/no)	38 (71.7) / 15 (28.3)
Previous psychosocial treatment: (yes/no)	15 (28.3) / 38 (71.7)
Breast conserving therapy	18 (34.0)
Mastectomy	35 (66.0)
Radiotherapy: (yes/no)	28 (52.8) / (47.2)
Hormonal therapy: (yes/no)	35 (66.0) / 18 (34.0)
Trait anxiety	18.7 ± 5.9 (range 11-33)

Mean ± standard deviation are presented for age and Trait anxiety, percentages are between brackets, except for age and Trait anxiety

Predictors of Quality of Life

Univariate linear regression analyses revealed that the patient factor (kids living at home) and clinical factors (type of surgery, hormonal therapy, radiotherapy) did not significantly contribute to the General QOL facet or any of the QOL domains. Therefore, these factors were not entered in the multivariable analyses.

More Physical problems (β= -.45; *p*=.001) and Depressive symptoms (β= -.37; *p*=.003) at Time-1 negatively affected the WHOQOL-100 Physical health domain at Time-2. Depressive symptoms (β= -.41; *p*=.003) and Body image (β= -.31; *p*=.021) at Time-1 were significant predictors of lower scores on the QOL domain Psychological health at Time-2. Age (β= .37, *p*=.002) and having no partner (β= .53; *p*<.001) at Time-1 were significant predictors for worse scores on the QOL domain Social relationships (Time-2). Having no partner (β= .52; *p*<.001), Physical problems (β= -.23; *p*=.039) and Depressive symptoms (β= -.31, *p*=.004) at Time-1 negatively affected the domain scores of Environment at Time-2. Overall QOL and General health at Time-2 was negatively affected by Physical problems (β= -.35; *p*=.014) and having no partner (β= .32; *p*=.024) at Time-1.

Quality of Life compared with norm population

The scores on the QOL domains Social relationships and Physical health were significantly different compared to the scores of a healthy norm population at Time-1 and Time-2 (*p*'s<.001). Physical health was lower compared to the norm population on both time

points Time-1 and Time-2 while Social relationships was higher at both time points (p's<.002). Overall QOL and General health was only significantly lower at Time-1 (p=.019). The domain Environment health and Psychological health did not significantly differ compared to the healthy norm population on both time points.

Table 2. Predictors of quality of life at three months after chemotherapy

		Beta	P-value	Confidence interval for B Lower Bound	Upper Bound	SE	Total Adj. R²
Physical health	Physical problems	-.45	.001	-.80	-.24	.14	44%
	Depressive symptoms	-.37	.003	-4.07	-.86	.80	
Psychological health	Depressive symptoms	-.41	.003	-2.44	-.52	.48	27%
	Body image	-.31	.021	-.73	-.06	.16	
Social relationships	Age	.37	.002	.03	.13	.03	42%
	Having no partner	.53	<.001	1.91	4.98	.76	
Environment	Having no partner	.52	<.001	1.83	4.28	.61	59%
	Physical problems	-.23	.039	-.35	-.01	.09	
	Depressive symptoms	-.31	.004	-2.37	-.47	.47	
Overall QOL & General health	Physical problems	-.35	.014	-.71	-.08	.15	27%
	Having no partner	.32	.024	.37	5.00	1.15	

QOL= Quality of life; Total Adj. R²= Total Adjusted R²-squared; SE= standard error

Table 3. Comparison of scores on the different WHOQOL-100 domains before start chemotherapy (Time-1) and three months after adjuvant chemotherapy (Time-2) with the norm scores

	Time-1	Time-2	Reference score	Comparison with the norm Time-1 p-value	Comparison with the norm Time-2 p-value
Physical health	13.6 ± 2.9	14.0 ± 3.0	15.9	<.001	<.001
Psychological health	14.3 ± 1.6	14.5 ± 1.7	14.4	.655	.712
Social relationships	16.7 ± 1.9	16.4 ± 2.3	15.3	<.001	.002
Environment	16.3 ± 1.8	16.4 ± 2.1	16.0	.234	.258
Overall QOL and General health	14.8 ± 2.7	15.4 ± 2.9	15.7	.019	.447

Time-1= before start of chemotherapy; Time-2= three months after chemotherapy

Discussion

The aim of this pilot study was to identify which factors of a psychosocial screening instrument (patient factors, clinical factors and psychosocial factors) contributed to patients' QOL three months after adjuvant chemotherapy. Another aim was to examine the QOL of breast cancer patients before the start of adjuvant chemotherapy and three months after finishing chemotherapy and to compare these scores with the scores from a healthy norm population. (HR)QOL has become an important outcome measure of treatment.

Based on this pilot study, paying special attention to younger patients and patients with high scores on Depressive symptoms, without a partner, having more physical problems and having problems with their body image may be needed because these patients may be at risk for an impairment of QOL shortly after chemotherapy. Although the current study is characterized by a limited sample size, the findings are in line with results found in other studies. For instance, Kiebert et al. [36] and Badger et al. [37] also found that having depressive symptoms and having problems with body image are factors that are related to a lower Psychological health [36, 37]. In this study, having no partner was a predictor of a lower QOL. This is consistent with the study of Engel et al. [38] on (HR)QOL in breast cancer patients. Moreover, Tuinman et al. [39] also found that age (younger and middle-aged patients) was related to high distress and a higher likelihood of being referred for additional psychosocial care. An unexpected finding was that Trait anxiety was not a significant predictor of QOL in this study. This finding is inconsistent with findings in the literature in which high trait anxiety had a negative impact on QOL [40, 41]. It has to be taken into account that these studies had a longer follow-up period and the study populations include both benign disease and breast cancer. These patients also received different types of treatment. Moreover, our study has a relatively small sample size and included only patients with adjuvant chemotherapy. Patients with adjuvant treatment with chemotherapy frequently visit the health-care provider and this may experience a sense of safety, while in the follow-up this feeling may have been lost without the frequently support from a health-care provider. Furthermore, in the current pilot study Financial problems and Sexual problems were not predictive for an impaired QOL at Time-2. It could be that these concerns will predict QOL in a later stage when patients have persistent complaints as a result of medical treatment and, therefore, problems with returning to work [42, 43] or problems with sexual functioning [14]. Moreover, State anxiety was not predictive for an impaired psychological QOL at Time-3. However, Schreier et al. [44] demonstrated that breast cancer patients with higher levels on State anxiety experienced lower QOL before the start of radiation therapy and post treatment. In the univariate analysis was State anxiety a predictor of lower QOL. The overlap between state anxiety and depressive symptoms may be the reason that State anxiety did not predict lower QOL in the multivariate analyses.

Compared with the norm population, patients have significantly lower scores on Physical health before the start of chemotherapy and three months after chemotherapy. This result is in line with previous studies [45, 46]. Despite that 32% of the patients scored

high on State anxiety and 28% scored high on Depressive symptoms on Time-1 the score on Psychological health was comparable to the norm population at both time points. An explanation for this could be that patients received more attention from friends and family during treatment, which resulted in an experience of higher levels of social support, which predict psychosocial well-being [47].

A strength of this study is that this is the first study examining the predictors of the different domains on QOL assessed with a screening instrument for psychosocial problems shortly after ending chemotherapy. However, this study has several drawbacks. First, the sample size of this pilot study is very small. Therefore, caution is needed when interpreting the findings. Another factor that may have influenced the results is that patients who had high levels of psychosocial problems were probably referred to a psychologist, psychiatrist or social worker and received additional help, which could have influenced Psychological health scores at Time-3. Third, at baseline the answers of the subscale assessing the risk factor (lack of) Social support did not show variation. For this reason this subscale could not be used in the regression analyses. Therefore, a multi-center study with longer follow-up with methods to control confounding must be conducted to examine whether different psychosocial problems predicting different domains of QOL across time and to make these findings more generalizable.

In summary, this pilot study implies that psychosocial screening provides useful information concerning the relationship between aspects of psychosocial problems and patients' QOL in breast cancer patients shortly after finishing adjuvant chemotherapy. Psychosocial screening is essential to select those patients in need for professional help in order to enhance their QOL.

