Individual psychosocial support for breast cancer patients

Quality of life, psychological effects, patient satisfaction, health care utilization and costs

CECILIA ARVING
Dissertation presented at Uppsala University to be publicly examined in Auditorium Minus, Gustavianum, Uppsala, Friday, September 7, 2007 at 09:00 for the degree of Doctor of Philosophy (Faculty of Medicine). The examination will be conducted in Swedish.

Abstract

A randomized intervention study, with the aim to compare the effects of individual psychosocial support provided by (1) oncology nurses specially trained in psychological techniques (INS), or (2) psychologists (IPS), to (3) standard care (SC). Breast cancer patients, living in Uppsala County, and about to start adjuvant treatment at the Department of Oncology, Uppsala, were consecutively included between 1998 and 2000. The patients were assessed seven times during two years by self-administered questionnaires. Study I revealed positive effects of both INS and IPS as compared to SC on global quality of life, side effects, and post-traumatic distress. A lower proportion of patients in the intervention groups had psychosocial support provided in routine care compared with the SC group. In study II the patients reported being highly satisfied with the intervention, irrespective of profession providing the support. However, patients in the INS group reported higher levels of benefit regarding disease-related problems than those in the IPS group. In study III total Health Care costs were lower in the intervention groups and since a gain in quality-adjusted life years (QALY) was seen (mean .1 QALY), the interventions dominated. The costs for the interventions were 44 291- 48 978 SEK. In study IV, daily reporting of anxiety, depression and activity on Visual Analogue Scales (VAS) were completed during two weeks before and after the Hospital Anxiety and Depression Scale (HADS) assessments. A point assessment with the HADS captured the situation better than four weeks assessment on three VAS in the diary. The HADS was considered preferable to the diary. The conclusion is that psychosocial support is beneficial for breast cancer patients and that the intervention delivered by nurses was as effective as that given by psychologists. The costs for the interventions were limited.

Keywords: Breast cancer patients, Individual psychosocial support, Intervention study, Randomized, Quality of life, Psychological effects, Patient satisfaction, Health care utilization and costs

Cecilia Arving, Department of Public Health and Caring Sciences, Uppsala Science Park, Uppsala University, SE-75183 Uppsala, Sweden

© Cecilia Arving 2007

ISSN 1651-6206
ISBN 978-91-554-6922-1
urn:nbn:se:uu:diva-7929 (http://urn.kb.se/resolve?urn=urn:nbn:se:uu:diva-7929)
To the memory of my mother

Finish every day and be done with it.
You have done what you could.
Ralph Waldo Emerson
List of papers included in the thesis

This thesis is based on the following papers, which are referred to in the text by their Roman numerals:


IV Arving C, Glimelius B, Brandberg Y. Four weeks of daily assessments of anxiety, depression and activity compared to a point assessment with the Hospital Anxiety and Depression Scale. Submitted 2007.

Reprints were made with the kind permission of the publishers.

The studies were approved by the Ethics Committee of the Faculty of Medicine at Uppsala University.
# Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introduction</td>
<td>11</td>
</tr>
<tr>
<td>Breast cancer</td>
<td>11</td>
</tr>
<tr>
<td>Psychosocial impact of the disease</td>
<td>12</td>
</tr>
<tr>
<td>Anxiety</td>
<td>12</td>
</tr>
<tr>
<td>Depression</td>
<td>13</td>
</tr>
<tr>
<td>Post-Traumatic Stress</td>
<td>15</td>
</tr>
<tr>
<td>Health Related Quality of Life (HRQoL)</td>
<td>16</td>
</tr>
<tr>
<td>Psychosocial support</td>
<td>18</td>
</tr>
<tr>
<td>Patient satisfaction</td>
<td>22</td>
</tr>
<tr>
<td>Health care utilization and costs</td>
<td>24</td>
</tr>
<tr>
<td>The individual psychosocial support project</td>
<td>25</td>
</tr>
<tr>
<td>Aims</td>
<td>26</td>
</tr>
<tr>
<td>Methods</td>
<td>27</td>
</tr>
<tr>
<td>Design</td>
<td>27</td>
</tr>
<tr>
<td>Patients</td>
<td>27</td>
</tr>
<tr>
<td>Study I</td>
<td>29</td>
</tr>
<tr>
<td>Study II</td>
<td>31</td>
</tr>
<tr>
<td>Study III</td>
<td>31</td>
</tr>
<tr>
<td>Study IV</td>
<td>31</td>
</tr>
<tr>
<td>Individual Nurse Support (INS) and Individual Psychologist Support (IPS) interventions</td>
<td>32</td>
</tr>
<tr>
<td>Standard care (SC)</td>
<td>33</td>
</tr>
<tr>
<td>Data collection</td>
<td>33</td>
</tr>
<tr>
<td>Questionnaires</td>
<td>36</td>
</tr>
<tr>
<td>Health care utilization and days with sick leave</td>
<td>38</td>
</tr>
<tr>
<td>Cost analyses</td>
<td>38</td>
</tr>
<tr>
<td>Effectiveness and Health-economic analyses</td>
<td>39</td>
</tr>
<tr>
<td>Sensitivity analyses</td>
<td>40</td>
</tr>
<tr>
<td>Statistical analyses</td>
<td>40</td>
</tr>
<tr>
<td>Baseline analyses</td>
<td>41</td>
</tr>
<tr>
<td>Study I</td>
<td>41</td>
</tr>
<tr>
<td>Study II</td>
<td>41</td>
</tr>
<tr>
<td>Study III</td>
<td>41</td>
</tr>
<tr>
<td>Study IV</td>
<td>42</td>
</tr>
</tbody>
</table>
Results...........................................................................................................44
   The effects on HRQoL, anxiety, depression and post-traumatic stress and
   utilization of psychosocial support offered in routine care ......................44
   Patients' utilization of, benefits from and satisfaction with the intervention
   ..................................................................................................................45
   Effect of randomization on utilization of health care resources and
   number of days with sick leave, and the cost-effectiveness......................45
   Comparison of daily registrations of anxiety, depression and activity with
   the HADS, and the factor structure of the HADS ....................................46
Discussion.....................................................................................................50
   General discussion....................................................................................50
   Methodological considerations.................................................................52
   Ethical considerations..............................................................................55
   Conclusions ..............................................................................................56
   Clinical implications ................................................................................56
Acknowledgement ........................................................................................58
Svensk sammanfattning ................................................................................60
References.....................................................................................................61
Abbreviations

SEK Swedish Crowns
HADS Hospital Anxiety and Depression Scale
DSM Diagnostic and Statistical Manual
PTSD Post-Traumatic Stress Disorder
IES Impact of Event Scale
HRQoL Health Related Quality of Life
WHO World Health Organization
CBT Cognitive-behavioural therapy
SCR Support-Care-Rehabilitation project
IPS Individual Psychological Support
IPHC Intensified Primary Health Care
STAI State-Trait Anxiety Inventory
RT Radiotherapy
POMS Profile of Mood States
BDI Beck Depression Inventory
ABMT Autologous Bone Marrow Transplantation
CED-D Center for Epidemiological Studies-depression scale
DES-IV Differential Emotions Scale-IV
MHI-5 Mental Health Inventory
SPSI-R Social Problem-solving Inventory-revised
CARES Cancer Rehabilitation Evaluation System
PMRT Progressive Muscle Relaxation Training
VAS Visual Analogue Scale
SDS Symptom Distress Scale
PFS Revised Piper Fatigue Scale
SAI State Anxiety Inventory
QLI Ferrans and Powers Quality of Life Index
SF-36 Medical Outcomes Study 36-item Short-Form general Health Survey
EORTC The European Organization for Research and Treatment of
QLQ C-30 Cancer Quality of Life Core Questionnaire, version 3
INS Individual Nurse Support
SC Standard Care
N1 Nodal status 1
T1 Tumour status 1
Ax.diss Axillary dissection
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEC</td>
<td>Fluorouracil, Epirubicin, Cyclophosphamide</td>
</tr>
<tr>
<td>QLQ-BR23</td>
<td>The EORTC QLQ Breast cancer module</td>
</tr>
<tr>
<td>PAS</td>
<td>Patient Administration System</td>
</tr>
<tr>
<td>IMX</td>
<td>Infomedix</td>
</tr>
<tr>
<td>CEA</td>
<td>Cost-effectiveness Analysis</td>
</tr>
<tr>
<td>LY</td>
<td>Life-Year</td>
</tr>
<tr>
<td>QALY</td>
<td>Quality-Adjusted Life Year</td>
</tr>
<tr>
<td>ICQR</td>
<td>Incremental Cost-QALY Ratio</td>
</tr>
<tr>
<td>SPSS®</td>
<td>Statistical Package for the Social Sciences</td>
</tr>
<tr>
<td>CV</td>
<td>Coefficient of Variation</td>
</tr>
<tr>
<td>SD</td>
<td>Standard Deviation</td>
</tr>
<tr>
<td>KMO</td>
<td>Kaiser-Meyer-Olkin measure</td>
</tr>
<tr>
<td>BTS</td>
<td>Bartlett Test of Sphericity</td>
</tr>
</tbody>
</table>
Introduction

Breast cancer

In Sweden today, breast cancer is the most common type of cancer among women and is the main cause of death in young and middle-aged women (15-64 years). In high incidence countries, like Sweden, the lifetime risk to develop breast cancer is around one out of nine women and approximately 6900 new cases are reported each year. Although there has been an increase in the incidence in breast cancer since the 1960s, the death rate has decreased. Women diagnosed with breast cancer have a relative five years survival of 86% and corresponding 10 years survival is more than 75%. Most new breast cancers are detected in women aged 55-59 years. Early detection increases the chance for survival and in Sweden all women are offered regular screening from approximately the age of 40-45 years up until the age of 70-74.

Surgery is the main treatment of breast cancer, and the majority of the patients are treated with breast conserving procedures (sector resection). For large or locally advanced tumours, mastectomy is performed. In those cases, preoperative chemotherapy alone or with radiotherapy is frequently used to reduce the tumour size and eradicate microscopic foci outside the primary tumour before surgery. Axillary lymph nodes are investigated in order to decide on further treatment. For most women postoperative radiotherapy is given during five weeks to decrease the risk of loco-regional recurrence. Women at higher risk of recurrence, systemic adjuvant chemotherapy and/or hormonal therapy (e.g. anti-oestrogen) are also frequently given. In occasional patients, an antibody, trastuzumab (Herceptin®) is given to decrease the risk of recurrence.

The total cost of breast cancer care in Sweden in 2002 was estimated at Swedish Crown (SEK) 3.0 billion. The direct costs were estimated to 895 million SEK (30%) and indirect costs were 2.1 billion SEK (70%). The reason why indirect costs is so high is explained by that most newly detected breast cancers occur in patients aged below 65, thus causing significant production losses due to sick leave, early retirement, and premature mortality (52% of the indirect costs).
Psychosocial impact of the disease

The diagnosis and treatment of breast cancer force the patients and families to live, cope with and adjust to the symptoms of the disease, treatment side effects and their impact on daily life. For the breast cancer patient, the diagnosis implies a number of decisions to make and adaptation to new information during the initial phase of mammography, percutaneous fine-needle aspiration for cytology, surgery and adjuvant therapy. Each woman who is diagnosed with breast cancer reacts individually. Most women perceive psychological distress after diagnosis. In general the psychosocial impact of the disease diminishes over time and only a few develop psychiatric problems. Studies have reported that after one year the psychological problems among breast cancer patients is similar to levels found in the general population. However, during treatment the impact on quality of life can be profound. Patient related factors, such as younger age, disease related symptoms, perceived lack of support from a close relative and previous psychological treatment have been found to be associated with psychological distress.

Anxiety

In the Diagnostic and Statistical Manual of Mental Disorders IV, Generalized Anxiety Disorders are described as excessive anxiety and worry, which the individual has difficulties to control and which occurs more days than not for a period of at least 6 months. It can occur on its own, but also during other Axis I disorders such as e.g. Panic Disorders and Post-traumatic Stress Disorders. It is stated in the manual that anxiety and worry should be accompanied by at least three additional symptoms such as: restlessness, being extremely fatigued, having difficulties to concentrate, irritability and sleeping difficulties.

The prevalence rates of anxiety vary among breast cancer patients during the trajectory of treatment. High levels of anxiety have been reported among 37% of preoperative patients. Hall et al. reported that 50% of breast cancer patients had anxiety disorder during the first three months after the initial surgery. In a study by Ramirez and colleagues the prevalence rate of anxiety decreased and was reported by 20% of the patients 3 and 12 months after surgery. In a Swedish study, including 222 breast cancer patients, the largest reduction in levels of anxiety was seen during the first three months after surgery. In a recent study by Groenvold et al. low levels of anxiety during chemotherapy were reported.

Prior to radiotherapy (RT) prevalence of anxiety has been reported in 10-18% of the breast cancer patients. However, in a recent study, 32% scored above the cut-off level for possible clinical cases on the Hospital Anxiety and depression Scale (HADS). Forty per cent of the patients have been reported to feel anxious about undergoing RT at the first day and
more than 50% were afraid of possible treatment side-effects. Further, at the last day of radiotherapy, 19% of the patients in one study reported being anxious most of the time or during the whole treatment.

After RT only 6% of the patients reported feelings of anxiety compared to 18% prior to radiotherapy. One year after chemotherapy anxiety disorders were found among 8% of the sample. However, Montazeri et al. report a prevalence rate of anxiety as high as 29% after adjuvant therapy. In a study using a structured clinical interview, it was discovered that in the year after diagnosis the prevalence of anxiety or depression or both was around twice that of the general female population. Thereafter, women in remission showed similar levels of anxiety and depression to the general female population. Independent of time since diagnosis, the levels of anxiety and depression in a sample of early onset breast cancer 2-43 months post-diagnosis, were lower compared with a group of population-based reference women.

Thus, the prevalence of anxiety among breast cancer patients varies considerably, both with time and between studies. However, the prevalence of anxiety and worry seems to be more profound at diagnosis and during adjuvant therapy, although not universally reported. After therapy, anxiety in most women seems to decrease and at assessment after one year since the breast cancer diagnosis, the levels of anxiety are similar to normal background population. Despite relatively low levels of anxiety in most women, a number of women suffer from anxiety of clinical relevance and should be offered treatment.

Depression

According to the Diagnostic and Statistical Manual of Mental Disorders IV, the DSM criteria for Major Depressive Episode is that five (or more) of the following symptoms should have been present during the same 2-week period and represent a change from previous functioning. The symptoms are: depressed mood most of the day, nearly every day (experienced by the individual or observed by others), and /or loss of interest or pleasure, followed by either weight loss/gain, insomnia / hypersomnia nearly every day, feelings of restlessness or being slowed down, fatigue or loss of energy most days, feelings of worthlessness or excessive guilt, concentration difficulties or indecisiveness and / or recurrent thoughts of death. The symptoms shall cause clinically significant distress or functional impairment and shall not be due to general medical condition, substance or bereavement. Finally, the symptoms shall not meet the criteria for a Mixed Episode. However, Major Depressive Episode is only one of the subgroups belonging to Depressive Disorders, which are one of several Mood Disorders.

This somewhat complex definition may be a reason why the prevalence of depression in breast cancer patients varies between studies from 1.5-37%. Ramirez and colleagues found a prevalence rate of 5% post-operatively. In
contrast, one study\textsuperscript{13} reported a prevalence rate of 37% among breast cancer patients three months after initial surgery. Adjustment disorders and major depressive disorders were identified in 34% of patients about to start adjuvant chemotherapy\textsuperscript{23}. In a recent study\textsuperscript{18} 88% of breast cancer patients report to score in the normal range for depression on the HADS prior to RT. However, it was also noted that a significantly higher percentage of patients, having received chemotherapy were “cases”. Stiegelis et al.\textsuperscript{24} concluded in a review that depression symptoms measured by the HADS seemed to be rather low in patients before they attended RT, ranging from 1.5 to 8%.

Interestingly, Stiegelis et al.\textsuperscript{24} concluded in their review that opposite to the low prevalence rates of depression prior to RT, depressive symptoms during RT were relatively high, ranging from 12 to 31%. In a Swedish study\textsuperscript{14}, the prevalence rates of cases with depression according to the HADS stayed almost the same during one year. Approximately three months after surgery 5% of the patients, which were mainly breast cancer patients, scored as cases of depression and this was also found 6 (4%) and 12 months (4%) after surgery. In a recent study\textsuperscript{15} the symptoms of depression were more pronounced among breast cancer patients who received chemotherapy compared to those who did not, but mean scores for depression according to HADS were generally situated in the normal range.

After RT, levels of depression were reported in 3% of breast cancer patients\textsuperscript{17}. However, another\textsuperscript{20} reported that 10% of breast cancer patients were diagnosed with Major Depressive Disorder according to DSM-III-R criteria one year after chemotherapy. Adjustment disorders with depressive mood were found in another 10%, assessed through a clinical interview. The prevalence of depression was 30% at the end of RT, but two weeks later the prevalence was similar to the established norm for adults and remained so for five months.

The great variation in prevalence of depression between studies is not easy to interpret. However, it can at least partly be explained by different definitions of the concept, by variations in the tools used for assessment and in the time of the assessment\textsuperscript{6, 20, 24, 25}. The conclusions are often based on data collected at single points of assessment\textsuperscript{26}. It is important to note that facets of anxiety and depression may also be reflections of common effects of the breast cancer disease and/or medical treatments e.g. weight loss/gain, fatigue and sleeping difficulties. Using DSM criteria or standard instruments for assessing the prevalence of psychological or psychiatric complications without taking this into account may lead to falsely overestimated prevalence rates\textsuperscript{27}.

The HADS\textsuperscript{28} is a brief self-administered questionnaire used extensively in cancer settings. The HADS aims at identifying clinical “cases” (possible and probable) of anxiety disorders and/or depression among somatically ill, non-psychiatric patients. The HADS ease, speed and patient acceptability have led to its use, both in research and as a screening instrument to detect cancer
patients’ psychiatric problems in different oncology settings. The HADS have been found to have sufficient reliability and validity for detecting anxiety and depression in somatically ill patients, also in breast cancer patients. When the HADS is criticized it generally concerns its psychometric properties. It has been discussed whether the HADS is a one dimensional mood scale and if it really differentiates between anxiety and depression. Evidence for a third factor, called restlessness, has been reported. Thus, the factor structure of the HADS seems to vary across studies and populations.

The HADS is a standardized questionnaire resulting in conclusions on the basis of data collected at single points of assessment. However, little is known about the variability of breast cancer patients’ psychological problems over time. Studies including prospective assessment of anxiety and depression on a daily basis among breast cancer patients are rare.

Post-Traumatic Stress

Post-Traumatic Stress Disorder (PTSD) is a debilitating anxiety disorder resulting from a trauma exposure. In the Diagnostic and Statistical Manual of Mental Disorders IV, life-threatening illness such as cancer is specified as an extreme traumatic event, capable of precipitating PTSD. Two common responses to stressful events have been revealed in clinical studies: intrusion and avoidance. Intrusion involves unbidden thoughts and images, troubled dreams, strong pangs or waves of feelings, and repetitive behaviour. Avoidance involves ideational constriction, denial of meanings and consequences of the event, blunted sensation, behavioural inhibition or counter-phobic activity, and awareness of emotional numbness.

Through a structured clinical interview, the prevalence of PTSD was assessed in 160 women diagnosed with breast cancer Stage I. The prevalence rate was 3% post-cancer diagnosis. Hellbom, in her thesis, presents data from a sample where the patients scored medium high levels of avoidance and intrusion on the Impact of Event Scale (IES) at the time point when they just had been informed about their diagnosis or that they were to undergo surgery for a suspected breast cancer. However, after 3 months the levels of intrusion were back to normal and they stayed at that level through the follow-up period of 12 months. For Avoidance the levels decreased, but still were categorized as medium high 12 months after diagnosis. In another study, 18% of 108 patients with breast cancer reported scores indicating PTSD on the Impact of Event Scale reversed version (IES-R) at diagnosis.

The prevalence of PTSD six months later was almost the same, 16%. Mundy and colleagues compared breast cancer patients receiving conventional treatments (n=20) with patients who had autologous stem cell transplantation (n=17). Through a retrospective structured clinical interview they found no differences between groups, but the cancer diagnosis caused ex-
pressions of PTSD among 16% of the total sample. Examining the rate of PTSD regarding the women’s entire experience with breast cancer, 24% would have been positive for a PTSD diagnosis according to Mundy and colleagues. In another study, 24% reported medium high and 38% high levels of post-traumatic stress symptoms according to the IES. The sample consisted of 150 breast cancer patients receiving treatment and they were 1-5 year post diagnosis.

Using the PTSD Checklist-Cililian, version 8 5% of 142 women, post-treatment for early stage breast cancer, scored >50 and were likely to have a PTSD diagnosis. After adjuvant chemotherapy and RT 14% of 106 breast cancer patients were likely to meet PTSD diagnostic criteria assessed 12 months post-surgery with IES.

It is difficult to draw conclusions from the literature on the prevalence of PTSD among women diagnosed and treated for breast cancer. The assessment methods of PTSD varied between the studies and the prevalence of current PTSD also varied between 3-38%. The same conclusion was made in a review by Smith et al. They identified four studies which concerned the prevalence of PTSD among breast cancer patients in conjunction with primary treatment or long-time survival. They stated that the assessment methods varied between studies and the prevalence of current PTSD also varied among between 2 and 22% of the samples.

Health Related Quality of Life (HRQoL)

HRQoL has been described as a dynamic concept, changing with time and conditions. Different aspects of HRQoL also attribute different weight and relevance to different individuals.

HRQoL is considered to be a broader concept of health. The World Health Organization (WHO) suggested that health is a state of physical, mental and social well-being in addition to the absence of infirmity and disease. The construct of HRQoL incorporates areas that is affected by a medical condition or its treatment. HRQoL refers to a multidimensional concept that comprises the level of functioning or symptoms in a number of dimensions (e.g. physical, emotional, social and cognitive function or symptoms such as pain, fatigue, nausea). In addition, more specific components are of great relevance such as sexuality, body image, spirituality, economic status, role performance and self-esteem, and are sometimes included in the instruments measuring HRQoL.

During the trajectory of treatment several aspects of HRQoL have been found to be negatively affected. Seventy per cent of 253 breast cancer patients reported physical and treatment-related problems, one month post-surgery, irrespectively if the patients had been operated with mastectomy or breast conservation.
During adjuvant chemotherapy negative effects have been reported for several HRQoL aspects e.g. physical functioning, role functioning, social functioning, Global QoL, fatigue, body image and systemic therapy side-effects\textsuperscript{59}. However, after treatment these effects tended to decline. In a recent study\textsuperscript{18} chemotherapy was reported to affect most HRQoL domains and results in worsened body image, sexual functioning, as well as breast and arm symptoms. No effects of hormonal therapy were, however, reported.

No statistically significant changes in overall HRQoL were reported during adjuvant RT in 23 young women with breast cancer\textsuperscript{60}. Geinitz et al.\textsuperscript{61} evaluated 41 breast cancer patients' symptoms before, immediately after RT and 2.5 years later. Fatigue did not differ from pre-treatment levels. In a recent study\textsuperscript{15} the cognitive function were negatively effected by chemotherapy and this effect was also found 9 months after start of chemotherapy.

After treatment with adjuvant chemotherapy, the sexual functioning decreased, physical well-being became lower and more shortness of breath was reported in a sample of young women with breast cancer\textsuperscript{62}. In addition, a decrease in social support was seen over time. However, the patients also reported improvement concerning physical functioning, psychological adjustment, functional adjustment and body image 6 months post-surgery. High levels of physical functioning and emotional functioning were reported in a sample of 558 breast cancer patients one month after the last component of primary treatment, i.e. surgery, RT or chemotherapy\textsuperscript{63}. Levels of mood were normal regardless of type of surgery. Sexual functioning was worse for women who received chemotherapy compared to those who did not, regardless of type of surgery.

Shimozuma et al.\textsuperscript{58} reported that poorer HRQoL one year after surgery was significantly associated with greater mood disturbance and body image one month after surgery. No significant differences in problems due to type of surgery were reported one year later. However, problems were reported concerning numbness, tightness or stretching in the chest wall or axilla, less energy or fatigue, sleeping difficulties and hot flashes. Most women also reported high levels of functioning and HRQoL one year after surgery. Factors found to be associated with reduction of HRQoL in breast cancer patients during the year after diagnosis were low income status, positive lymph node involvement in conjunction with primary treatment, body image and mood disturbance\textsuperscript{58}. Bloom et al.\textsuperscript{9} interviewed 185 women under age 50 at diagnosis. Five years later 92 \% rated their health as good or excellent. Significant improvements were reported for surgical symptoms, worry about the future, intrusiveness of treatment, but there was a decrease in emotional support and size of social network.

The consequences of adjuvant therapy on HRQoL in breast cancer patients have been reported in several studies and these studies conclude that during treatment various negative aspects of HRQoL, such as physical and treatment related problems are frequent. Most patients, however, report lev-
Psychosocial support

Psychosocial support is a broad concept including both support from professionals, peers, family and friends. It can encompass a variety of different psychosocial activities such as communication, emotional support, education/information, cognitive functioning, social interaction and/or physical activity.

Psychosocial support interventions frequently aim at minimizing the psychosocial impact of the breast cancer disease and treatment. The interventions have been conducted either in group settings or on an individual basis. In recent years, the majority of studies have concerned group settings. Group therapy is as effective as individual therapy in reducing anxiety and depression among cancer patients, according to a meta-analysis.

Most studies exploring the potential efficacy of individual psychosocial support were performed during the 1980s. Moorey et al. reported that in a randomized individual intervention study improvements were seen in both groups. However, the group who received a cognitive-behavioural treatment (CBT) specially developed for cancer patients, improved to a greater extent compared to the group receiving supportive counselling regarding anxiety and use of coping strategies.

Methods derived from CBT have been employed in a number of structured as well as problem-focused intervention studies. These methods include techniques based on classical and operant conditioning as well as techniques to change maladaptive thinking. Methods derived from CBT has been suggested to effectively reduce emotional distress and controlled side effects in cancer patients. Jacobsen and Hann also stated that treatments using techniques derived from CBT are possible to administer in a brief period of time in order to quickly gain control of problems. Another advantage is that, during the course of illness and treatment, it can be tailored to the symptoms and problems experienced by the individual cancer patients. These techniques can be exemplified by distraction, cognitive restructuring, activity scheduling and coping self-statements. In the studies exploring the effects of psychosocial interventions using techniques derived from CBT, these have often been performed by psychologists.

A Swedish randomized study, the “Support-Care-Rehabilitation” project (SCR), with the aim of exploring the effectiveness of psychosocial interventions for cancer patients, recruited patients between 1993 and 1995 in Uppsala. Patients newly diagnosed with breast, colorectal, gastric or prostate cancer (n=527) were included. One intervention was intensified support, consisting of individual psychological support (IPS) and intensified primary health care (IPHC). The IPS comprised contact with a psychologist, working...
with techniques derived from CBT, such as ways to improve communication, activity scheduling, and relaxation, and distraction\textsuperscript{14,76}. There were no major impacts reported of the IPS on anxiety, depression, post-traumatic stress responses or various aspects of HRQoL compared to the patients in the control group. Both the IPS and control groups improved considerably and to similar extent over time. IPHC entailed extended contacts with the home care nurse in the patient’s residential area. In addition to working directly with medical problems, the nurse provided psychosocial support to the patient\textsuperscript{77}. This intervention increased follow-up contacts (90\%) in primary care compared to control patients (26\%). A majority of the patients (70\%) in the intervention group stated that the first contact was made at the “right time” and that the nurses gave expected support to a large or very large extent (67\%).