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Chapter 7

GENERAL DISCUSSION
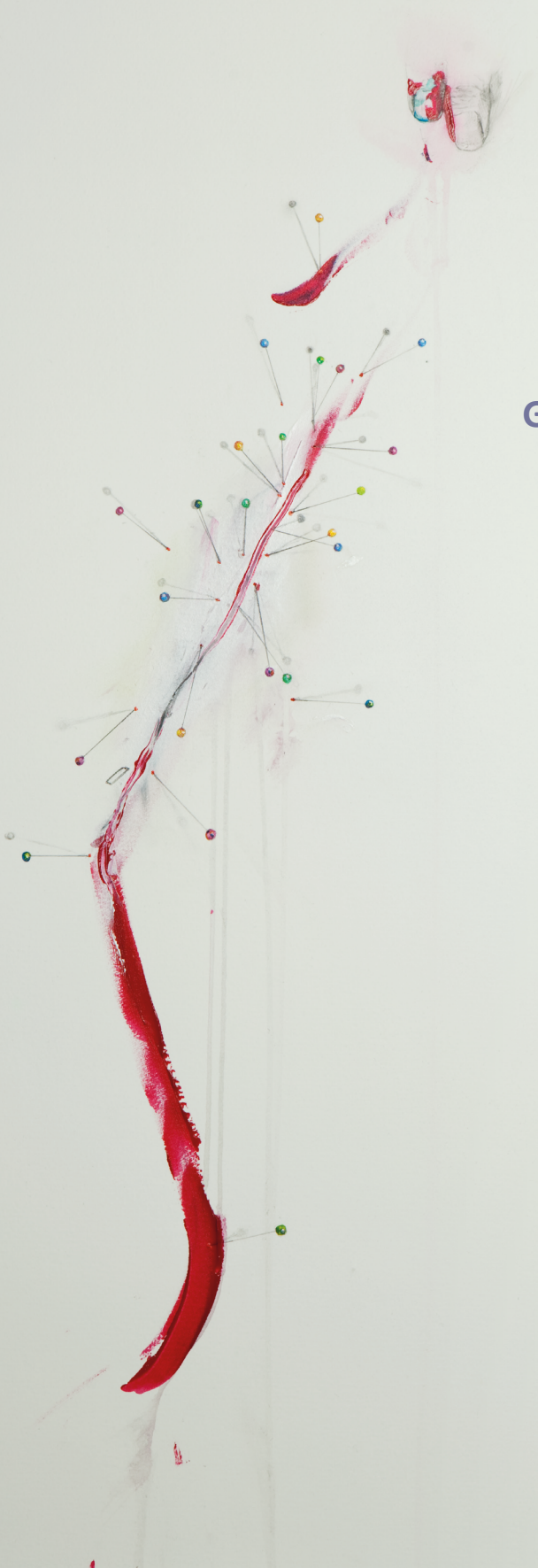
In the Netherlands, breast cancer is the most frequently diagnosed malignant disease, with more than 14,000 new cases diagnosed in 2014 [1] and a still increasing incidence. The survival rate has increased due to improvement in medical treatments [2]. However, the prolonged survival reveals that breast cancer has become a long-lasting disease with physical complaints and a profound impact on psychological and social functioning [3-5]. In general, many patients are reluctant to discuss psychosocial issues and, therefore, psychosocial problems often go unrecognized [6-8]. The National Cancer Control Programme stated [9] that cancer patients with psychosocial needs should be identified and extra psychosocial care should be offered to improve patients' psychosocial well-being [9]. When this study was started in 2006, no comprehensive, reliable and valid screening instrument was available to screen a broad picture of psychosocial problems in (breast) cancer patients.

The primary aim of this thesis was to develop and to examine the psychometric properties of the Psychosocial Distress Questionnaire-Breast Cancer (PDQ-BC), a screening instrument for psychosocial problems suited for early-stage breast cancer patients. Using the PDQ-BC the course of anxiety and depressive symptoms was evaluated before the start of chemotherapy up to one year after ending chemotherapy. Furthermore, risk factors for higher scores on State anxiety, Depressive symptoms and an impaired Quality of Life (QOL) were identified. In this present chapter the main findings are summarized and discussed in relation to the literature. Next, strengths and limitations of this thesis are addressed. Finally, ideas and suggestions for future research and clinical implications are presented.

Discussion of the main findings

Part A of this thesis is focused on the development and psychometric properties of the PDQ-BC.

In Chapter 2, the conceptual frame work of the PDQ-BC was discussed. Psychosocial problems were defined as a composite of frequently reported psychological and social problems including specific issues that are known to effect patients' (HR)QOL, and risk factors that are associated with patients' psychosocial well-being for whom referral for extended psychosocial care by a psychosocial health care provider would be helpful. Psychosocial problems were assessed with nine subscales. These subscales were determined by an extended literature search and opinions of a multi-disciplinary project group of experts in the field of psychosocial care, including a person from the Comprehensive Cancer Center South. The initial idea was to use short existing reliable and validated questionnaires to establish content validity for the different subscales. However, this generated too many questions for the purpose of screening and, therefore, the validated questionnaires were not suited to implement in daily practice. To establish the subscales Trait anxiety and State anxiety, the questions from the short-form versions [10, 11] were used. To reduce the number of items on the subscales Depressive symptoms, Physical problems, Body image, Financial problems, and Sexual problems factor analyses

on the data of a prospective follow-up study concerning the role of personality factors on QOL in breast cancer patients were performed [12, 13]. For each scale the items with a factor loading above 0.70 were used. To provide the information needed to determine whether or not patients should be referred to a social worker the subscales Social problems, Social support and Financial problems were developed. The project group decided to adapt one question from the WHOQOL-100 for the subscales Financial problems and Social support. In addition, the four questions on the subscale Social problems were developed by the project group because there was no existing questionnaire that assessed the specific aspects relevant for social work (i.e., work, family, social functioning). The subscale Sexual problems consist of one question adapted from the WHOQOL-100, based on the clinical experience that patients indicated to get irritated when they have to complete more questions about sexuality in the phase of treatment with chemotherapy.

Confirmatory factor analyses were performed and showed that the a priori model of the PDQ-BC had a good fit. During the development phase of the PDQ-BC ten patients were interviewed about the comprehensiveness of the constructs and the adequacy of the response scale. Patients indicated that de PDQ-BC was easy to complete, not burdensome, and the questions were perceived as relevant. In clinical practice, the PDQ-BC is a good tool to systematically discuss those psychosocial problems that are most relevant based on the scores, resulting in a more patient-tailored discussion. Moreover, only focusing on those problems that patients perceive as relevant is more efficient, given the limited time of physicians and nurses for each patient.

The psychometric properties support the usefulness of the PDQ-BC to identify psychosocial problems in early-stage breast cancer patients with adjuvant chemotherapy [14-16].

With regard to the reliability of the PDQ-BC, the internal consistency of each subscale was good, except for the subscale Social problems. The low alpha of the subscale Social problems before adjuvant chemotherapy can be explained by the fact that the subscale was designed to tap into different aspects of social problems, such as work, family and social activities. The high internal consistency (0.95) of the subscale Social problems in the post-treatment group suggested that the reliability is driven by the variance in a more heterogeneous group in comparison to the group of patients in an active treatment phase (homogeneous group) [17]. At the same time subgroups in the post-treatment group produced lower or higher scores on the Social problems subscale which results in a high alpha.

As hypothesized almost all the subscales of the PDQ-BC were significantly correlated with each other. The subscales Trait anxiety, State anxiety, and Depressive symptoms had the highest correlations with each other. This can be explained by the fact that women with high scores on Trait anxiety have a tendency to respond with higher levels on State anxiety to situations perceived as threatening [18, 19]. Furthermore, studies have shown that these women, irrespective of diagnosis, also score high on fatigue (i.e., physical problem) [20] and are at risk for more psychological distress [19, 21]. Psychological distress concerns both anxiety and depressive symptoms. These two psychological

problems have been shown to have substantial overlap [22-24]. The PDQ-BC subscales Physical problems, Financial problems, Social support, Sexual problems and Body image had lower correlations with the other PDQ-BC subscales. These subscales focus on (HR)QOL issues that may interfere with patients' psychosocial well-being during treatment phase and the follow-up [25-28].