An overview of individual intervention studies using techniques derived from CBT for breast cancer patients are displayed in Table 1. The term “methods and techniques derived from CBT” was broadly defined and included any intervention containing components of either behavioural or cognitive techniques. Fifteen intervention studies were identified. Distress was the primary outcome and was measured most frequently with different self-administered standardized questionnaires. All were randomized trials, but the samples were often small. Positive effects were reported in twelve of the studies. None of the studies reported negative effects compared to control groups\textsuperscript{78-92}. 
<table>
<thead>
<tr>
<th>Author, year</th>
<th>Purpose/Instrument</th>
<th>Assessment points</th>
<th>Patients</th>
<th>CBT techniques</th>
<th>Therapists</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Davis, 1986</td>
<td>Distress: STAI</td>
<td>Baseline and 8 months</td>
<td>19</td>
<td>Biofeedback and relaxation stress training (identification of dysfunctional attitudes, positive imagery, positive self-talk, coping behaviours and relaxation)</td>
<td>Trained experienced therapist led Biofeedback: 45 min / 10 biweekly sessions (n=8) + weekly sessions (n=3) CBT: 8 weeks same format as biofeedback in three phases, education, rehearsal, application</td>
<td>Distress ↓</td>
</tr>
<tr>
<td>Larsson and Starrin, 1992</td>
<td>Distress: Faces mood scale</td>
<td>Baseline and post-radiotherapy treatment</td>
<td>64</td>
<td>Autogenic training and relaxation</td>
<td>Nurses</td>
<td>Distress ↓</td>
</tr>
<tr>
<td>Arathuzik, 1994</td>
<td>Distress: POMS</td>
<td>Baseline and after treatment</td>
<td>24</td>
<td>Relaxation &amp; visualization</td>
<td>Nurses led 20 min exercise in relaxation and 20 min guided visualization</td>
<td>Distress → Pain ↓</td>
</tr>
<tr>
<td>Marchiono et al., 1996</td>
<td>Distress: BDI</td>
<td>Baseline, 1, 3, 6 and 9 months</td>
<td>36</td>
<td>Cognitive therapy (based on Beck’s model)</td>
<td>Weekly 50 min sessions with Psychologist</td>
<td>Distress ↓</td>
</tr>
<tr>
<td>Walker et al., 1999</td>
<td>Distress: Mood rating scale HADS</td>
<td>Baseline, start of chemo-therapy, 3, 6, 9, 12, 15 and 18 weeks</td>
<td>96</td>
<td>Guided imagery (Visualization) and relaxation</td>
<td>Live training lessons (n=5) during 18 weeks &amp; audiotape and record with coloured cartoons</td>
<td>Distress ↓</td>
</tr>
<tr>
<td>Gaston-Johansson et al., 2000</td>
<td>Distress: BDI STAI</td>
<td>Baseline, 2 days before ABMT, 7 days after ABMT</td>
<td>110</td>
<td>Cognitive restructuring, imagery, and relaxation</td>
<td>Live training with Social worker (n=1) + reinforcement by nurse (n=3) + 5 min audiotape</td>
<td>Distress → Pain →</td>
</tr>
<tr>
<td>Sandgren et al., 2000</td>
<td>Distress: POMS</td>
<td>Baseline, 4 and 10 months</td>
<td>53</td>
<td>Cognitive restructuring, coping skills training, problem solving and relaxation</td>
<td>10-30 min telephone sessions</td>
<td>Distress ↓ Pain ↓</td>
</tr>
<tr>
<td>Study</td>
<td>Distress Measures</td>
<td>Timepoints</td>
<td>Intervention Description</td>
<td>Distress Impact</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-----------------------</td>
<td>-------------------</td>
<td>------------</td>
<td>------------------------------------------------------------------------------------------</td>
<td>-----------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Allen et al., 2002</td>
<td>IES, MHI-5, SPSI-R, CARES</td>
<td>Baseline, 4 and 8 months</td>
<td>Nurses In-person session (n=2) + Telephone sessions (n=4) during 12 weeks</td>
<td>Distress ↓ Unmet need ↓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Molassiotis et al., 2002</td>
<td>POMS, STAI</td>
<td>Baseline, 7 and 14 days</td>
<td>Instruction + 30 min video training program</td>
<td>Distress ↓ Duration of Nausea and Vomiting ↓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Montgomery et al., 2002</td>
<td>VAS</td>
<td>Baseline and 2 months</td>
<td>Hypnosis</td>
<td>Distress ↓ Pain ↓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schneider et al., 2003</td>
<td>SDS, PFS, SAI</td>
<td>Baseline and after chemo-therapy session</td>
<td>Tutorial with Investigator (n=1) + intervention during chemotherapy (n=1)</td>
<td>Distress → Fatigue → Anxiety ↓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hidderley and Holt, 2004</td>
<td>HADS</td>
<td>Baseline and 2 months</td>
<td>Autogenic training</td>
<td>Trained AT practitioners 2 months weekly</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Williams and Schreider, 2004</td>
<td>STAI</td>
<td>Baseline, 4 and 12 week</td>
<td>Relaxation</td>
<td>Audio taped self-care education</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mishel et al., 2005</td>
<td>POMS</td>
<td>Baseline and 10 months</td>
<td>Audio taped cognitive-behavioural coping skills and self-help manual</td>
<td>Nurses weekly telephone calls (n=4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Doorenbros et al., 2006</td>
<td>SF-36</td>
<td>Baseline, 10, 20 and 32 weeks</td>
<td>Cognitive behavioural theory guided problem-solving, communication skills,</td>
<td>Nurses lead sessions (n=10) during 18 weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Physical function ↑</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
In a review\textsuperscript{93}, it was stated that there is evidence that cognitive-behavioural counselling has a positive effect on depression in cancer patients. It was also noted that the highest effectiveness was achieved by counsellors with counselling training, but irrespective of their profession (surgeon, psychologist, social worker, and palliative counsellor), and suggested that it is important that the counsellor is knowledgeable about the cancer disease and the specifics of treatment. However, it was found that the studies reviewed lacked detailed descriptions of the credentials of the counsellors. This was true particularly for those studies that demonstrated moderate or small effects.

The quality of several of the trials included in the meta-analyses, as well as the quality of the meta-analyses themselves, can be discussed. Thus, they do not fulfil many of the requirements of evidence-based medicine. Based upon a systematic overview of the literature, Newell and colleagues\textsuperscript{74} concluded that therapist-delivered interventions for cancer patients involving individual CBT warrant further exploration with regard to short- and long-term benefits before recommendations can be made concerning their use in routine care.

Today, social workers, but very few psychologists, are employed for the treatment of psychosocial problems among cancer patients in Sweden. It has been suggested that nurses should be educated in techniques to relieve psychosocial problems\textsuperscript{94}. According to Lovejoy and Matteis\textsuperscript{95}, nurses trained in cognitive-behavioural skills should take an active role in preventing and managing cancer-related depression. An important reason for exploring the effects of psychosocial support performed by other professionals is therefore the availability of nurses with special psychosocial training and the lack of psychologists employed in oncology departments.

Patient satisfaction

Psychosocial support interventions for cancer patients are often evaluated in terms of anxiety, depressive symptoms, coping and HRQoL, as assessed by standardized questionnaires. In addition, it is vital that patient satisfaction is evaluated due to the complexity of psychosocial support interventions\textsuperscript{96}.

Carr-Hill\textsuperscript{97} defines human satisfaction as a derived complex concept that is related to a number of factors including life style, past experiences, future expectations and the value of both individuals and society. It is used as an important indicator of quality of care\textsuperscript{98, 99}. The concept “Patient satisfaction” has, however, been criticized both theoretically\textsuperscript{100} and methodologically by researchers. Sitzia\textsuperscript{100} concluded that the greatest weakness is that theoretical work has concentrated on development of models which explain the results of satisfaction studies, rather than questioning the theoretical foundations on which the concept “satisfaction” and its “measurement” are based. Sitzia\textsuperscript{101}
points out that many studies exploring patient satisfaction lack awareness of non-response bias, methodological rigor and present limited evidence of instrument reliability and validity.\(^{102}\)

Patient satisfaction is associated with continuity of care and with communication skills. Breast cancer patients who were followed-up by their general practitioner were more satisfied with care than those who were followed-up in hospital out-patient departments.\(^{103}\) In “the follow-up by general practitioner group”, 90\% met with a doctor who knew them well, compared to 50\% in “the hospital group”. More patients in “the general practitioner group” than in “the hospital group” could see the doctor on the same day for urgent problems and had enough time to discuss problems with their doctor. Further, dissatisfaction was related to aspects of patient-physician communication. The doctor should listen more to what the patient said.

Patient satisfaction is also of importance to enhance psychological adjustment and coping with the disease. In a study\(^{104}\) investigating cancer patients’ experience of and satisfaction with emotional support, support from family and senior doctors was considered most important, followed by support by consultants. Patients’ satisfaction with that emotional support was also high. Less than half of the patients who used the ward nurse for emotional support were satisfied and 39\% were satisfied with the support given by other patients. Patients’ ratings regarding support groups showed that doctor- or nurse-led groups were preferable to psychologist- and psychiatrist-led groups. Patients who expressed dissatisfaction with the emotional support received had significantly higher anxiety and depression scores on the HADS.

In a review by Mandelblatt and colleagues\(^{105}\) regarding outcomes including communication, satisfaction and HRQoL following breast cancer treatment in older women, satisfaction was enhanced if the surgeon initiated a conversation about treatment concerns. Older patients preferred that their physicians provided information in person compared to written material. Intensive nurse case management programs were found to improve mood and reduce feelings of uncertainty. Further, having less social support was associated with decreased satisfaction with the breast cancer care.

Six months after a psycho-educational intervention for 41 breast cancer patients, satisfaction with information about breast cancer increased and methods for coping with cancer were significantly associated with lower total mood disturbance scores.\(^{106}\)

Patient satisfaction with an individual psychosocial support intervention performed by psychologists was measured in the previously described Swedish intervention study.\(^{76}\) The patients stated that their problems were addressed to great extent. Further, those who reported having problems perceived more benefits as compared to patients reporting having no problems to address in the intervention. An overwhelming majority of the patients would recommend the support intervention to a close friend.
Health care utilization and costs

Health care decision makers have to decide what greatest health benefits can be extracted from a given budget and make priorities among equally effective interventions. The commonly held notion that an intervention can be considered to be adopted if it proves to be effective is fallacious. Therefore, it has been a request for costs to be included as an additional outcome, also of psychosocial intervention research in breast cancer care [107].

Psychological distress among patients may lead to increased utilization of health care resources [108-110]. Young age, fatigue and arm problems were related to higher use of health care services among breast cancer patients [111]. Breast cancer patients with anxiety and depression requested additional investigations as a part of routine follow-up visits more often [112].

A meta-analytic review [113] reported a cost reduction of about 20% associated with psychological interventions in all types of disorders. Simpson and colleagues [114] report similar results in their study. In that study, breast cancer patients receiving a cognitive-behavioural group intervention reported better psychological well-being and HRQoL than the control group. The intervention group showed a 24% reduction of direct health care costs as compared to the control group.

In the Swedish study [115], described earlier, an intervention consisting of IPHC, nutritional support and IPS, reduced the number of admissions and the number of days of hospitalization in regular hospital care among older cancer patients.

Economic analyses in psycho-oncology are, however, rare. In a review [116], 2 studies were identified exploring the utilization of health care resources among breast cancer patients. Except for the study by Simpson et al. another study by Ashbury et al. [117] reported that higher levels of fatigue increased health care utilization.

Additionally, three studies using economic or resource utilization outcomes associated with the interventions have been identified. Lemieux and colleagues [118] examined the impact of group psychosocial support on health care costs in metastatic breast cancer. They found no statistically significant differences in total costs between the groups who received psychosocial support compared to those who did not. No significant decrease in costs in favour of the intervention was revealed by an exploratory cost-effectiveness analysis (CEA). The effects of advanced nursing care on HRQoL and cost outcomes of women diagnosed with breast cancer revealed no significant cost differences between the intervention group and standard care [119]. Two forms of stress management training interventions for cancer patients undergoing chemotherapy were evaluated [120]. Costs for the self-administrated intervention were 66-68% less compared to professionally administrated intervention and in addition, patients in the self-administrated intervention group
scored better HRQoL compared to the standard care group. This was not the case in the professionally administrated intervention group.

The individual psychosocial support project

As described earlier, a breast cancer diagnosis and treatment have a number of psychological implications and often result in decreased HRQoL. Thus, development of methods to help breast cancer patients to deal with their problems is requested. Based upon the experiences from the “Support-Care-Rehabilitation-project”, described earlier, a prospective randomized intervention study, the “Individual psychosocial support-project” for breast cancer patients was initiated in autumn 1997. The project started with a training course in psychological techniques for Oncology nurses. The project recruited breast cancer patients in Uppsala County between December 2nd 1997 and December 31st 1999. Data collection was terminated in January 2002 and subsequently analyzed. The patients were randomized in blocks of 9 to one of three alternatives: Individual psychosocial support performed by (1) specially trained oncology nurses (INS) (n= 60), (2) psychologists (IPS) (n=60) or (3) standard care (SC) (n=59). The results of this study are the basis for this thesis.
Aims

The overall aim was to compare the effects of individual psychosocial support to breast cancer patients provided by (1) oncology nurses specially trained in psychological techniques “Individual nurse support” (INS), or (2) “Individual psychologist support” (IPS), to (3) standard care (SC) in a randomized intervention study, the “Individual psychosocial support project”. It was hypothesized that the two interventions would perform equal, but better than the SC group.

Specific aims of the separate studies:

I  To study the effects of individual nurse vs. psychologist psychosocial support on HRQoL, anxiety, depression and post-traumatic stress and utilization of psychosocial support offered in routine care compared to standard care.

II  To evaluate patients' utilization of, benefits from and satisfaction with the interventions.

   To explore differences in satisfaction between the interventions provided by the two professions according to whether they reported having problems or not, or if they reported scores indicating being cases of depression, anxiety or distress on the HADS and IES questionnaires, respectively.

III  To explore the effects of individual psychosocial support by INS, or IPS, compared to SC, on utilization of health care resources and number of days with sick leave, and the cost-effectiveness from the date of inclusion to two years later.

IV  To explore the variability and to what extent daily registrations of anxiety (“calm-worried”), depression (“happy-sad”) and activity (“active-passive”) in a prospective continuous diary mirror a point assessment with the HADS, and further, to examine the psychometric properties and the factor structure of the HADS in the present sample.
Methods

Design
This thesis consists of three empirical studies and one methodological study based on data from the prospective randomized, controlled intervention study the “Individual psychosocial support-project”.

Patients
A total of 425 consecutive patients, living in Uppsala County, Sweden, diagnosed with breast cancer and about to start adjuvant chemotherapy, endocrine therapy or loco-regional radiotherapy were eligible. Exclusion criteria were ongoing psychiatric illness, previous cancer diagnosis or inability to speak and understand Swedish. Out of these eligible, a consecutive series of patients (n=288) were approached by research staff and asked to participate after receiving information about the adjuvant treatment at the Department of Oncology at the Uppsala University Hospital. One hundred and seventy-nine (62%) accepted participation (Figure 1). Of the 179 patients who had accepted, 8 (4%) discontinued participation before answering the baseline questionnaires and being informed about the randomization results (Figure 1). Demographic and medical data for the whole sample are shown in Table 2.
Figure 1. Design and attrition in the “Individual psychosocial support-project”.
Patients recently operated for a primary breast cancer or planned for operation of a primary breast cancer were referred to the Department of Oncology, for primary medical consultation. The patients had undergone surgery; mostly sector resection with axillary exploration or modified radical mastectomy with axillary exploration or were planned to undergo surgery (Table 2). The patients were seen simultaneously by an oncologist and a surgeon. The strategies for post- or preoperative therapy were discussed. In general premenopausal patients with lymph node positive disease or node negative disease with ‘high risk criteria’ received adjuvant polychemotherapy, mostly FEC based therapy (Table 2). When tamoxifen was used it was given after completion of chemotherapy. Postmenopausal patients with receptor positive disease received tamoxifen at 20 mg for five years according to regional predefined recommendations (Table 2.). Polychemotherapy was given to postmenopausal patients with high risk for relapse (Table 2). Postoperative RT was given according to regional and local therapy recommendations (Table 2). A statistically significantly higher proportion ($\chi^2 = 8.83$, df=2, $p=0.01$) randomized to INS were diagnosed in stage N0 as compared to remaining groups. As a consequence, fewer INS patients received adjuvant chemotherapy, but this difference was not statistically significant.

Study I

Forty-two patients (23%) decided to discontinue participation within 6 months or did not complete all assessments due to administrative failure or illness (Figure 1). Thus, the sample size was 129. There were no statistically significant differences in attrition between the groups.
Table 2. Demographic-medical background data of the study sample and those who declined participation. Numbers in parentheses indicate percentages unless otherwise indicated

<table>
<thead>
<tr>
<th>INS</th>
<th>IPS</th>
<th>SC</th>
<th>Total</th>
<th>Declined</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>60</td>
<td>60</td>
<td>59</td>
<td>179</td>
</tr>
<tr>
<td>Age, years</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (range)</td>
<td>55 (34-72)</td>
<td>55 (23-75)</td>
<td>55 (25-87)</td>
<td>55 (23-87)</td>
</tr>
<tr>
<td>Residential area:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uppsala town</td>
<td>32 (53)</td>
<td>33 (55)</td>
<td>39 (66)</td>
<td>104 (58)</td>
</tr>
<tr>
<td>Rural district</td>
<td>28 (47)</td>
<td>27 (45)</td>
<td>20 (34)</td>
<td>75 (42)</td>
</tr>
<tr>
<td>Social status:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married/cohabitant</td>
<td>48 (80)</td>
<td>46 (77)</td>
<td>42 (71)</td>
<td>136 (76)</td>
</tr>
<tr>
<td>Single, divorced, widowed</td>
<td>12 (20)</td>
<td>14 (23)</td>
<td>15 (25)</td>
<td>41 (23)</td>
</tr>
<tr>
<td>Missing information</td>
<td>0</td>
<td>0</td>
<td>2 (3)</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Children</td>
<td>52 (87)</td>
<td>54 (90)</td>
<td>51 (86)</td>
<td>157 (88)</td>
</tr>
<tr>
<td>Stage</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>43 (72)</td>
<td>44 (73)</td>
<td>43 (73)</td>
<td>130 (73)</td>
</tr>
<tr>
<td>T2</td>
<td>12 (20)</td>
<td>11 (18)</td>
<td>12 (20)</td>
<td>35 (20)</td>
</tr>
<tr>
<td>T3/T4</td>
<td>5 (8)</td>
<td>5 (8)</td>
<td>4 (7)</td>
<td>14 (8)</td>
</tr>
<tr>
<td>N0</td>
<td>41 (68)*</td>
<td>28 (47)</td>
<td>30 (51)</td>
<td>99 (55)</td>
</tr>
<tr>
<td>Type of surgery</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sector resection + ax. diss.</td>
<td>50 (83)</td>
<td>45 (75)</td>
<td>44 (74)</td>
<td>139 (77)</td>
</tr>
<tr>
<td>Mastectomy + ax. diss.</td>
<td>9 (15)</td>
<td>13 (22)</td>
<td>15 (25)</td>
<td>37 (21)</td>
</tr>
<tr>
<td>No operation</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>3 (2)</td>
</tr>
<tr>
<td>Postoperative treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No treatment</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Radiotherapy (RT)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RT local only</td>
<td>39 (65)</td>
<td>31 (52)</td>
<td>30 (51)</td>
<td>100 (56)</td>
</tr>
<tr>
<td>RT loco-regional</td>
<td>19 (32)</td>
<td>27 (45)</td>
<td>25 (42)</td>
<td>71 (40)</td>
</tr>
<tr>
<td>Hormonal therapy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tamoxifen</td>
<td>24 (40)</td>
<td>31 (52)</td>
<td>33 (56)</td>
<td>88 (49)</td>
</tr>
<tr>
<td>Adjuvant polychemotherapy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEC:</td>
<td>17 (28)</td>
<td>29 (48)</td>
<td>23 (39)</td>
<td>69 (38)</td>
</tr>
<tr>
<td>‘Classic’, tailored and dose escalated*, with G-CSF**</td>
<td>13 (22)</td>
<td>21 (35)</td>
<td>19 (32)</td>
<td>53 (30)</td>
</tr>
<tr>
<td>Died within 6 months</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>1 Year after diagnosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recurrence-free</td>
<td>58 (97)</td>
<td>59 (98)</td>
<td>56 (95)</td>
<td>173 (97)</td>
</tr>
<tr>
<td>Deceased</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2 (1)</td>
</tr>
<tr>
<td>2 Years after diagnosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recurrence-free</td>
<td>55 (92)</td>
<td>57 (95)</td>
<td>53 (90)</td>
<td>165 (92)</td>
</tr>
<tr>
<td>Deceased</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td>6 (3)</td>
</tr>
<tr>
<td>2 Years after diagnosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recurrence-free</td>
<td>55 (92)</td>
<td>57 (95)</td>
<td>53 (90)</td>
<td>165 (92)</td>
</tr>
<tr>
<td>Deceased</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td>6 (3)</td>
</tr>
</tbody>
</table>

*Statistically significant difference, p=0.05
†Patient files were not found for three patients due to incorrect id-number
‡One patient was given both oophorectomi and tamoxifen
§FEC= fluorouracil (600mg/m²), epirubicin (60mg/m²), cyclophosphamide (600mg/m²) IV q 3 weeks x 9 excluding epirubicin and fluorouracil during the RT
¶This information is not available in the records for all patients who declined participation.
Study II

Patients randomized to INS (n= 60) and IPS (n=60) were included, thus patients in the Standard care group were excluded. Of the original 120 patients, 112 patients attended at least one session. Directly after termination of the intervention 30 (27%) patients, 12 in the INS group and 18 in the IPS group, did not answer the assessment, due to illness (n=1), the patient was deceased (n= 2), had decided to discontinue participation (n=7), or due to administrative failure or for unknown reasons (n= 20).

Fifty-seven (51%) patients completed all three scheduled assessments, 27(47%) in the INS-group and 30(53%) in the IPS-group. The reasons for not completing all assessments were illness (n=1), the patients were deceased (n=2), the patients had decided to discontinue participation (n=27), or due to administrative failure or for unknown reasons (n=25). Ten patients stated reasons for discontinuation. These reasons were "Don't want to be reminded by answering questionnaires" (n=4) and "It is tiresome to answer questionnaires" (n=6).

There were no statistically significant differences in attrition between the groups.

Study III

All patients who had answered the baseline questionnaires (n=171) was included, since analyzes were made according to intention-to-treat and only three patients randomized to the interventions did not attend a first session with the INS or IPS. Further, the stated main reason for discontinuation of participation in the project was discontent with answering the questionnaires. Data from the county hospitals utilization database were not retrieved for three patients (2%) because of incorrect id-number. Thus, 168 patients, INS (n= 55), IPS (n=57) or SC (n=56), respectively, were included with follow-up until January 2002.

Study IV

The total sample (n=171) was included except for those who did not answer the baseline questionnaires. At the three months assessment 122 patients (71%) completed both the HADS and the diary. The twelve months assessment was completed by 98 patients (57%). Twenty-one patients (12%) discontinued participation before completing the three months assessment and 28 patients did not complete the three months assessments. Reasons for not participation were: “Don’t want to complete the diary” (n=3), “Forgot” or “too sick” (n=3), “Misunderstood the instruction to complete the diary” (n=4), “The time period between the diary and HADS did not correspond” (n=4) and Administrative failure such as “Not reaching the patients by phone
to remind them to reply”, “Gone missing in the mail” or for unknown rea-
sons (n= 14). At the 12 month assessment, another 11 patients had discon-
tinued participation, 3 patients were deceased and 38 patients did not com-
plete the assessment. Reasons for not participation were: Don’t want to
complete the diary (n=3), “Forgot”, “too sick” (n=2), “Misunderstood the
instruction to complete the diary” (n=2), “The time period between the diary
and HADS did not correspond” (n=10), Administrative failure: “Not reach-
ing the patients by phone to remind them to reply”, “Gone missing in the
mail” or for unknown reasons (n= 21). Six patients did not answer the three
month assessment, but participated in the twelve month assessment.

Individual Nurse Support (INS) and Individual
Psychologist Support (IPS) interventions.

INS was the intervention carried out by nurses, and IPS was carried out by
psychologists. Both interventions used the same techniques, which were
derived from CBT72, 122. Techniques such as problem-solving, expressing
negative emotions, relaxation, distraction, graded task assignment, activity
scheduling, and ways to improve communication were employed. The INS
was carried out by two oncology nurses' specially trained in psychosocial
support of cancer patients during a four months period123. In the training
program basic techniques for assessment of psychosocial problems, for re-
lieving anxiety and depression, solving problems in conjunction with treat-
ment and disease, and ways to improve communication were taught. Partici-
pants met for four 3 h weekly lesions. Participants met between meetings to
train assessment and techniques. Follow-up discussions were held at termi-
nation and 5 months later.

Two psychologists performed the IPS. Both psychologists had theoretical
knowledge about cancer diseases and treatments. Both nurses and psycholo-
gists received supervision once every third week by a psychologist or a nurse
with extensive clinical experience of psychosocial support to cancer patients.
The supervision included analysis of tape recordings of sessions with the
patients and discussions on problems perceived by the professionals. The
intention was that both professionals should perform the interventions in a
similar fashion.

The patient was asked to relate her disease history in the first session. An
interview guide covering the following areas: Worry/anxiety; depression;
sleep disturbances; view of prognosis and future; social situation and support
from spouse, family and friends in general and with respect to the disease in
particular; communication with hospital staff; the impact of dis-
ease/treatment on the patient’s activity level such as working capacity, lei-
sure time activities and management of household tasks, was used. An esti-
mation of which problems were expected to occur in the near future, e.g. if the patient was waiting for test results or was to go through burdensome treatments was also included in the assessment.

It was jointly decided if further sessions were warranted at the end of the first session. The main reason for continuation was the presence of problems in any of the areas covered in the initial assessment. Every session was scheduled to last for forty-five to sixty minutes. The patient’s problems were identified and strategies such as problem solving, relaxation and distraction techniques, ways to improve communication, as well as activity scheduling that could help her to manage these were taught to the patient. Oral and written instructions how to practice these strategies at home were given to the patients and during the following sessions the outcome was reported. Some sessions (n= 91, 19%) were held by telephone because of long traveling distances. They had essentially the same content as sessions held face-to-face.

At the termination of the intervention, the patient was encouraged to contact again, should new problems arise. The number of sessions and the time interval between them varied, according to the need and desire of the individual patients.

Standard Care (SC)

Patients randomized to this condition were given standard care for patients in Uppsala County. This included regular contact with the patient’s oncologist and medical staff. Contact with a psychiatrist or a counsellor, e.g. social worker and/or staff at the Hospital church, for discussion of psychosocial issues was arranged if the patient’s physician or other medical staff at the oncology wards judged this to be necessary or if the patient herself made a specific request.

Data collection

Data were collected by self-administered questionnaires before randomization and 1, 3, 6, 12, 18 and 24 months later. Points of assessment and questionnaires used for the different studies are displayed in Table 3. The patients completed the baseline assessment prior to being informed about the randomization result, most frequently at the Department of Oncology, Uppsala University Hospital. At the subsequent assessments the questionnaires were mailed to the patient accompanied by written instructions and a prepaid return envelope. In order to secure the points of assessment, the patient was contacted by telephone within a fortnight if completed questionnaires had not been returned. The project staff checked the returned questionnaires for incomplete responses and contacted the patient by phone to eliminate these.
For "The Patient satisfaction questionnaire" (study II) one point of assessment was within a week after termination of the intervention, the others at fixed time-points, 6, 12 and between 18-24 months after inclusion.