Test-retest reliability calculated with the intra class correlation in a stable group early-stage breast cancer patients was good. Patients completed the PDQ-BC twice within a one week interval in the same test conditions. They received the second questionnaire after the first was send back, to prevent that the first administration would influence the second administration. Between the two completion moments none of the patients reported having experienced an event that they considered stressful, which was explicitly asked. Therefore, all patients were considered stable during the interval period.

Regarding the construct validity a priori formulated hypotheses were tested. All the hypotheses, except two, were confirmed. Two associations were lower than expected: the PDQ-BC subscale Sexual problems with Sexual activity (WHOQOL-100) and the PDQ-BC subscale Physical problems with the facet Energy and Fatigue (WHOQOL-100). The PDQ-BC subscale Depressive symptoms was tested against the Center for epidemiological Studies depression Scale (CES-D, chapter 2). High correlations were expected as seven items in the subscale were adapted from the CES-D to be in line with the other questions in the PDQ-BC. However, the correlations between the subscale and the CES-D without the item overlap was also high. In addition, the construct validity of the subscale Depressive symptoms (PDQ-BC) was also tested against the depression scale of the Hospital Anxiety Depression Scale (HADS-D). As expected, the PDQ-BC subscale Depressive symptoms had a moderate correlation with the HADS-D because the questions of the HADS-D focus on the ability to experience pleasure (anhedonia) [29] while the adopted questions of the CES-D focus on depressed affect [30]. Moreover, the PDQ-BC subscales had low correlations with non-related questionnaires.

We expected to find floor effects on the subscales Social problems, Body image, Sexual problems, and Financial problems before start of chemotherapy. It is possible that before start of treatment patients are less bothered by social problems, body image and sexual problems because they are worried about the side effects of their first chemotherapy cycle. Among breast cancer patients social problems, sexual problems and problems with their body image often occur during treatment phase and in the later follow-up [3, 25, 31]. The ceiling effect on Social support can be explained by the fact that patients in general receive sufficient support from family and friends.

An appropriate psychosocial screening instrument which is linked to an adequate norm-based referral system identifies only those patients who are in need of psychosocial care. This improves adequate referral to appropriate psychosocial health services, thus efficiently using available resources. Given the large group of breast cancer patients, a low sensitivity will affect many patients who will be under treated whereas low specificity will result in higher costs and unnecessary visits to psychosocial health care providers. Tested against the HADS, the PDQ-BC is accurate in identifying patients with severe anxiety and depressive symptoms and those without.

Studies evaluated the effectiveness and acceptability of screening for distress reported that 20% to 30% of patients with a referral advice for psychosocial treatment accepted this referral for psychosocial treatment [32, 33]. In this study, 18% of the patients accepted the referral advice according to the results of the PDQ-BC. Patients mentioned several reasons for refusal. Some patients preferred to resolve their problems by themselves. An explanation could be that they would experience the acceptance of the referral as a failure. Other patients believed that these feelings of anxiety would decline after the first cycle of chemotherapy. This was the case in patients with only high scores on State anxiety and not on Trait anxiety. Moreover, based on the PDQ-BC more patients were referred to a psychologist (~25%; Chapter 2 and 4) than to a social worker (~18%; Chapter 2 and 4). The fact that more patients were referred to a medical psychologist than to a medical social worker was due to a high prevalence of patients with high scores on Trait anxiety in combination with high scores on State anxiety and/or Depressive symptoms. Studies showed that breast cancer patients with high scores on trait anxiety before diagnosis are at risk for higher levels of anxiety [18, 19], depressive symptoms [19, 21] and an impaired QOL at six [13, 34-36] and 12 months after diagnosis [37]. The development of the referral system of the PDQ-BC was based on these studies and supported by the medical psychologists. Therefore, patients with such combinations get a referral advice for a medical psychologist because these patients may benefit from psychological interventions [36, 38, 39]. The number of referral advices according to the PDQ-BC was compared to the Distress Thermometer (DT) because the DT is the recommended instrument in the Dutch breast cancer guidelines. There were less referral indications according to the PDQ-BC compared with the DT. Before chemotherapy was started 47% of the patients had a referral advice based on the PDQ-BC, while 61% of the patients had a referral indication according to the DT (Chapter 4). This difference may be explained by the fact that distress, as assessed by the DT, can also be caused by other factors, such as physical side effects of therapy. Given the difference in aims between the PDQ-BC (assessing psychosocial problems) and the DT (assessing distress according to the definition of the NCCN [39] these results are difficult to compare.

Anxiety, depressive symptoms, and QOL

In Part B of this thesis, the course and predictors of State anxiety and Depressive symptoms as well as the relationship between Psychosocial problems (PDQ-BC) and QOL (WHOQOL-100) were examined. Knowledge about the predictors of State anxiety and Depressive symptoms and QOL helps to identify patients who are at risk and who would benefit from special attention by the nurse practitioner.

Highest levels of State anxiety and Depressive symptoms were registered before the start of chemotherapy; these levels declined in the first year after chemotherapy. This study showed that risk factors for higher scores on State anxiety and Depressive symptoms are: no partner, scheduled for radiotherapy, high scores on Trait anxiety, more Physical problems and a lack of Social support. This is consistent with studies concerning

predictors on anxiety and depressive symptoms in breast cancer patients [19, 37, 40-42]. In addition, we found that hormonal therapy was only a predictor for depressive symptoms. In contrast to the study of Burgess et al. [40], previous psychological treatment did not predict State anxiety and depressive symptoms. This result is difficult to compare with the current study, due to the study design (e.g. instruments, time points in the follow-up). For example, Burgess et al. [40] carried out a clinical interview to identify anxiety and depression (not depressive symptoms) and data were collected for more than one year after treatment. However, we did not register the reasons why patients had received previous psychosocial counselling. In our study patients may have received psychosocial counselling for other reasons than anxiety and/or depressive symptoms.

Concerning the predictors of QOL it was not expected that high Trait anxiety did not predict QOL at three months after chemotherapy. Van der Steeg et al. [13] and Keyzer et al. [36] showed that high Trait anxiety at baseline (before diagnosis) negatively influenced QOL at six months follow-up irrespective of diagnosis. Possible explanations could be that first, the difference in time point of screening may play a role because until three months after chemotherapy patients visit the nurse practitioner more frequently, which may give a sense of safety. After three months, regular contacts are becoming less frequent and thus may reducing the sense of safety and patients with high Trait anxiety may start experiencing a lower QOL later in follow-up. This information is not available because in the study we only examined patients' QOL at three months after chemotherapy. Second, the sample size in the present study is too small to draw solid conclusions.

Strengths and limitations

Overall there was a high participation rate (>76%) and different populations of breast cancer patients were used to examine the referral system of the PDQ-BC. To examine the construct validity and the sensitivity and specificity of the PDQ-BC the CES-D, WHOQOL-100, DT and HADS were used, which have been extensively validated in the field of cancer patients [43-45]. The participants in the present study included a sample of early-stage breast cancer patients visiting an out-patients clinic. Thus, the study results can probably be generalized, at least across the Netherlands.

To examine the course of State anxiety and Depressive symptoms and its predictors, a prospective longitudinal study was conducted and data were analyzed with linear mixed models. This is a sophisticated statistical method in the way it deals with missing data and, therefore, an optimal use of available information. In addition, this study identified longitudinal predictors and not only predictors assessed at baseline, i.e., before start of the chemotherapy.

To our knowledge, this is the first study that identifies predictors on QOL measured with a screening instrument for psychosocial problems in breast cancer patients with adjuvant chemotherapy. Knowledge about these predictors of QOL may help healthcare providers to identify patients at risk for a low QOL at an early stage and offer them personalized psychosocial support.

This study has some major limitations. First, items on the different PDQ-BC subscales were derived from existing well-established questionnaires using factor analysis. More detailed information about the psychometric quality of the subscales can be obtained from latent trait models, such as Item Response Theory (IRT) analysis and Rash models that belong to the IRT models [17]. Second, there is international consensus that the target population should be involved in the development of a patient reported outcome measurement. In 2006, when the PDQ-BC was developed, such consensus did not exist and patients were only interviewed during their hospital visit. The nurse practitioner who performed the ten interviews was focused on getting insight in patients' perspective of the content of psychosocial problems. These patients were also asked if they missed relevant important aspects or items in the PDQ-BC to measure the different constructs. In addition, they judged the adequacy of the response options. Nevertheless, the PDQ-BC was developed based on the literature and based on discussions in the expert group. Patients did not participate in the expert meetings, something that is common nowadays.