The "Diary" (Study IV) supplied daily registrations of anxiety, depression and activity during two weeks just before and after the 3 and 12 months HADS assessments. Four weeks of diary recordings were chosen to secure that the daily reporting of anxiety, depression and activity captured the week preceding the HADS assessments, i.e. the time frame for the HADS assessment. The two assessment points, three and twelve months, were chosen because they represented a time period of active treatment (chemo- and radiotherapy) and a period of follow-up, respectively. The patients were contacted by telephone before diary recording was about to start and informed about the diary and how to report each evening during 4 weeks. The diary and the HADS were mailed separately to the patient accompanied by written instructions and prepaid return envelopes.

Patient files provided demographic and medical data, data on patient's utilization of psychosocial support offered in routine care and the number of sessions in the intervention groups.
Table 3. Points of assessment and questionnaires used for the four different studies in the “Individual psychosocial support project”

<table>
<thead>
<tr>
<th>Study</th>
<th>Questionnaires</th>
<th>Baseline</th>
<th>1 months</th>
<th>3 months</th>
<th>6 months</th>
<th>12 months</th>
<th>18 months</th>
<th>24 months</th>
<th>After termination of intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>EORTC QLQ C-30</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>EORTC QLQ BR-23</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>HADS</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>IES</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>STA1</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>Patient Satisfaction Questionnaire</td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>HADS</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>IES</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>EORTC QLQ C-30 Global QoL</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HADS</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td></td>
<td>IES</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>HADS</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diary</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Questionnaires

The EORTC QLQ-C30 questionnaire was developed by the European Organization for Research and Treatment of Cancer Quality of Life Study Group for assessment of HRQoL in cancer trials. Version 3 consists of 30 items, of which the first 28 items have a four-grade Likert scale format. They concern physical, role, emotional, cognitive and social functioning, and symptoms (nausea/vomiting, diarrhoea, fatigue, dyspnoea, insomnia, appetite loss, constipation, pain and financial difficulties). The remaining two items assess global quality of life and health status, respectively, both on seven-graded scales. Subscale scores are transformed to 100-grade scales, on which a higher score indicates better functioning on the function subscales and global quality of life/Health status scales, and more symptoms on symptom scales and single items. Version 3.0 has been tested in EORTC field studies.

The EORTC QLQ Breast cancer module, QLQ-BR23 comprises 23 questions, constituting five multi-item scales assessing disease symptoms such as arm and breast symptoms, side effects of treatment (surgery, chemotherapy, radiotherapy and hormonal treatment), body image and sexual functioning. In addition, single items assess sexual enjoyment, hair loss and future perspectives. The scoring system for the QLQ-BR23 is identical to that for the function and symptom scales/single items of the QLQ-C30. The module has been developed according to the EORTC QLQ guidelines. Validation studies have been completed.

The Hospital Anxiety and Depression Scale (HADS) is a fourteen-item questionnaire with two subscales measuring anxiety (HAD-A, 7 items) and depression (HAD-D, 7 items), suited for patients with somatic illness. The patient is asked to rate the presence of problems during the preceding week on a four-graded scale from 0 to 3. The scores for each subscale are summed, giving a maximum of 21. Two cut-off scores have been recommended: 8-10 to indicate cases that warrant further psychiatric investigation, and > 10 for clinical level of anxiety/depression. The Swedish version has been translated and validated.

The Impact of Event Scale (IES) is a fifteen-item scale for assessment of post-traumatic stress responses including two subscales: intrusive thoughts and images (Intrusion=IES-I), and avoidance/denial behaviours (Avoidance=IES-A). The patient indicates on a four-graded scale to what extent her experiences during the last week correspond to experiences described in each statement. Responses are weighted (i.e. the lowest score is given the value of 0, the next 1, the third 3, and the fourth 5) and coded into two sets of sums, giving a maximum of 40 for Avoidance and of 35 for Intrusion. Cut-off scores to indicate cases of low (= 8), medium (9-19) and high (≥20) levels of distress have been recommended. The IES is still one of the most...
widely used self-report measures of posttraumatic stress. The psychometric properties of the IES are satisfactory.130

The State-Trait Anxiety Inventory (STAI) includes two twenty-item instruments measuring state and trait anxiety on four-graded scales, ranging from 1 to 4.131 The STAI was used as a complement to the HAD-A in order to achieve a more detailed picture of the anxiety responses. The STAI has been used to assess anxiety among medical patients and as an outcome measure in more than 200 studies of counselling, psychotherapy, and behavioural and cognitive treatment.131 Patients were asked to answer the Trait-anxiety instrument before randomization and the State-anxiety instrument at randomization and at the following assessments. In the present study, the Trait-anxiety version was completed only at baseline (data not included) and the State-anxiety version at baseline and the following assessments.

The Patient satisfaction questionnaire includes 25 items developed for assessment of patient satisfaction. It was an extended version of the ‘IPS-patient satisfaction questionnaire’, which was used in an earlier study of psychosocial support interventions.11 Using category scales, the patient was asked to rate, e.g., the extent to which the number of sessions was sufficient, if the timing was right and whether she would recommend support of this kind to a close friend in a similar situation. The patient was also asked to score the perceived benefit of the support with respect to twelve areas, e.g., ‘Worry about the disease’, ‘Feeling depressed’, ‘Problems in relation to family, friends and others’ on a four graded scale (0= ‘None at all’, 1= ‘Some’, 2= ‘Much’ and 3= ‘Very much’). The questionnaire has not been formally validated. However, it has shown expected differences between patients with and without problems in the previous study as well as differences in scoring between items in the scale, suggesting that it is sensitive to group differences and that the patients discriminate between the items in the questionnaire (Appendix A).

The Diary was composed of three dimensions “anxiety” (calm-worried), “Depression” (happy-sad), and “Activity” (active-passive). The patients were asked to score each of the three dimensions on a 100 mm long visual analogue scale (VAS) at the end of each day during four weeks. The end-points “Calm”, “Happy” and “Active” were valued 10. Correspondingly “Worried”, “Sad” and “Passive” were valued 0. The diary was developed by Professor Lennart Melin, Department of Psychology, Uppsala. The diary has not been formally tested for validity and reliability. VAS-scale assessment of mood is, however, an established method in clinical psychology and frequently used in many similar studies (Appendix B).
Health care utilization and days with sick leave

Data on patients’ in- and out-patient visits to different professions at the Uppsala County hospitals in Study III were retrieved, retrospectively, from the “Patient administration system” (PAS) and “Infomedix” (IMX), which were the two computerized systems used by the Uppsala County during that time. All reported out-patient hospital visits to different health care professionals at the oncology, internal medicine and surgery departments in Uppsala County were summed to obtain “Out-patient hospital visits”. All calculations were made of admissions for all reasons and the length of hospitalization stay was calculated as follows: the day of admission and discharge were counted as 1 day in all, but no days were counted if admission and discharge took place on the same day. The length of stay of each admission was summed to obtain “Days of hospitalization”. Days of sick leave were retrieved from the Swedish Federal Bureau of Health Assurance, recording all sick leaves longer than 14 days. Number of sessions with the INS or IPS was retrieved from patient files and summed.

Cost analyses

The retrospective assessment of the costs for health care enclosed two years from the date of inclusion and was obtained from the Uppsala University Hospital, Uppsala, Sweden and are presented in SEK. Costs for psychosocial support by nurses and psychologists, radiation-, chemo- and hormone therapy, follow-up visits to the oncology department, other out-patient visits and for hospitalization were based on the fiscal period 2006. The cost was calculated individually for each patient and was based on the billing system used by the Uppsala University Hospital.

The individual support intervention performed by nurses or psychologists was calculated to SEK 1160 per session. Both interventions received the same cost since they were similar and the differences in wages are small. We did not include a cost for the training program prior to patient inclusion. If the patient received RT she was assigned a calculated cost of SEK 60 200, which were the average cost for postoperative breast cancer radiation with 50-54 Gy in 25-27 fractions. According to stage and other risk categories some patients also received different chemotherapy regimens. In 77% of the cases receiving chemotherapy, they received a standard regime including 5-fluorouracil, epirubicin, and cyclophosphamide (FEC). A standard FEC regime was therefore chosen to evaluate costs for chemotherapy, and were calculated to be SEK 39 650, which were assigned to the patient in the cost calculations. The costs for an implantable port, which most patients received, were not included. The cost for a 20 minutes out-patient hospital visit without x-ray was SEK 2 180, which are the cost for a visit to a physician. According to the same billing system, the hospitalization cost for a patient with complications was SEK 7 500 per day.
Effectiveness and Health-economic analyses

The effectiveness of the interventions were explored through descriptive statistics of the questionnaires EORTC QLQ C-30 global QoL subscale, and HAD-D and HAD-A subscales at the seven points of assessment. The IES-I and IES-A subscales at two points of assessment were also explored. For survival, all patients were censored after two years from inclusion.

It was hypothesized that the amount of “out-patient hospitals visits” among the present sample mainly was generated by the breast cancer treatment, and secondly, on recurrence and the co-morbidity an increasing age may produce. It was believed that these are predictors which an individual psychosocial support intervention hardly could influence, even if a previous study reported reduced utilization among elderly patients receiving IPHC. However, the intervention performed in the present study did not include home care, which was an important component in the study by Johansson and colleagues. But “out-patient hospital visits” which were not due to breast cancer treatment, recurrence and/or age might be influenced by the intervention. Studies have shown that psychological distress among patients leads to an increased utilization of health care resources and the intervention aimed at reducing psychological distress. Therefore, a hierarchic linear regression analysis was performed to determine whether the addition of information regarding psychological distress, HRQoL and randomization improved the prediction of utilization of “out-patient hospital visits” “days of hospitalization” and “days with sick leave” beyond that afforded by breast cancer treatment, recurrence and modified by age.

The following predictors were entered into the model: if the patient had received RT yes/no, chemotherapy yes/no, had a recurrence during two year from inclusion yes/no, was diseased during two years from inclusion yes/no and the patients age. Second was data from the baseline assessment with EORTC QLQ C-30 global QoL, HAD-A, HAD-D, IES-A and IES-I entered into the model and finally randomization to INS yes/no and IPS yes/no entered as dummy variables with standard care as reference variable. The same procedure was performed with “days of hospitalization” and “days with sick leave”.

A CEA was made. Life-years (LY) for the study sample were calculated for each patient and descriptive statistics provided a mean value for each randomization group. Mean Global QoL was calculated from the mean scores of the EORTC QLQ C-30 at seven points of assessment. The quality-adjusted life year (QALY) was calculated with the algorithm [(LY x mean Global QoL)/100] and the incremental QALY was calculated with the algorithm (Intervention QALY-SC QALY). The incremental cost-QALY ratio (ICQR) was calculated with the algorithm [(Difference in Cost)/(Difference in QALY)] using the cost for the interventions. The perspective of the
health care system was chosen, which meant that services, paid for by the patients were not included in the cost estimations.

Fewer individuals in the intervention groups than in the SC group used psychosocial support, provided in routine care. Thus a calculation was made to estimate the cost for psychosocial support in routine care. The number of visits that each individual could have were estimated so that the total cost for the psychosocial support, whether given as a planned intervention to all and/or as part of routine care to those in need for it, became the same in all groups. It was assumed that the cost for each routine psychosocial support visits was the same as for an intervention visit and that the mean number of routine visits was the same for all groups.

Sensitivity analyses

The robustness of the results was assessed with different methods. Firstly two methods were used to test the utilization of health care between randomization groups. In method I all patients were included. Whereas in method II, all outliers were excluded in the hierarchic linear regression analysis, > 97 in “out-patient hospital visits” (IPS, n=3 and SC, n= 3) and ≤10 in “out-patient hospital visits” (SC, n=2). Regarding “days of hospitalization”, outliers were defined as ≥ 83 (SC, n=3). No outliers were found among “days with sick leave”. Secondly, since we found that the health care costs were lower in the intervention groups, i.e. dominated the costs in the control group, a CEA was made, where all differences in health care costs were identical between groups, only counting the costs of the interventions. Thirdly, we performed a CEA assuming that there was no difference in survival between groups. Finally, we performed CEA on the subgroups who scored ≥ 8 on the HAD subscales.

It was considered unlikely that varying each component of resource utilization or cost would have resulted in a different conclusion, if similar conclusions were reached using these four approaches.

Statistical analyses

Sample size considerations were based on recommendation by Kazdin, who stated that the differences between treatment and no treatment is likely to be relatively large, as reflected in a reasonably large effect size (e.g., 0.70 to 0.80). Small sample sizes (e.g., 10-30 cases per group) are often quite sufficient to detect differences when effect size is large. Therefore, it was hypothesized that a sample of 179 breast cancer patients would be enough.

The statistical analyses were made according to the ‘intention to treat principle’. For all questionnaires substitution of missing values was made,
with the mean of each patient's responses to the remaining subscale items, provided that at least half of these had been completed. Substitution of a missing questionnaire was made, for the "Patient Satisfaction Questionnaire", when the points of assessments overlapped or when the patient made a written statement to refer to the previous questionnaire.

Baseline analyses
For all four studies analyses of significant differences at baseline between the three randomization groups was performed with the SPSS® Chi-2 tests for categorical data and One-way ANOVA for continuous variables. One-way ANOVA was chosen because parametric tests it is often robust enough to handle distributions which do not fulfil all requirements. Two-tailed t-test was used for assessment of differences for continuous variables and Chi-2 exact tests for categorical data between participants and drop-outs.

Study I
The SPSS® ANOVA with repeated measures was used to analyze the effects of randomization on HRQoL, anxiety, depression, post-traumatic stress. The analyses are based on data from patients who completed all assessments. Clinically significant differences in quality of life for patients in EORTC HRQLQ scores were interpreted, according to Osoba et al., in terms of small (5-10p), moderate (11-19p) and large (> 20p) changes and analyzed with Chi-2 tests to detect group differences. Patients clinical levels of depression, anxiety and distress were categorized according to recommended cut-off scores for the HADS and IES questionnaires. Chi-2 tests were performed for assessment of differences between the three groups regarding use of psychosocial support provided in routine care.

Study II
Chi-2 tests were performed for comparisons between the two groups regarding utilization and satisfaction of the interventions. T-tests were performed for assessment of differences regarding patients’ perceived benefit of the psychosocial support after termination of the intervention and to assess initial differences at the 6 months assessment in study II. The SPSS® ANOVA with repeated measures was used to analyze the effects of randomization on perceived benefits of the intervention.

Study III
Outliers, normality, homoscedasticity and multicollinearity were checked by the SPSS®. Normality was found to be satisfactory for “out-patient hospital
visits”, but there were outliers (described earlier). HAD-D and IES-I were removed from the analyses due to high correlations with the anxiety predictor, which made it difficult to draw inferences about the relative contribution of each predictor variable to the success of the model (multicollinearity). For “days of hospitalization” there was a small positive shrewdness in the distribution and there were outliers (described earlier). HAD-D and IES-I were also removed from the analyses due to multicollinearity. There were no outliers found for “days with sick leave. Patients’ clinical levels of anxiety and depression, avoidance and intrusion were analyzed by descriptive statistics. Assessment of significant differences between randomization groups was performed with the SPSS® Chi-2 exact tests for categorical data and One-way ANOVA for continuous variables. A hierarchic linear regression analyzes in the SPSS® using the enter method with three blocks, as described above, was used to explore which variables that might have influenced the “out-patient hospitals visits”, “days of hospitalization” and “days with sick leave”. A p-value less than 0.05 were considered statistically significant.

Study IV
The analyses were based on those who completed both the HADS and the diary at the two assessments, respectively. The means on the HADS of each patient were compared with baseline data, using paired sample t-test. Since the point assessment with the HADS represented a mean rated by the patient of the presence of problems during the preceding week, for the diary, the mean of each patient’s answer to each dimension for the week (the “HADS week”) preceding the completion of the HADS were calculated individually. Most frequently, the “HADS week” took place between the 7th and 15th day, as scheduled, at the two assessments. For the diary, also, the mean of each patient’s answer to each dimension for every four weeks at both assessments were also calculated individually. These four weeks’ means were compared, using paired sample t-test, with the mean for the “HADS week”.

The correlations between these means and each patient’s scores on the HADS subscales for the same period were analyzed using the SPSS® Pearson product moment correlation (r), bivariate, two-tailed.

The coefficient of variation (CV) was calculated as the standard deviation (SD) divided by the mean and expressed as a percentage for each patient in order to show symptom fluctuations.

Cronbach’s alpha was used to examine internal consistency of the HADS. Following Rogers et al.

Following Rogers et al.40, an exploratory factor analysis with a maximum likelihood factor extraction procedure with oblique rotation as proposed by Munro139, was performed on the full 14-items HADS in order to establish the factor structure in the present sample. The HADS was firstly forced into three factors, and secondly, an eigenvalue greater than one was chosen, in order to determine that an extracted factor accounted for a reasonably large
proportion of the total variance. The three and twelve month assessments were chosen to evaluate if the factor structure was stable over time. The Kaiser-Meyer-Olkin measure (KMO) was conducted on the data prior to factor extraction to test sampling adequacy and the Bartlett Test of Sphericity (BTS) was conducted to evaluate if the correlation matrix is suitable for factor analysis.
Results

The results of the studies of “The individual psychosocial support project” can be summarized as follows:

The effects on HRQoL, anxiety, depression and post-traumatic stress and utilization of psychosocial support offered in routine care

At baseline, those who did not complete all assessments reported statistically significant lower levels of Cognitive functioning than those who did. Except for Financial difficulties, which were more pronounced in the Standard Care (SC) group, no statistically significant group differences were found at baseline between participants.

Significant Group by Time interactions between the randomization groups were found for the subscales Global quality of life/health status, Nausea and vomiting, and Systemic therapy side effects, all in favour of the interventions groups.

The INS and IPS groups improved significantly more than the SC group in the subscales Insomnia, Dyspnoea and Financial difficulties. Also, the INS group experienced less Intrusion compared with the SC patients. This was also shown in the analyses of clinically significantly changes, where more patients in the intervention groups as compared to the SC group improved clinically from "Higher levels of distress" to “Lower levels of distress” on the IES-I. Several subscales improved statistically significantly over time in all groups, with the exception of Dyspnoea, which worsened over time in all groups.

Finally, significantly fewer patients in the intervention (INS, n=8; IPS, n=8) groups used psychosocial support provided by the hospital as compared with the SC group (n=16). Those who received psychosocial support provided in routine care had significantly higher scores at baseline in the HAD-A and IES-I subscales compared to those who did not.

The results indicate that psychosocial support was beneficial for breast cancer patients and that the intervention given by nurses was as effective as that given by psychologists.
Patients' utilization of, benefits from and satisfaction with the intervention

The results showed no significant differences in the utilization between the two intervention groups. Patients in the INS group attended between 0 and 16 sessions (mean=3.8, median=2.0) and those in the IPS group between 0 and 23 sessions (mean=4.5, median=3.0). For the patients who had more than 1 session, the mean (median) duration between the first and the last session was 172 (106) days in the INS group and 210 (178) days in the IPS group, respectively. The mean (median) time between sessions was 35 (28) days in the INS group and 45 (37) days in the IPS group, respectively. Forty-one (37%) patients continued their sessions with the nurse or the psychologist for more than 6 (n= 21), 12 (n=14) or 18 months (n= 6). No statistically significant differences were found between the groups in the duration of the intervention or in the time between sessions.

The patients were highly satisfied with the number of sessions and the timing of individual psychosocial support, irrespective of which profession provided the support. In addition, many patients reported that their problems, if present, were addressed to a large extent during the sessions and that these had fully or partly helped them in dealing with their situation. Nearly all patients stated that they would recommend the INS or IPS to a close friend in a similar situation.

Statistically significant differences were found concerning benefits of the interventions in the areas 'Worry about the disease', 'Worry about test and treatment', 'In receiving and handling information about the disease and treatment' and 'Contact with hospital', all in favour of the INS group. This was true regardless if all patients were analyzed or only those who reported having problems to assess or scored as cases/doubtful cases on the HADS and the IES at baseline.

In conclusion, the breast cancer patients were highly satisfied with an individual psychosocial support intervention, and the psychosocial support performed by nurses was not inferior to and as appreciated as that by psychologists. In fact, in areas dealing with somatic aspects, the INS group did better than the IPS group.

Effect of randomization on utilization of health care resources and number of days with sick leave, and the cost-effectiveness

Besides the differences found during the first 6 months, reported in study I, and favouring the intervention, additional statistically significant group differences were found in the present study. When analyzing each assessment
point separately, 24% of the assessed psychological measurements were statistically significant, all in favour of the intervention groups.

The average number of “out-patient hospital visits” was 51 for the INS, 57 for the IPS and 53 for the SC group, respectively. Regarding “days of hospitalization” the average number of days was numerically more than twice as many for the SC group (28 days) than for the INS (13 days) and the IPS (11 days), respectively. Average number of “days with sick leave” was 297 for the INS, 334 for the IPS and 380 days for the SC group, respectively.

Numerically, the total health care costs were almost 30% less in the intervention groups, and in the regression analyses, the interventions significantly explained some of the variability in “days of hospitalization”, constituting a substantial part of the total costs. However, these results were not stable in the sensitivity analysis excluding the outliers. Death, radiotherapy, chemotherapy and anxiety significantly influenced and increased “out-patient hospitals visits”. “Days with sick leave” were significantly influenced and increased if the patient received chemotherapy and had a recurrence.

It was not possible to calculate any cost-effectiveness ratio since the calculated costs in the intervention groups were lower than in the SC group, and the number of QALY’s higher. Thus, the intervention dominated the SC group.

In the sensitivity analyses the robustness of the result was not entirely established, although mostly similar conclusions were reached. Our results indicate that providing psychosocial support for breast cancer patients has a cost-effectiveness ratio approximately between 44 291- 48 978 SEK /QALY under the assumption that the interventions did not influence the health care utilisation. When the subgroups who scored ≥ 8 on the HAD subscales were analyzed the incremental QALY became slightly higher and consequently the ICQR decreased.

The individual psychosocial support intervention for breast cancer patients performed in the present study is thus relatively cheap and seems beneficial for breast cancer patients. However, more studies are needed to explore if such an intervention could produce net savings in addition to improved health.

Comparison of daily registrations of anxiety, depression and activity with the HADS, and the factor structure of the HADS

Patients who did not complete the 12 months assessment, i.e. were dropouts, were more depressed (HAD-D, p=0.04) than those who did. Both total HADS scores and HAD-A decreased from the 3 to the 12 months assessment, whereas depression did not (Table 6). In the diary mean values of
anxiety, depression and activity did not differ between the three and twelve month assessments (Table 6). With one exception, no differences in the mean diary scores between the weeks were found.

The CV was about 30% for all assessed aspects (Table 6) and did not differ between the two assessment points. Thus, even if a substantial proportion of the patients had either RT or chemotherapy during the first but not during the second 4-week period, this was not reflected in the variability. The day-to-day variability was rather constant for most individuals despite the nine months interval between assessments, and the difference in treatment intensity.

At both assessments, the scores of the total HAD-scale and subscales correlated with the dimensions of anxiety, depression and activity in the diary for the same week. The Calm/worried dimension in the diary showed the strongest correlation coefficients between 0.56 and 0.72, with the lowest correlation with the HAD-D and the highest for the total HADS. The Happy/sad dimension in the diary showed the lowest correlations coefficient with the HAD-A (r=0.51) and the highest with the HAD-D (r=0.66). The Active/passive dimension showed the weakest correlations, 0.36 for the HAD-A to 0.53 for the total HADS.

The Cronbach’s alpha coefficient for the total HADS, HAD-D and HAD-A showed sufficient values at both assessments. The factor analyzes demonstrated at both time points, more or less, a two-factor structure corresponding to HAD-A and HAD-D.

In conclusion, the HADS is a reliable and valid instrument for the assessment of anxiety and depression in women undergoing adjuvant treatment for breast cancer during the first year after their diagnosis. A point assessment with the HADS also seems to capture the situation of breast cancer patients at least as well as compared to four weeks assessment on three VAS in a diary. Diary recordings put more effort on the patients and the instructions might be misunderstood. The HADS is therefore preferable to the diary.
Table 6. Mean values (SD), range and CV for the total HADS and for the HADS-A and HADS-D, and for dimensions of anxiety, depression and activity in the “Diary” during four weeks and the individual “HADS week” at three points of assessment