Further limitations of the study are the adequacy of the referral indications according the PDQ-BC. First, although all referrals were judged as correct by the social worker and psychologist in the St. Elisabeth Hospital (Tilburg, the Netherlands) only the referral advices of the patients who wanted to be referred were examined. No information is available about the correctness of the referral advices of patients which did not accept referral. Moreover, there were no patients referred to a psychiatrist based on the PDQ-BC score. As a consequence we do not know if these scores justified a referral to psychiatry. Second, the sensitivity and specificity of the PDQ-BC subscales Depressive symptoms and State anxiety do not provide information on the validity of the referral system of the PDQ-BC. The referral system of the PDQ-BC is based on a combination of the scores on the subscales State anxiety, Depressive symptoms, and Trait anxiety. However, the PDQ-BC seems to be accurate in identifying anxiety and depressive symptoms and ruling out patients without these symptoms. Based on the mentioned limitations a multi-centered study should be performed to reveal whether the referral indication is correct for patients that do not have a referral advice and patients that have a referral advice but refuse.

The study was conducted during daily practice of one nurse practitioner of the internal medicine department. Therefore, all data, except data from the Elkerliek Hospital which stopped the inclusion of patients because the DT was implemented, were collected among breast cancer patients scheduled for adjuvant systemic therapy in one hospital. However, the PDQ-BC was validated in the group patients with adjuvant chemotherapy it is not to be expected that the quality of the PDQ-BC will be different in breast cancer patients without adjuvant chemotherapy. This is supported by the fact that in the few women who received neo-adjuvant chemotherapy the PDQ-BC did not perform differently (results not shown). Moreover, almost all patients were native Dutch speakers. This paper does not include male patients, since no male breast cancer patients were scheduled for chemotherapy. This is mainly caused by the fact that male breast cancer is a relatively rare cancer in men [1]. Finally, the psychosocial state of patients during the transition phase from active treatment to resuming their lives was not examined. Studies have shown that patients in the transition phase experience more distress [46].

Future perspective and research

As mentioned previously, guidelines with regard to psychosocial oncology recommend systematic distress screening to determine the need for professional psychosocial support as part of the regular care in cancer patients [47, 48]. However, there is a lack of evidence from well-conducted randomized controlled trials (RCT's) that show benefits of distress screening for patients' HRQOL outcome. To my knowledge the effect of psychosocial screening on HRQOL was examined in seven RCTs [49-55] in which patients with different types of cancer and disease stages were examined, including breast cancer patients. Of these studies only two studies showed a positive effect on HRQOL [49, 51]. In the study of Velikova et al. [49] patients in the attention-control (screening alone) and intervention group (screening with feedback) reported a better HRQOL compared to the control group (no screening). In the intervention group the use of HRQOL data (feedback) positively influences physician-patient communication, improved HRQOL and emotional functioning in some patients [49]. In the study of Klinkhammer et al. [51] patients received more therapeutic options from their clinician when they scored low on HRQOL before they left the hospital after breast surgery, which resulted in an improvement of HRQOL at six months after surgery [51]. Moreover, in a crossover randomized trial Detmar et al. [56] showed the positive effect of using HRQOL assessments in the intervention group compared to the control group. Patients in the intervention group more frequently discussed HRQOL issues which resulted in increased levels of counseling from their physician on how to manage their health problems. The other RCTs showed no significant differences between the intervention and control groups on HRQOL [50, 52-55] and reported difficulties with the adaptation of a psychosocial screening program in the daily care for cancer patients. However, one study showed that the intervention improved patients' communication with the health-care team and resulted in an increasing number of referrals to psychosocial health-care services [54]. Thus, five [50, 52-55] out of seven RCTs failed to show significant benefits on patient reported HRQOL [50, 52-55].

With regard to the RCTs examining the effect of psychosocial screening on distress two RCTs that also include breast cancer patients exist [33, 57]. Carlson et al. [33] showed a positive effect on distress in the full-screening group (screening with feedback) and the triage group (full screening and additionally a triage assessment to discuss referral options with the patients) compared to the minimal-screening group (screening and no feedback). Patients in the full-screening or triage group who received a referral for psychosocial health care services had decreased levels of anxiety and depression [33]. The other study on distress showed no significant differences in distress between the intervention and control groups [57]. The existing reviews all concluded that there is no conclusive evidence that screening reduces distress and improves patients' HRQOL [32, 57, 58]. The studies are difficult to compare due to the heterogeneous group of cancer patients with different stages of disease and treatment, and different time points of screening and psychosocial interventions. Moreover, psychosocial screening was performed by using different measurements tools. Mitchell [32] concluded that simply implementing a screening

instrument for psychosocial problems in cancer care is usually not sufficient to establish a change in HRQOL.

Nowadays, there is a theoretical debate concerning screening for distress in cancer patients. Detractors stated that screening for distress should only be mandated if there is solid evidence that patients will benefit from screening with reduced stress levels [4, 59]. In addition, patients who were identified as distressed do not always wish to receive psychosocial care. Therefore, detractors argued that the efforts invested in screening programs would be better deployed in other ways to improve mental health [4, 59]. Advocators stated that studies with inconclusive results with regard of the effectiveness of distress screening is caused by major design limitations in terms of a lack of staff training, appropriate referral pathways, and follow-up care [32, 60]. They stated that distress screening itself is not enough to show improvement patients' HRQOL [32, 60]. Moreover, the wish for psychosocial support seems unrelated to the levels of distress [61, 62]. Screening for unmet needs additionally to distress screening in order to differentiate between psychological versus psychosocial and practical needs have potential benefit to better manage patients' concerns [60, 63].

There is more research needed to understand the impact of routine psychosocial screening using the PDQ-BC in breast cancer patients on patient-reported outcomes (PROs), including QOL. In the near future, another study in breast cancer patients will be initiated. This study will examine the effects of screening on QOL and costs using the PDQ-BC during the whole trajectory of treatment up to two years after treatment. To provide more insight into the psychosocial state of patients in the transition phase from active treatment to resuming their lives all breast cancer patients will be screened for psychosocial problems before surgery, before start of chemotherapy, after ending chemotherapy (i.e., before start radiotherapy) and at 3, 6, 9, and 12 months follow-up. Furthermore, studies have to be conducted to develop an appropriate psychosocial care plan for patients at risk for psychological problems. In the future it is also necessary to not only examine the potential increase in the number of psychosocial treatments (and related costs due to screening for psychosocial problems), but also to examine the possibility that screening at an early stage saves costs as patients may seek less medical support.

The PDQ-BC is considered to be a psychosocial screening instrument with adequate to good psychometric properties in early-stage breast cancer patients with adjuvant chemo-therapy. However, it can be argued that this instrument can also be considered to be a basic module which can be applied to patients diagnosed with another type of cancer. Specific questions in turn could be added similar to the European Organization for research and Treatment of cancer (EORTC) quality of life instruments [64]. The EORTC consist of a generic module (EORTC-QLQ-C30) to which specific add-ons can be added (EORTC-QLQ-BR23) [65]. As a consequence, only questions relevant for patients will be measured [66]. In this respect studies have to be conducted in order to examine which topics or risk factors should be added to a module for patients with other types of cancer or metastatic disease. For instance, items could be adapted for patients with a more advanced disease stage, since patients may also face existential questions, which cover a

range of issues related to the meaning of life and death issues [67]. Patients with lung cancer may feel more guilt and shame if smoking was involved [68]. Social isolation is often a result of (i) physical disfiguration in patients with advanced head and neck cancer and (ii) problems with swallowing lead to impairments in communication [69]. Recently, Eijzenga [70] reported that patients who undergo genetic counseling worry about the hereditary predisposition. Furthermore, experiencing cancer in the family may interfere with their psychosocial well-being [69].

The subscale Social problems of the PDQ-BC has suboptimal psychometric properties in the acute phase of treatment. To date, item banks can be helpful to select additional questions to optimize the reliability of the subscale Social problems [71]. These items are calibrated using Item Response Theory (IRT) models. IRT calibrated measurements provide the opportunity (i) to determine the relative contribution of each item to the measurement precision of the scale and to determine which items are most related to the interested construct; (ii) the possibility to develop short forms measurements containing items of most relevance to specific population [71]; and (iii) the ability to measure more precisely by assessing fewer questions by using Computer Adaptive Testing (CAT), a system by which the item being administered to the patient is chosen according to her/his response on the previous item [72].

In order to generalize our findings to breast cancer patients without adjuvant chemotherapy, male breast cancer patients and other ethnicities should be included in a study with more diverse study populations.

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Appendix

THE PSYCHOSOCIAL DISTRESS QUESTIONNAIRE-BREAST CANCER
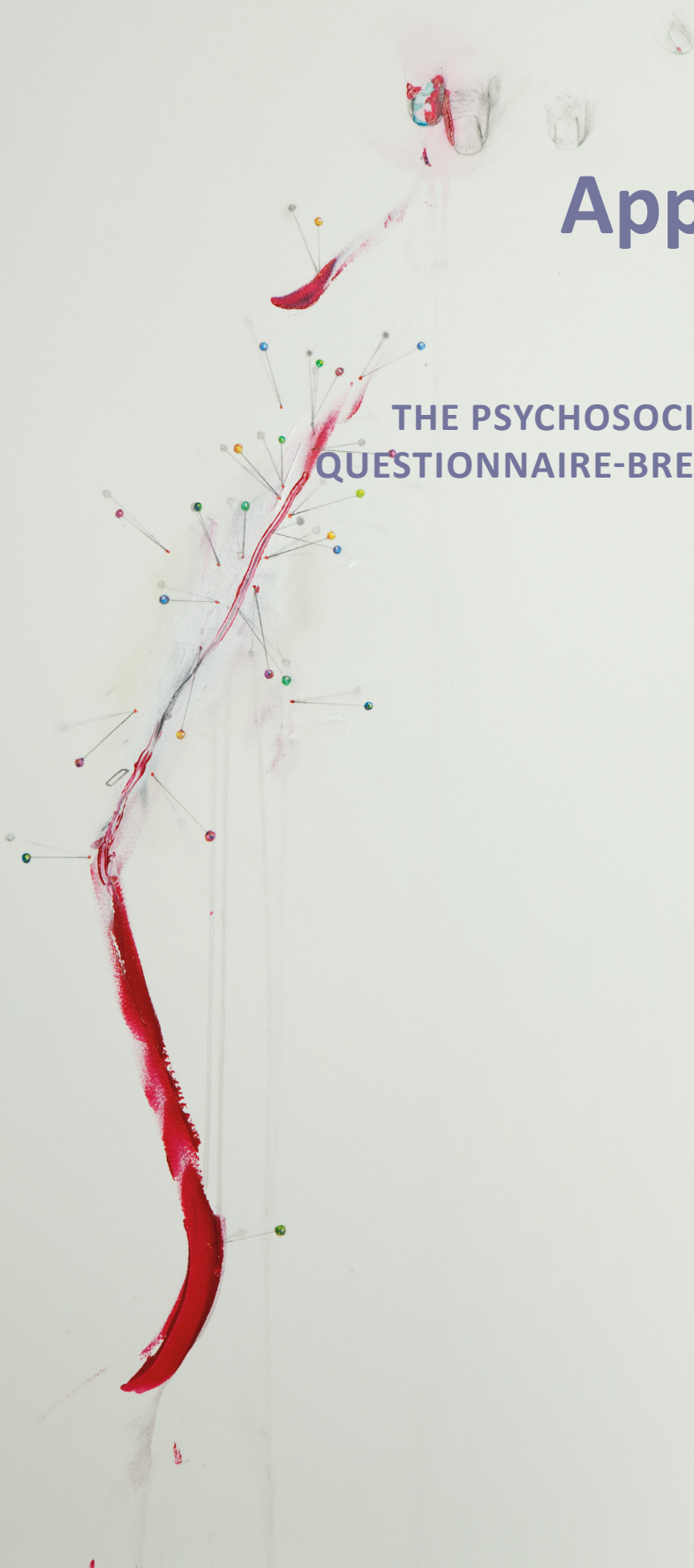
The Psychosocial Distress Questionnaire-Breast Cancer (PDQ-BC)

Omcirkel achter elke vraag of uitspraak het cijfer dat <u>in het algemeen</u> het beste bij u past	1 = Geheel niet	2 = Een beetje	3 = Tamelijk veel	4 = Zeer veel
AT 1 — Ik voel mij nerveus en onrustig.	1	2	3	4
AT 2 — Ik voel mij rustig en beheerst.	1	2	3	4
AT 3 — Ik voel dat de moeilijkheden zich opstapelen op zo'n manier dat ik er niet meer tegenop kan.	1	2	3	4
AT 4 — Ik pieker teveel over dingen die niet zo belangrijk zijn.	1	2	3	4
AT 5 — Ik word geplaagd door storende gedachten.	1	2	3	4
AT 6 — Ik voel mij veilig.	1	2	3	4
AT 7 — Ik voel mij op mijn gemak.	1	2	3	4
AT 8 — Ik ben gelijkmatig van stemming.	1	2	3	4
AT 9 — Er zijn gedachten die ik heel moeilijk los kan laten.	1	2	3	4
AT 10 — Ik raak helemaal gespannen en in beroering als ik denk aan mijn zorgen van de laatste tijd.	1	2	3	4

Omcirkel achter elke vraag of uitspraak het cijfer dat het beste bij u past <u>de afgelopen week</u>	1 = Geheel niet	2 = Een beetje	3 = Tamelijk veel	4 = Zeer veel
SP 1 — Ik ontvang voldoende steun van de mensen om mij heen.	1	2	3	4
SO 1 — Er zijn praktische problemen met betrekking tot mijn gezin.	1	2	3	4
DE 4 — Ik voelde mij gedeprimeerd.	1	2	3	4
DE 2 — Ik bleef maar in de put zitten, zelfs als familie of vrienden me probeerden er uit te halen.	1	2	3	4
PH 1 — Ik ben tevreden met de energie die ik heb.	1	2	3	4
SO 2 — Mijn medische toestand en behandeling heeft mij belemmerd in mijn sociale omgang.	1	2	3	4
DE 5 — Ik had het gevoel dat alles wat ik deed mij moeite kostte.	1	2	3	4
BO 2 — Ik vind het moeilijk om mijzelf naakt te zien.	1	2	3	4
DE 7 — Ik was treurig.	1	2	3	4
DE 1 — Ik stoorde mij aan dingen die mij gewoonlijk niet storen.	1	2	3	4

Omcirkel achter elke vraag of uitspraak het cijfer dat het beste bij u past <u>de afgelopen week</u>	1 = Geheel niet	2 = Een beetje	3 = Tamelijk veel	4 = Zeer veel
PH 3 Ik heb pijnklachten.	1	2	3	4
SO 3 Er zijn praktische problemen met betrekking tot mijn werk.	1	2	3	4
FI 1 Ik maak mij zorgen over mijn financiële situatie.	1	2	3	4
DE 3 Ik had moeite mijn gedachten bij mijn bezigheden te houden.	1	2	3	4
PH 2 Ik heb problemen met slapen.	1	2	3	4
PH 4 Pijnklachten belemmeren mijn dagelijkse bezigheden.	1	2	3	4
BO 1 Ik voel me lichamelijk minder aantrekkelijk ten gevolge van mijn ziekte of behandeling.	1	2	3	4
DE 6 Ik voel me bang.	1	2	3	4
SE 1 Ik heb problemen met mijn seksuele relatie.	1	2	3	4

Omcirkel achter elke vraag of uitspraak het cijfer dat het beste bij u past <u>op dit moment</u>, met andere woorden <u>hoe u zich nu voelt</u>	1 = Geheel niet	2 = Een beetje	3 = Tamelijk veel	4 = Zeer veel
AS 1 Ik voel mij kalm.	1	2	3	4
AS 2 Ik voel mij gespannen.	1	2	3	4
AS 3 Ik ben in de war.	1	2	3	4
AS 4 Ik ben ontspannen.	1	2	3	4
AS 5 Ik voel mij tevreden.	1	2	3	4
AS 6 Ik maak me zorgen.	1	2	3	4