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Week</th>
<th>N</th>
<th>Mean (SD)</th>
<th>Range</th>
<th>CV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>HADS</td>
<td>122</td>
<td>10.3 (7.1)</td>
<td>0.0-27.0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HAD-A</td>
<td>62</td>
<td>6.5 (4.5)</td>
<td>0.0-16.0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HAD-D</td>
<td>62</td>
<td>3.8 (3.2)</td>
<td>0.0-15.0</td>
<td></td>
</tr>
<tr>
<td>3 months</td>
<td>HADS</td>
<td>122</td>
<td>7.6 (6.4)</td>
<td>0.0-27.0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HAD-A</td>
<td>62</td>
<td>4.0 (3.8)</td>
<td>0.0-16.0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HAD-D</td>
<td>62</td>
<td>3.6 (3.3)</td>
<td>0.0-15.0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>“Calm/Worried”, individual week</td>
<td>122</td>
<td>6.8 (1.8)</td>
<td>2.6-10.0</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td>week 1</td>
<td>62</td>
<td>6.7 (2.0)</td>
<td>2.0-9.9</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td>week 2</td>
<td>62</td>
<td>6.8 (1.8)</td>
<td>1.0-10.0</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td>week 3</td>
<td>62</td>
<td>6.7 (2.0)</td>
<td>2.7-9.9</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td>week 4</td>
<td>62</td>
<td>6.8 (2.0)</td>
<td>0.6-9.9</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td>“Happy/Sad”, individual week</td>
<td>122</td>
<td>6.6 (1.8)</td>
<td>1.2-9.8</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td>week 1</td>
<td>62</td>
<td>6.3 (1.7)</td>
<td>2.6-9.9</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>week 2</td>
<td>62</td>
<td>6.6 (1.7)</td>
<td>1.0-10.0</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>week 3</td>
<td>62</td>
<td>6.5 (1.9)</td>
<td>1.3-9.9</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td>week 4</td>
<td>62</td>
<td>6.6 (1.8)</td>
<td>0.7-9.9</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>“Active/Passive, individual week</td>
<td>122</td>
<td>6.1 (1.8)</td>
<td>2.1-10.0</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>week 1</td>
<td>62</td>
<td>6.2 (1.8)</td>
<td>0.8-9.9</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td>week 2</td>
<td>62</td>
<td>6.2 (1.8)</td>
<td>0.7-10.0</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td>week 3</td>
<td>61</td>
<td>6.1 (2.0)</td>
<td>1.2-9.6</td>
<td>32</td>
</tr>
<tr>
<td></td>
<td>week 4</td>
<td>64</td>
<td>6.4 (1.9)</td>
<td>0.3-9.9</td>
<td>33</td>
</tr>
<tr>
<td>12 months</td>
<td>HADS</td>
<td>98</td>
<td>8.2 (6.7)</td>
<td>0.0-29.0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HAD-A</td>
<td>62</td>
<td>5.0 (4.2)</td>
<td>0.0-18.0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HAD-D</td>
<td>62</td>
<td>3.2 (3.2)</td>
<td>0.0-12.6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>“Calm/Worried”, individual week</td>
<td>94</td>
<td>6.6 (1.9)</td>
<td>2.0-10.0</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>week 1</td>
<td>94</td>
<td>6.7 (1.9)</td>
<td>1.8-10.0</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>week 2</td>
<td>94</td>
<td>6.8 (1.8)</td>
<td>2.0-10.0</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td>week 3</td>
<td>93</td>
<td>6.6 (2.1)</td>
<td>1.1-10.0</td>
<td>32</td>
</tr>
<tr>
<td></td>
<td>week 4</td>
<td>91</td>
<td>6.6 (2.1)</td>
<td>1.1-9.7</td>
<td>32</td>
</tr>
<tr>
<td></td>
<td>“Happy/Sad”, individual week</td>
<td>93</td>
<td>6.6 (1.8)</td>
<td>1.6-10.0</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>week 1</td>
<td>93</td>
<td>6.5 (1.8)</td>
<td>1.6-9.7</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>week 2</td>
<td>94</td>
<td>6.7 (1.9)</td>
<td>1.6-10.0</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>week 3</td>
<td>93</td>
<td>6.5 (1.9)</td>
<td>1.8-9.8</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>week 4</td>
<td>91</td>
<td>6.4 (2.0)</td>
<td>0.8-9.7</td>
<td>32</td>
</tr>
<tr>
<td></td>
<td>“Active/Passive, individual week</td>
<td>94</td>
<td>6.8 (1.9)</td>
<td>0.3-10.0</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>week 1</td>
<td>94</td>
<td>6.8 (1.7)</td>
<td>1.7-10.0</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>week 2</td>
<td>94</td>
<td>6.8 (1.8)</td>
<td>1.7-10.0</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>week 3</td>
<td>93</td>
<td>6.7 (1.9)</td>
<td>0.3-10.0</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td>week 4</td>
<td>91</td>
<td>6.8 (1.7)</td>
<td>1.8-9.7</td>
<td>26</td>
</tr>
<tr>
<td>Anxiety items</td>
<td>Anxiety</td>
<td>Depression</td>
<td>Scared</td>
<td>Anxiety</td>
<td>Scared</td>
</tr>
<tr>
<td>--------------------------------------------------</td>
<td>---------</td>
<td>------------</td>
<td>--------</td>
<td>---------</td>
<td>--------</td>
</tr>
<tr>
<td>(1) I feel tense or “wound up”</td>
<td>0.86</td>
<td>0.08</td>
<td>-0.59</td>
<td>0.80</td>
<td>-0.01</td>
</tr>
<tr>
<td>(3) I get a sort of frightened feeling as if something awful is about to happen</td>
<td>0.14</td>
<td>0.13</td>
<td>0.77</td>
<td>0.06</td>
<td>-0.86</td>
</tr>
<tr>
<td>(5) Worrying thoughts go through my mind</td>
<td>0.51</td>
<td>0.20</td>
<td>0.39</td>
<td>0.51</td>
<td>-0.45</td>
</tr>
<tr>
<td>(7) I can sit at ease and feel relaxed</td>
<td>0.81</td>
<td>0.08</td>
<td>-0.10</td>
<td>0.60</td>
<td>0.08</td>
</tr>
<tr>
<td>(9) I get a sort of frightened feeling like “butterflies” in the stomach</td>
<td>0.76</td>
<td>-0.07</td>
<td>0.16</td>
<td>0.78</td>
<td>-0.34</td>
</tr>
<tr>
<td>(11) I feel restless, as if I have to be on the move</td>
<td>0.69</td>
<td>0.22</td>
<td>-0.14</td>
<td>0.66</td>
<td>0.05</td>
</tr>
<tr>
<td>(13) I get a sudden feeling of panic</td>
<td>0.64</td>
<td>0.02</td>
<td>0.18</td>
<td>0.45</td>
<td>-0.17</td>
</tr>
<tr>
<td>Depression items</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(2) I still enjoy the things I used to enjoy</td>
<td>-0.01</td>
<td>0.77</td>
<td>-0.14</td>
<td>-0.01</td>
<td>-0.07</td>
</tr>
<tr>
<td>(4) I can laugh and see the funny side of things</td>
<td>0.16</td>
<td>0.62</td>
<td>0.16</td>
<td>0.01</td>
<td>-0.28</td>
</tr>
<tr>
<td>(6) I feel cheerful</td>
<td>0.20</td>
<td>0.61</td>
<td>-0.01</td>
<td>0.29</td>
<td>-0.06</td>
</tr>
<tr>
<td>(8) I feel as if I am slowed down</td>
<td>-0.05</td>
<td>0.47</td>
<td>0.17</td>
<td>0.09</td>
<td>0.05</td>
</tr>
<tr>
<td>(10) I have lost interest in my appearance</td>
<td>0.22</td>
<td>0.35</td>
<td>-0.03</td>
<td>-0.07</td>
<td>0.03</td>
</tr>
<tr>
<td>(12) I look forward with enjoyment to things</td>
<td>-0.04</td>
<td>0.91</td>
<td>0.00</td>
<td>0.02</td>
<td>0.04</td>
</tr>
<tr>
<td>(14) I can enjoy a good book or TV program</td>
<td>0.54</td>
<td>0.22</td>
<td>-0.17</td>
<td>0.34</td>
<td>0.16</td>
</tr>
</tbody>
</table>
Discussion

General discussion

We explored in a randomized study whether breast cancer patients had less distress and better HRQoL after an individual psychosocial intervention performed by either an oncology nurse specially trained in psychological techniques, or a psychologist. Differences indicating positive effects of the interventions were seen regarding disease and treatment related problems and intrusion, but also to some extent regarding anxiety and depression. The individual psychosocial support intervention for breast cancer patients performed is relatively cheap and appeared to have a positive effect on the speed of improvements seen spontaneously in the majority of patients.

The lack of marked effects in the present study might have several explanations. The overall high scores on functional scales and the few symptoms reported, i.e. “floor” or “ceiling” effects, made it difficult to improve patient well-being in the intervention groups compared to the SC group and is likely a major explanation behind the limited positive effects. Our results correspond well with many other studies reporting quite high general well-being and few symptoms among breast cancer patients. Although most of the patients scored low levels of problems, 16 patients (27%) in the SC group made use of the psychosocial support provided in routine care. This resulted in a statistically significant group difference between the intervention groups and the SC group with respect to use of psychosocial support in routine care. An interpretation is that there is a need for psychosocial support among breast cancer patients, and that the interventions provided here can diminish this.

It has been suggested that inclusion of cancer patients in psychosocial interventions should be based on the presence of psychological problems rather than on medical status. This could enhance the possibility of finding positive results in studies of these interventions. However, in “The Individual psychosocial support-project” the intervention was offered to all patients with no previous screening for psychosocial problems. At the time of the start of the project, no instruments were recommended for screening of psychosocial problems. Today, there is still debate on which instrument or cut-off scores to use. In addition, experiences from an earlier study of psychosocial support revealed that it is difficult to predict to what extent problems will arise in breast cancer patients during adjuvant treatment.
Thus, patients experiencing problems later and in need for psychosocial interventions might not be considered for psychosocial interventions.

Lack of power is another possible explanation behind the lack of marked effects. The studies performed earlier, reporting positive effects of individual psychosocial support using techniques derived from CBT\textsuperscript{78, 79, 81} had sample sizes smaller than was chosen in the “Individual psychosocial support-project”. When the present project was initiated in 1997 it was hypothesized that a sample of about 150 patients of the same sex and cancer diagnosis, randomized between three conditions and prospectively assessed, should enable the detection of statistically significant group differences, if present. However, there was a large amount of missing data, reducing the sample size further and which might have caused small but relevant group differences to go undetected. Considering the knowledge gained in the present project, the question remains whether a sample of 150 patients is large enough to detect relevant group differences from psychosocial interventions or whether the effects of psychosocial interventions are only limited? To answer that question more studies replicating previous studies are needed.

Lack of skills among the professionals providing the support could be a third explanation behind the lack of marked effects. Both nurses and psychologists were, however, specially trained and had continuous supervision during the study period. In addition, the patients were highly satisfied with the support provided in the project. The positive results seen in study II are similar to those reported in an earlier study of psychosocial support provided by psychologists\textsuperscript{76}. The patients expressed great satisfaction with the offered interventions regarding timing, number of sessions and additionally, that their problems, if present, were addressed to a large extent during the sessions. In addition, they stated that the interventions had fully or partly helped them in dealing with their situation. In the present study, the differences found between the IPS and INS groups in areas dealing with somatic aspects, consistently favouring the INS group, could be a result of the nurses’ larger knowledge about breast cancer and its treatment. In addition, they were more familiar with hospital routines, specific knowledge used by the nurses in the intervention. This finding is in accordance with the suggestion by Sellick and Crooks\textsuperscript{93} that it is important that the counsellor has knowledge about the cancer diagnosis and the specific treatments. Another possible explanation is that the psychosocial support intervention performed in the present study did not meet the need of the majority of the breast cancer patients. The general well-being among breast cancer patients appeared to be rather high. Satisfaction with health care has been found to increase with the opportunity to discuss and choose treatment together with the physicians\textsuperscript{105}. Breast cancer patients have expressed that they want their fears and concerns listened to, and they want emotional support\textsuperscript{140}. However, it has been reported\textsuperscript{104} that patients preferred support from family and senior doctors. Patients’ ratings
regarding support groups showed that doctor- or nurse-led groups were preferable to psychologist- and psychiatrist-led groups.

The health-economic evaluation of the interventions showed that the cost for the intervention was small and improved QALY with one month. Gain HRQoL was mainly produced during the first six month, which was a period of active treatment. Out-patient hospitals visits” was significantly influenced by death, adjuvant therapy, i.e. RT and chemotherapy, and psychological problems, but not by the interventions. However, what influenced “days of hospitalization” was more unpredictable. Both psychological factors and the interventions appeared to have some impact on the number of hospitalization days. Numerically, the interventions performed dominated the SC groups regarding both ”days of hospitalization”, “days with sick leave” and health care costs. The costing exercise revealed that the costs for providing the interventions to all patients diagnosed with breast cancer were limited. In addition, there is a possibility that the interventions might produce net savings in addition to improved health. Thus, health care providers have to consider if the benefits for some breast cancer patients in providing psychosocial support at a rather limited cost are large enough to be incorporated in already restrained budgets. Compared to the costs for breast cancer treatment 5 seems the cost reported here for individual psychosocial support neglect able.

The diary recordings showed relative consistency across the weeks, during two four-week periods, indicating that the HADS-reporting, corresponding to the situation during one week, covers a sufficient time period to reflect the situation of breast cancer patients. This is an important finding when using results of points of assessment to generalize about levels of anxiety and depression in these patients. Further, the results indicate that existing variations in scorings from day to day are consistent regardless of whether the patient is going through a period of active treatment or a period of follow-up. The high Cronbach’s alpha coefficients indicate that the internal consistency of the total HADS and both subscales were not challenged in a breast cancer population at two different time points, during active treatment and during follow-up. This corresponds to the findings in other studies including other populations 32, 33, 40, 134. Thus, our results support earlier findings that the HADS appear to be a valid instrument in many patient populations and in different situations. The factor analyses revealing differences in the factor structure at the two assessments are not immediately easy to interpret. However, at both time points the HAD-D and HAD-A were defined, more or less, by the factors retrieved from the analyses.

Methodological considerations

Due to the complexity of HRQoL, and psychological issues, these measurements mostly include numerous statistical tests. Therefore, there is always a
risk of finding statistically significant differences by chance (mass significance). This can not be excluded here and findings should therefore be interpreted cautiously. However, all differences detected either favoured one or both of the interventions as compared to SC, which is a highly unlikely finding if only a reflection of chance. The fact that also those in the SC group improved could at least partly be due to that about 27% of the patients in the SC group used the psychosocial support provided in routine care, being a statistically significantly higher proportion than in the intervention groups. In addition, reduction of psychosocial problems by time from diagnosis have been found in a number of studies, thus our results were expected in this respect6, 14, 19, 59. Our findings suggest that the instruments used were sensitive enough, and that the natural course of patient adjustment to the situation is responsible for the larger part of the improvements.

The great variation in prevalence of anxiety and depression between studies is a problem. It makes it difficult to compare and interpret the effects of different interventions. The variation in prevalence might, at least partly, be explained by different definitions of the concept and by variations in the tools used for assessment6, 20, 24, 25. Greater care has to be taken when report and interpret the results of an intervention with respect to definition of concepts and instruments used141.

The extended version of the ‘IPS-patient satisfaction questionnaire’76, developed for the assessment of patient satisfaction, has not been formally reliability tested or validated. It was, however, developed and used in the preceding “Support-Care-Rehabilitation” project 76 with similar results. There were also differences in the present study concerning reported benefits between the areas, which well correspond with other reports of problems perceived by cancer patients24, 76, 93, 142. Social desirability is a well-known problem when patient satisfaction is measured97. In order to give the patients an opportunity to express their honest opinion, whether favourable or not, the questionnaires were distributed by an independent investigator. The patients (Study II) were also not reminded to answer in order to diminish the problem, although it potentially increased the drop-out frequency. Another problem in measuring patient satisfaction in terms of benefit is that it is confounded with whether the respondent had any problems to address or need for help regarding that specific item. One fourth of the patients also stated having no problems to address and a similar proportion that they had no need for help. It is important in future studies, to screen the patients before inclusion in order to provide support to those who need it.

There was a large attrition in the “Individual psychosocial support-project”. The internal and external validity of studies I, II and III could therefore be questioned. Comparisons of the trajectory of scores prior to drop-out revealed that patients who dropped out reported more problems (data not shown). How this imbalance influenced the results is difficult to tell, since it could work in either direction, i.e. patients with more psychological prob-
lems might have benefited more from the interventions and improved to a greater extent. Thus, the effects of the interventions could have increased compared to standard care. Or, patients with more psychological problems might not have had benefit from the intervention and therefore the effects of the interventions could have decreased.

One methodological difficulty in study IV was that the purpose of the "diary" was to explore the variability of patients’ well-being during four weeks and to compare it to a point assessment with a standardized questionnaire. However, it was hypothesized that since the point assessment with the HADS28 represented a mean rated by the patient of the presence of problems during the preceding week, it would be comparable to a calculated mean for the diary dimension for the week (the “HADS week”) preceding the completion of the HADS. The mean of each patient’s answer to each dimension in the diary were therefore calculated individually and compared with scores on the HADS. The coefficient of variation (CV) was chosen in order to in some way show symptom fluctuations for each patient. This is a measure commonly used in economic and medical studies and not so frequently applied in psychological studies. The interpretation of the values and comparison with other ways of measuring variability could therefore be difficult. However, in this case, a CV of 30% means a change of 30 mm on a 100 mm scale and this is a rather large change. According to Osoba138 changes on the EORTC QLQ-C30 100 per cent scale, ≥ 20 points represent large clinically relevant changes.