AT= Trait anxiety; SP= Social support; SO= Social problems; PH= Physical problems; DE= Depressive symptoms;
BO= Body image; SE= Sexual problems; FI= Financial problems; AS= State anxiety

SUMMARY

Summary

Breast cancer is the most common malignancy in women worldwide [1]. In the Netherlands, 13% of all Dutch women will develop breast cancer and 70% to 86% of all breast cancer patients will still be alive after five years [2]. The number of women with breast cancer is increasing due to early detection and the advancements in treatment [3]. Breast cancer diagnosis and treatment are not only associated with substantial physical complaints which interfere with daily activities [4, 5], but are also related to psychosocial problems (i.e., a combination of psychological and social problems) [6-9]. In general, these problems are experienced by 10% to 53% of the women during treatment and follow-up [6, 7, 9] and have a negative impact on patients' experience of (health-related) quality of life (HR)QOL [4, 5]. Despite the high prevalence of psychosocial problems identifying patients with psychosocial problems by the physician is difficult [10-12]. Patients are often reluctant to express their emotional problems to their physician [10, 13] because they think that the doctor has not enough time and that it is not a doctor's role to help them with their emotional problems [10]. Another consideration is that in cancer patients depressive symptoms, such as fatigue, sleep disturbance, and loss of appetite may also be attributable to the side effects of treatment [10, 14].

Nowadays, screening for psychosocial problems in cancer patients receives much attention and is recommended by several organizations [15-18]. However, in 2006, when this study was started there was no reliable and valid psychosocial screening instrument available in Dutch, despite the fact that the National Cancer Control Program had already stated in 2004 that psychosocial screening was important and should be incorporated in 2010 [16]. To facilitate the communication between the medical health care providers and patients about psychosocial problems the Psychosocial Distress Questionnaire-Breast Cancer (PDQ-BC), a screening instrument for psychosocial problems, was developed and incorporated in the standard routine care. The availability of such an instrument provides the opportunity to screen a substantial part of the ambulant cancer population.

In this thesis psychosocial problems is defined as a composite of frequently reported psychological and social problems, including specific issues that are known to effect patients' (HR)QOL, and risk factors that are associated with patients' psychosocial well-being for whom referral for extended psychosocial care by a psychosocial health care provider would be helpful [15, 19, 20]. The content of the PDQ-BC was based on the literature and discussions in a multi-disciplinary project group ('Verwijs-Wijzer') of psychosocial health care providers. The PDQ-BC consists of nine subscales (i.e., Trait anxiety, State anxiety, Depressive symptoms, Physical problems, Social support, Social problems, Body image, Financial problems, Sexual problems) using 35 questions. The majority of these questions (31) were derived from existing reliable and valid questionnaires. The cut-off scores for these questions were derived from the norm scores of the original longer questionnaires. For the remaining scales the cut-off scores were determined during discussions within the project group. In addition, the project group also decided which combination of scores above the cut-off scores indicated a referral to social work, psychology, or psychiatry. During the development phase of the PDQ-BC ten

patients were interviewed about the comprehensiveness of the constructs and the adequacy of the response scale.

Regarding the internal structure most of the subscales were significantly correlated with each other. Moreover, the confirmatory factor analysis supported the internal structure of the PDQ-BC. In addition, structural equation modelling showed that the structure of the a priori model of the PDQ-BC had a good fit [21].

The PDQ-BC subscales appear to have a good reliability [21, 22]. The Cronbach's alpha coefficients of the subscales Trait Anxiety, State Anxiety, Depressive Symptoms, Body Image, and Physical Problems ranged from 0.70 to 0.87. However, the subscale Social problems had a much lower Cronbach's alpha (0.39) because this subscale contains items that measures different aspects of social functioning [21, 22]. To determine the reliability of the PDQ-BC across time the test-retest reliability was examined using the Intraclass Correlation Coefficient (ICC) among a stable group of disease free breast cancer patients [23].

In absence of a golden standard the hypotheses testing approach was chosen to evaluate the construct validity of the PDQ-BC subscales [24]. The a priori stated hypotheses could be confirmed except for the PDQ-BC subscales Physical problems and Sexual problems. The former subscale had a slightly lower correlation with the facet Energy and Fatigue of the World Health Organization Quality of Life Assessment Instrument (WHOQOL-100) than hypothesized. The PDQ-BC subscale Sexual problems had a lower correlation with the facet Sexual activity (WHOQOL-100) than expected. In this study the construct validity could not be confirmed for the subscale Sexual problems. Regardless of the reason, from clinical experience we know that the question concerns problems with sex. Therefore, one can use this subscale in daily practice to facilitate communication about Sexual problems. The usefulness of the subscale for research purposes is less evident.

Floor effects for the PDQ-BC subscales Financial problems, Social problems, Body Image, and Sexual problems and the ceiling effect of the PDQ-BC subscale Social support were expected at time of completing. Floor effects for the subscales Body image and Sexual problems indicate that these topics are not a serious issue before start of chemotherapy. However, these problems occur frequently during follow-up [25-28]. The floor effect for the subscale Financial problems can be explained by the income protection insurance in the Netherlands. The ceiling effect for Social support was expected because most patients receive a lot of support and attention between diagnosis and end of treatment (not including hormone treatment).

Because no total score is calculated for the PDQ-BC the sensitivity and specificity should be calculated for separate subscales. Therefore, it was decided to investigate the sensitivity and specificity of the PDQ-BC subscales State anxiety and Depressive symptoms, two frequently present problems. The subscales State anxiety and Depressive symptoms appeared to have a satisfactory sensitivity and specificity compared to the HADS-A and HADS-D, respectively.

Regarding the referral advice of the PDQ-BC before start of chemotherapy ~47% of the patients had an indication for referral, of whom ~31% were actually referred [21, 23].

This percentage is in accordance with percentages found in existing studies on psychosocial problems [29, 30]. Based on the discussions during multidisciplinary meetings between health care professionals it was concluded that all referrals based on the PDQ-BC were correctly made. More patients were referred to a psychologist than to medical social worker (PDQ-BC) due to a high prevalence of patients with high scores on Trait anxiety in combination with high scores on State anxiety and/or Depressive symptoms. Patients with high levels of Trait anxiety have a tendency to respond with a rise in anxiety in stressful situations and are at risk of experiencing, for instance, more psychological distress [31, 32] and a low QOL [32, 33]. These patients may benefit from psychotherapy [34].

There were less referral indications according to the PDQ-BC (~47%) compared to the Distress Thermometer (~61%; DT). Distress has been defined as "an unpleasant experience of an emotional, psychological, social, or spiritual nature that interferes with the ability to cope with cancer treatment" [15]. The DT accompanied by the Problem List (DT-PL) is recommended in the Dutch guidelines to identify distress in cancer patients [23]. In the DT-PL distress is operationalized differently in the sense that physical problems is added to the PL. Therefore, distress can also be caused by factors such as side effects from chemotherapy, for which psychosocial care during medical treatment is not indicated. Given the difference in constructs of interest between the PDQ-BC (assessing psychosocial problems) and the DT (assessing distress) these results are difficult to compare.

In a longitudinal study on the course of State anxiety and Depressive symptoms up to one year after chemotherapy the socio-demographic, clinical, and patient factors as predictors of State anxiety and Depressive symptoms were identified. Patients completed the PDQ-BC before the start of adjuvant chemotherapy, three weeks, three months, and a year after completion of chemotherapy. Linear mixed-effects models with a specified covariance pattern model were used to examine the course and predictors of anxiety and depressive symptoms. Overall, State anxiety and Depressive symptoms declined over time. Patients without a partner, having more Physical problems, high scores on Trait anxiety, a lack of Social support and scheduled for radiotherapy are at risk for higher levels of State anxiety and Depressive symptoms and hormonal therapy is a risk factor for higher levels of Depressive symptoms. This information is useful for health care providers since it helps them to identify patients who are at risk for high scores on State anxiety and Depressive symptoms. These patients can also be offered a psychological intervention for these psychological problems.

In a pilot study, the relationship between a psychosocial screening instrument and quality of life (QOL) was examined. Patients completed the PDQ-BC and the WHOQOL-100 before start of chemotherapy (Time-1) and three months after chemotherapy (Time-2) was ended. Multiple linear regression analyses identified that patients with more physical problems, depressive symptoms, having problems with their body image and patient' factors (i.e., younger age, no partner) predicted lower scores on different QOL domains 3 months after chemotherapy. Compared to the norm scores, before start of chemotherapy the study group had significantly lower scores on the General QOL facet. Moreover, significantly lower scores were found on the domain Physical health at both time points and higher scores on the domain Social relationships at Time-1 and Time-2.

Guidelines with regard to psychosocial oncology recommend systematic psychosocial screening as part of the regular care for breast cancer patients [15, 18, 35]. Patients should be screened before start of treatment, post-treatment and every three months in the follow-up [35]. However, there is little empirical evidence that these efforts result in reducing distress and increasing patients' (HR)QOL. Questions are raising about the efficiency of screening programs because the wish for psychosocial support seems unrelated to the levels of distress [29, 36, 37]. To improve patients' well-being screening for distress alone seems insufficient. A broader focus including identification and addressing unmet needs may be necessary [38, 39]. More research is needed to understand the impact of routine psychosocial screening in breast cancer patients on patient-reported outcomes (PROs) by using the PDQ-BC.

Concerning the implementation of a psychosocial screening program in the outpatient clinic for breast cancer, it is important to communicate the strategic plan to all stakeholders. This guarantees the psychosocial follow-up care [39]. Without stakeholders' acceptance and involvement screening for psychosocial problems is useless [39]. Furthermore, studies have to be conducted to develop an appropriate psychosocial care plan for patients at risk for psychological problems.

The PDQ-BC can be considered as a feasible and reliable screening instrument for screening psychosocial problems in early stage breast cancer patients with adequate psychometric properties. Moreover, structural screening with the PDQ-BC facilitates the communication about psychosocial problems and provides adequate referral indications for extended psychosocial healthcare.

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NEDERLANDSE SAMENVATTING

Samenvatting

Wereldwijd is borstkanker de meest voorkomende kanker bij vrouwen [1]. In Nederland is borstkanker de meest voorkomende kwaadaardige aandoening bij vrouwen boven de 30 jaar [2]. Dertien procent van alle Nederlandse vrouwen krijgt borstkanker [2]. Het aantal vrouwen met borstkanker neemt toe als gevolg van uitgebreidere behandelings-mogelijkheden [3]. De diagnose borstkanker en de behandelingen zijn niet alleen geassocieerd met een aanzienlijke hoeveelheid lichamelijke klachten die interfereren met de dagelijkse activiteiten [4, 5], maar zijn ook gerelateerd aan psychosociale problemen [6-8] (d.w.z. een combinatie van psychische en sociale problemen). Aangezien 70% tot 86% van alle borstpatiënten een ziektevrije overleving van 5 jaar heeft [2], overleven steeds meer patiënten die moeten leven met de gevolgen van de ziekte en de behande-ling. In het algemeen ervaart 10% tot 53% van de borstkankerpatiënten psychosociale problemen tijdens de behandeling en follow-up [6, 7, 9]. Dit heeft een negatieve invloed op hun (gezondheidsgerelateerde) kwaliteit van leven (HR)QOL [4, 5]. Ondanks de hoge prevalentie worden psychosociale problemen door de artsen en verpleegkundigen vaak over het hoofd gezien [10-12]. Hiervoor zijn verschillende oorzaken aan te wijzen. Patiënten zijn vaak terughoudend om hun emotionele problemen te uiten aan hun zorgverleners omdat ze denken dat die niet genoeg tijd hebben. Daarnaast denken patiënten dat het niet de taak van hun zorgverleners is om hen te helpen met hun emotionele zorgen [10]. Een andere reden is dat de zorgverleners depressieve klachten zoals vermoeidheid, slaapstoornissen, verminderde eetlust vaak verwarren met lichame-lijke klachten als bijwerking van de behandeling [10, 13].

Tegenwoordig, is er veel aandacht voor het detecteren van psychosociale problematiek bij patiënten met kanker. In 2006, toen dit onderzoek is gestart, stond screenen naar psychosociale problematiek nog in de kinderschoenen en was er geen betrouwbaar en valide screeningsinstrument voor handen dat een breed scala aan psychosociale klachten meet. Om de communicatie tussen de zorgverleners (verpleeg-kundige, arts, verpleegkundig specialist) en patiënt te faciliteren en om borstkanker-patiënten met psychosociale problematiek tijdig te kunnen identificeren is de Psychosocial Distress Questionnaire-Breast Cancer (PDQ-BC) ontwikkeld en geïmplementeerd in de standaard borstkankerzorg rondom chemotherapie in het St. Elisabeth Ziekenhuis te Tilburg.

De term psychosociale problemen is in dit proefschrift gedefinieerd als een samenspel van frequent gerapporteerde psychische en sociale problemen, met inbegrip van specifieke kwesties waarvan bekend is dat ze effect hebben op (gezondheids-gerelateerde) kwaliteit van leven, alsmede risicofactoren die interfereren met het psychosociaal welbevinden van patiënten waarvoor psychosociale zorg door een psycho-sociale zorgverlener nuttig kan zijn.

De verschillende domeinen van de PDQ-BC zijn gebaseerd op een literatuurstudie en de discussies met experts op het gebied van psychosociale zorg. De PDQ-BC bestrijkt negen domeinen (angst dispositie, momentane angst, depressieve symptomen, licha-melijke problemen, sociale steun, sociale problemen, body image, financiële problemen,

seksuele problemen) die worden gemeten met 35 vragen. Hiervan zijn 31 vragen afkomstig uit bestaande vragenlijsten die betrouwbaar en valide zijn. De afkapwaarden voor verwijzing zijn afgeleid van de normscores van de oorspronkelijke, langere vragenlijsten. Van de subschalen waar de afkapwaarden niet konden worden afgeleid uit bestaande vragenlijsten, zijn de afkapwaarden voor verwijzing binnen de projectgroep bepaald. Daarnaast heeft de projectgroep besloten welke combinatie van scores een verwijzing indiceren naar maatschappelijk werk, medische psychologie of psychiatrie.

Het onderzoek naar de psychometrische kwaliteiten van de PDQ-BC laat zien dat de meeste subschalen significant met elkaar correleren [14]. De confirmatorische factoranalyse ondersteunt de interne structuur van de PDQ-BC. Bovendien laat structural equation modeling zien dat het factormodel van de PDQ-BC voorafgaand aan de analyses goed past [14].

De PDQ-BC subschalen hebben een goede betrouwbaarheid. De Cronbach's alpha coëfficiënten van de subschalen varieerden van 0.70 tot 0.87. Echter, de subschaal Sociale problemen had een lage Cronbach's alpha (0.39). Dit kan verklaard worden doordat deze subschaal items bevat die verschillende gebieden (werk, familie, vrije tijd) van sociaal functioneren meten [14, 15]. De test-hertest betrouwbaarheid, onderzocht middels de intraclass correlatiecoëfficiënt (ICC) in een stabiele groep ziektevrije borstkankerpatiënten die hun aanvullende behandeling met chemotherapie drie jaar eerder hadden afgerond, is goed [16].

Om de constructvaliditeit van de PDQ-BC te evalueren zijn vooraf gedefinieerde hypothesen getoetst. De PDQ-BC subschalen waren sterk gecorreleerd met de gerelateerde facetten van de World Health Organization Quality of Life Assessment Instrument (WHOQOL-100), de Lastmeter (Praktisch), de Center for Epidemiologic Studies Depression Scale (CES-D) en de Hospital Anxiety and Depression Scale (HADS-D). De constructvaliditeit van de PDQ-BC subschaal Seksuele problemen is niet bevestigd. Deze schaal bestaat uit een algemene vraag over seks, die in de dagelijkse praktijk goed blijkt te kunnen worden gebruikt om problemen met seks te bespreken. De bruikbaarheid van deze subschaal in onderzoek lijkt minder goed te zijn. Lage correlaties zijn gevonden tussen de PDQ-BC subschalen en vragenlijsten waarvan verwacht werd dat ze niet gerelateerd zijn.

De vloereffecten op de subschalen Financiële problemen, Sociale problemen, Body Image, en Seksuele problemen en het plafondeffect op de subschaal Sociale steun worden verwacht op het moment van afname van de PDQ-BC. Het geeft aan dat deze problemen voor de start van de chemotherapie minder vaak voorkomen. Het vloereffect op de subschaal Financiële problematiek kan worden verklaard door de Wet op inkomensbescherming in Nederland. Het plafondeffect van de subschaal Sociale steun geeft aan dat patiënten voldoende ondersteuning ervaren gedurende de fase van behandeling. Dit komt overeen met andere studies die rapporteren dat deze problemen voornamelijk voorkomen in de latere follow-up [17-19]. Omdat er geen totaal score wordt berekend voor de PDQ-BC, is besloten de sensitiviteit en specificiteit van de subschalen momentane angst en depressieve symptomen te toetsen met de HADS-A (angstschaal) en HADS-D

(depressieve symptomen). De subschalen momentane angst en depressieve symptomen hebben een goede sensitiviteit en specificiteit vergeleken met de HADS-A and HADS-D.

Vóór aanvang van de chemotherapie had ~47% van de patiënten volgens de PDQ-BC een indicatie voor verwijzing voor psychosociale hulpverlening. Daarvan werd ~31% uiteindelijk doorverwezen. Op basis van de besprekingen in het multidisciplinaire psychosociale team is geconcludeerd dat alle verwijzingen op basis van de PDQ-BC correct waren. In dit onderzoek hadden meer patiënten een verwijzing voor medische psychologie dan voor medisch maatschappelijk werk. Dit kan verklaard worden doordat de PDQ-BC dispositionele angst meet. De combinatie dispositionele angst met hoge scores op momentane angst en/of depressieve symptomen resulteert in een verwijzing naar medische psychologie. Er waren minder doorverwijzingen volgens de PDQ-BC (~47%) in vergelijking met de Lastmeter (~61%). De Lastmeter welke bestaat uit een thermometer en probleemlijst wordt in de Nederlandse richtlijn aanbevolen om distress te meten bij patiënten met kanker [20]. Distress is gedefinieerd als "een onaangename ervaring van emotionele, psychologische, sociale of geestelijke aard die interfereert met het vermogen om effectief om te gaan met de behandeling van kanker" [21]. Refererend naar deze definitie is de DT-PL anders geoperationaliseerd. In de probleemlijst zijn fysieke klachten opgenomen waardoor distress mede veroorzaakt kan worden door de bijwerkingen van chemotherapie. Voor deze fysieke klachten is psychosociale zorg niet geschikt tijdens de behandeling met chemotherapie. Omdat de PDQ-BC psychosociale problemen meet en de Lastmeter distress zijn de resultaten van screening moeilijk met elkaar te vergelijken.

In een longitudinaal onderzoek naar het verloop van momentane angst en depressieve symptomen tot een jaar na chemotherapie zijn de socio-demografische, klinische en patiënt factoren als voorspellers van momentane angst en depressieve symptomen geïdentificeerd. Patiënten vulden de PDQ-BC in vóór start van de chemo-therapie, drie weken, drie maanden en één jaar na voltooiing van de chemotherapie. Lineaire gemengde modellen met een gespecificeerde covariantiepatroon zijn gebruikt om het verloop en voorspellers van momentane angst en depressieve symptomen te onderzoeken. Patiënten zonder partner, met meer fysieke problemen, hoge scores op dispositionele angst, een gebrek aan sociale steun en radiotherapie hebben meer kans op verhoogde angst en depressieve symptomen. Hormonale therapie is een risicofactor voor meer depressieve symptomen. Deze informatie is bruikbaar om patiënten met een hoger risico op angst en depressieve symptomen te identificeren en daarmee gericht aan deze subgroep patiënten extra steun en een tijdige doorverwijzing naar een psychosociale zorgverlener te bieden. Hierdoor kan een verslechtering van de (gezondheids-gerelateerde) kwaliteit van leven mogelijk worden voorkomen. In een pilot studie is de relatie tussen screenen op psychosociale problemen en kwaliteit van leven (KvL) onder-zocht. Patiënten vulden de PDQ-BC en de WHOQOL-100 in op twee momenten: voor aanvang van de chemotherapie (tijdstip-1) en drie maanden nadat de chemotherapie was afgerond (tijdstip-2). Meervoudige lineaire regressie analyses lieten zien dat leeftijd <40 jaar, het hebben van geen partner, fysieke problemen, depressieve symptomen en problemen met lichaamsbeeld lagere scores voorspelden op de verschillende domeinen van KvL drie maanden na de chemotherapie. Voor aanvang van de chemotherapie had de

studiepopulatie significant lagere scores op het facet Algemene kwaliteit van leven in vergelijking met de normpopulatie. Bovendien werden er significant lagere scores op het domein Lichamelijke gezondheid en hogere scores op het domein Sociale relaties op beide tijdstippen gevonden. Inmiddels is in Nederland de richtlijn "Detecteren behoefte psychosociale zorg" opgesteld. Bij alle patiënten met kanker die extra psychosociale zorg nodig hebben, dient deze behoefte gesignaleerd te worden als onderdeel van de reguliere zorg [20]. Patiënten moeten worden gescreend voor aanvang van de behandeling, na de behandeling en om de drie maanden in de follow-up [20].

Omtrent screenen naar distress is wereldwijd discussie gaande [22-24]. Studies tonen weinig empirisch bewijs dat deze screenings inspanningen resulteren in het verminderen van distress en het verbeteren van de KvL van patiënten. Daar komt bij dat uit onderzoek blijkt dat de wens voor psychosociale ondersteuning niet lijkt samen te hangen met de mate van distress [25-27]. Screening lijkt op zichzelf dus niet voldoende te zijn om de KvL te verbeteren. Het zou breder getrokken moeten worden waarbij de klachten en behoeften van patiënten zorgvuldig in kaart worden gebracht waardoor juiste interventies kunnen worden aangeboden [28, 29]. Er is echter meer onderzoek nodig om het effect van routinematige psychosociale screening met de PDQ-BC en het effect op de patiënt gerapporteerde uitkomsten vast te stellen. Studies moeten worden opgezet om passende psychosociale interventies te ontwikkelen voor patiënten met een verhoogd risico op psychische problemen.

Bij de implementatie van een psychosociale screenings programma is het belangrijk om alle belanghebbenden te betrekken te informeren en te vragen om feedback. Zonder acceptatie en betrokkenheid van belanghebbenden is screening naar psychosociale problemen nutteloos. Daarbij moet de psychosociale nazorg worden gegarandeerd.

Uit dit onderzoek is gebleken dat de PDQ-BC betrouwbaar is en beschikt over adequate psychometrische eigenschappen. De PDQ-BC faciliteert zorgverleners om in gesprek te gaan met borstkanker patiënten over psychosociale problemen en is gekoppeld aan een adequaat verwijssysteem.

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Dankwoord

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LIST OF PUBLICATIONS

List of publications

- Bogaarts MP, Den Oudsten BL, Roukema JA, Van Riel JM, Beerepoot LV, De Vries J. Development of the Psychosocial Distress Questionnaire-Breast Cancer (PDQ-BC): A breast cancer-specific screening instrument for psychosocial problems. Support Care Cancer 2011;19:1485-93.

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ABOUT THE AUTHOR

About the author

Mirjam Bogaarts was born on September 1, 1966 in Gouda, the Netherlands. After completing the HAVO at the Dongemond College in Raamsdonksveer, she started her nursing career as a bedside nurse specializing in oncology and intensive care. After working at the St. Elisabeth Hospital (Tilburg, the Netherlands) within the intensive care unit for 14 years she applied for the Master's degree programme Advanced Nursing Practice (MNAP). Thereafter she started the research project 'Psychosocial screening in early-stage breast cancer patients' in September 2006. During this phase she founded a cancer support home for cancer patients and their loved ones in Tilburg, something she had long desired to accomplish.