The diary used in study IV showed consistency over time and the individual CVs for the three dimensions were rather constant. Lack of sensitivity of the instrument could be an explanation of this finding. However, the variation in diary scorings shows that there is room for variation in scoring between patients and that recording during only one or a few days is insufficient to reflect the situation of the women adequately. One week, as used in the HADS, appears optimal. Thus, the diary seemed to be a sensitive instrument and the dimensions calm/worried and happy/sad produced results in correlation with the results of the HADS.

The great variability in psychosocial problems between individuals together with the marked improvement with time after diagnosis tell that the scientific rigor must be much higher than was the case in this randomized trial in order to reveal, or exclude clinically relevant effects of a psychological intervention. This problem is shared with (virtually) all other similar intervention studies. Actually, a textbook in clinical psychological research design137 gave misleading, too simplified recommendations about e.g. patient numbers needed to detect differences. Presently, power calculations must be much stricter also in clinical psychological research. The rather limited trials performed so far, including the present one, have even if underpowered and subject to problems with both external and internal validity problems, yielded at least some indications that these interventions can be valuable.
together with valuable information how to design future trials. It is then particularly important to target only those who are in greatest need for or have the greatest chance to respond to the interventions and to define the proper end-points and their effect sizes. However, since the prevalence of psychological morbidity among breast cancer patients may be rather low, single case studies may be an alternative approach.

The methodological problems to detect relevant differences, if present in the health economic study were even more difficult. There has been a request for costs to be included as an additional outcome of psychosocial intervention research in breast cancer care in order to better evaluate the effects. But the knowledge how to collect valid data on utilization of health care and days with sick leave was limited in psychological research when the project was planned and to some extent still is. Therefore the data collected was insufficient making it difficult to analyze the data as previously planned. The possibility to retrospectively retrieve data for the study sample about patients’ in- and out-patient visits to different professions at the Uppsala University hospital and their days with sick leave was the reason for choosing the statistical method used and to perform an exploratory cost-effectiveness analyzes. However, with the knowledge gained it would have been better to prospectively collect health economic data and define the proper end-points and their effect sizes.

Ethical considerations

In the “Individual psychosocial support-project” the intervention was offered only to some patients. However, it was considered ethically acceptable since psychosocial support was available in the routine care for those who did not receive it in the project. Further, this design made it possible to explore if the intervention caused negative effects.

At inclusion patients approached by research staff were given oral and written information about the project. They were also informed that they were free to discontinue their participation at any time, without having to state a reason for this. This was also done by some (11%) even if the majority stated reasons for discontinue their participation in the project.

The patients were included in the project by the nurses and psychologists who provided the support in INS and the IPS. Differences between inclusion performance and rates were checked by directors of the project and found to be equal and satisfactory. Randomization protocols and procedures were performed by persons not involved otherwise in the project. During the first six months of the project period the INS and IPS support was monitored by tape recording some of the sessions in order to detect differences in performance. The INS and IPS was found to be equal and satisfactory by the supervisors. The IPS psychologists collected data for the INS and SC groups.
Correspondingly, collection of the data from the IPS group was performed by INS nurses. In the beginning this procedure worked excellent. However, a large amount of missing data in the INS and SC group occurred when one of the psychologists stopped her employment and moved away. Analysis of data was performed by one of the INS staff (CA), but all data and analyses were checked and controlled by directors of the project and co-authors. During the study period of two years the patients were asked to answer several questionnaires at seven points of assessment. This was the main stated reason for discontinue participation in the project. Patients stated that they did not wanted to be remained about the disease and its treatment, or that the questions did not seem relevant any longer. This is not an uncommon fact, and a selection of questionnaires was carefully done, in order to choose questionnaires that were well known for ease, speed and patient acceptability. However, this kind of experimental study requires several instruments and assessment points in order to properly explore the effect of the intervention. To jeopardize a proper evaluation of the interventions by limiting the amount of instruments and assessment points further was considered to be even more unethical.

Conclusions
The randomized study revealed positive effects on HRQoL, side effects, and post-traumatic distress of the interventions. The patients' satisfaction with the intervention was high, strengthening significant group differences, favouring the interventions. The interventions could decrease utilization of health care resources and reduce the need for psychosocial support provided in routine. Providing psychosocial support for breast cancer patients costs approximately 5000 SEK and gives 0.1 QALY, thus, it is a highly cost-effective intervention. The HADS seems to be a reliable and valid instrument for the assessment of anxiety and depression in women undergoing adjuvant treatment for breast cancer during the first year after their diagnosis. Our results indicate that professional psychosocial support by specially trained nurses is as effective as that given by psychologists, and more effective than standard care.

Clinical implications
Our results indicate a need for psychosocial support among breast cancer patients, and our results suggest that the type of intervention provided here can fulfil some of that need. During the first six months, i.e. during active treatment, some statistically significant differences were seen between groups regarding the psychological measures, all in favour of the interven-
tion groups, telling that the intervention has an effect on the speed of improvements seen spontaneously in the majority of patients. However, health care providers have to consider if there are enough benefits gained by providing psychosocial support, although at a rather low cost. An individual psychosocial support by specially trained nurses can be a realistic alternative to psychologists in routine cancer care. Accordingly, specially trained psychosocial nurses may also be beneficial in screening cancer patients for patient-related factors that might influence psychosocial adjustment to cancer among heterogeneous group of patients. Thus, the individualized treatment may be further developed and psychosocial support could reach those mostly in need for it. When assessing psychological problems among breast cancer patients it is important to have the appropriate tools. In our study the diary recordings put more effort on the patients and the instructions were sometimes misunderstood. Our results indicate that a point assessment with the HADS seems to capture the situation of breast cancer patients and therefore in the clinical settings the HADS is preferable to the diary, because of its ease, speed and patient acceptability.

Further, studies replicating previous intervention studies are needed to confirm or reject the reported results. Screening patients for psychological problems before inclusion in psychosocial intervention studies could enhance the possibility to detect statistically significant group differences.
Acknowledgement

I would like to express my sincere gratitude and appreciation to all of you that have supported me and contributed to my graduate studies and to my work in the "Individual psychosocial support" project in different ways.

Especially, I would like to thank:

All the patients who participated in the "Individual psychosocial support" project, for sharing their experiences and feelings with us.

Bengt Glimelius, my supervisor, for always so generously sharing your vast scientific knowledge with me, for constructive criticism and for quickly responding to my questions. I also want to thank you for believing and supporting me from the beginning in the early 1990s up until now, when I, among other nurses at the clinic, was involved in different project, aiming at improving the care for cancer patients.

Yvonne Brandberg, my co-supervisor, for sharing with me your deep knowledge within the field of psychooncology, for enthusiasm, and excellent guidance both as a clinical psychologist and researcher.

Per-Olow Sjödén, my late supervisor, for his unique scientific knowledge within the field of psychooncology and valuable involvement in my work and in the project.

All the members of the “Individual psychosocial support” project, Annika Thalén Lindström, Elisabet Wasteson, Heléne Karlsson, Jennifer Kurland, Margareta Schmidt, Maria Hellbom, and Ulla-Lena Gustavsson for guidance, help, and fruitful discussions. A special thanks to you, Jonas Bergh, for your constructive and helpful comments on my work. I particularly also would like to thank Inger Hjertström Östh for all help and administrative support at the Clinic. It has been invaluable.

Marianne Carlson, head of the department, for revealing the world of science to me when I was writing my first composition and Per Lindberg, head of the unit, for being so helpful and for your valuable advises.
Birgitta Johansson and Lena-Marie Petersson for being my friends and for introducing me to the world of being a PhD student.


All the former and present staff and friends at the Department of Oncology, University Hospital, Uppsala, who helped out in this project. In particular I want to thank Annika Lidin Lindqvist, for encouraging me and others to improve the cancer care at the ward and Lotta Meuller Danielsson for your challenging discussions and ideas. A special thanks to Didde Simonsson Westerström for administrative support.

My wonderful friends Aysegul, Eva, Fia, Karin, Katarina, Lena and Lotta for “being there” throughout the years, sharing feelings and experiences about life with me.

The families Eiderstedt, Anderson Ekedahl, Sjöström Ekedahl, Forsman and my “mother-in-law” Elsa Ekedahl for all pleasant dinners and fun activities.

My parents, Ulla and Lars, for your never-ending love and support. My brothers Hans and Magnus, and sister Kerstin for always supporting me and bring me up with laughter, fights, activities and lots of loud dinner discussions. I also want to thank your families and May for bringing joy to our life’s now days.

Finally, I would like to thank Mats for your love, for caring about my nutrition status and for making me laugh during all these years. I also would like to thank my hero Jonathan, our son, for being who you are and for your indulgence with my absence from “family life” during these past months. You two are the essence of my life.

The research presented in this thesis was made possible by grants from the Swedish Cancer Society.

Uppsala in April 2007

Cecilia Arving/<AFK>
Svensk sammanfattning

I ett projekt, ”Stöd-projektet”, med randomiserad design, var syftet att jämföra effekten av en individuell psykosocial stödintervention utförd av (1) onkologsjuksköterska special utbildad i psykologiska hanteringstekniker (INS), med (2) samma stöd men utfört av psykolog (IPS) och med (3) sedanvanligt omhändertagande (SC). Projektet startade 1998 och inkluderede konsekutivt under två år patienter diagnostiserade med bröstcancer, boende i Uppsala län och som skulle starta adjuvant behandling vid onkolog kliniken på Akademiska sjukhuset i Uppsala. Patienterna utvärderades vid sju tillfällen under två år med olika frågeformulär, såsom the Hospital Anxiety and Depression Scale (HADS). Studie I påvisade positiva effekter av interventionerna jämfört med SC med avseende på Global livskvalitet, behandlingsbiverkningar och stress symptom. Färre patienter i intervention grupperna utnyttjade psykosocialt stöd i rutinsjukvård jämfört med SC. Studie II påvisade att patienterna var mycket nöjda med den individuella psykosociala stödintervention de erhållit oberoende av vem som utförde interventionen. Dock rapporterade patienterna i INS gruppen högre nivåer av nytta med interventionen avseende problem relaterade till sjukdom och behandling. Efter att justerat för bröstcancer behandling, återfall, död och ålder i studie III kunde inga skillnader mellan randomiserings grupper rapporteras avseende besök i sjukvården, men interventionerna hade färre vårddagar på sjukhus. Inga skillnader kunde ses avseende sjukskrivning. Kostnaden för interventionen var 43 660-50 880 Svenska kronor för varje livskvalitet justerat år (QALY). I studie IV registrerades dagligen oro, nedsatt samhälle och aktivitet på visual analog skalar (VAS) under två veckor före och efter en punkt mätning vid 3 och 12 månader efter inklusion med HADS. HADS verkade fånga patienternas psykiska situation bättre än fyra veckors mätning på tre VAS i en dagbok och kan därför anses som mer användbar. Konklusionen är att individuellt psykosocialt stöd är till nytta för patienter med bröst cancer och att det individuella stödet utfört av sjuksköterskor var lika effektivt som det psykologerna utförd, samt att kostnaden för denna intervention var ringa.
References

15. Groenvold M, Fayers PM, Petersen MA, Sprangers MA, Aaronson NK, Mouridsen HT. Breast cancer patients on adjuvant chemotherapy report a


83. Gaston-Johansson F, Fall-Dickson JM, Nanda J, et al. The effectiveness of the comprehensive coping strategy program on clinical outcomes in breast


Appendix A
Här följer några frågor om de samtal du haft med Stöd-projektets sjuksköterska. Även om du bara har haft ett samtal med sjuksköterskan och ni sedan tillsammans bestämt att inte ha fler samtal är det värdefullt att du besvarar frågorna.

1. Hur många samtal har du haft med sjuksköterskan?
   _____ samtal

2. Har du fortfarande kontakt med sjuksköterskan?
   ☐ Ja ☐ Nej

3. Vem har tagit initiativet till samtalen? (Kryssa för ett svar)
   ☐ Alltid sjuksköterskan
   ☐ Alltid jag
   ☐ Det har varierat

4. Vad tyckte du om samtalen?
   ☐ Inte tillräckligt, skulle vilja ha fler samtal
   ☐ Tillräckligt, men skulle vilja ha möjlighet till fler samtal om jag får nya problem
   ☐ Tillräckligt
   ☐ För många, några samtal kändes onödiga

5. Vad tyckte du om tidpunkten för samtal?
   ☐ För tidigt, jag behövde inte stöd då, men senare
   ☐ Passade rätt i tiden
   ☐ För sent, hade behövt stöd tidigare

6. Vad tyckte du om innehållet i samtalen?
   ☐ Mina problem togs upp helt och hållet
   ☐ Mina problem togs upp delvis
   ☐ Mina problem togs knappast alls upp
   ☐ Mina problem togs inte alls upp
   ☐ Jag hade inga problem att ta upp
7. I hur hög grad var samtalen som du förväntat dig?
   - Helt och hållet
   - I hög grad
   - I viss grad
   - Inte alls
   - Jag hade inga förväntningar

8. Har du fått skriftliga råd av sjuksköterskan?
   - Ja
   - Nej

9. Om ja, vad tyckte du om dem?
   - De var mycket användbara
   - De var ganska användbara
   - De var inte alls användbara

10. Har samtalen hjälpit dig att hantera din situation?
    - Ja, de har varit en stor hjälp
    - Ja, de har varit till ganska stor hjälp
    - De har varit till viss hjälp
    - Nej, de var inte alls till hjälp
    - Nej, det kändes snarast värre
    - Jag behövde ingen hjälp

11. Skulle du rekommendera denna typ av samtal till en vän i samma situation som du?
    - Ja
    - Kanske
    - Troligen inte
    - Absolut inte
12. Hur mycket nytt hade du av samtalen när det gäller (ringa in en siffra)

<table>
<thead>
<tr>
<th></th>
<th>Ingen nyta alls</th>
<th>Lite nyta</th>
<th>Ganska mycket nyta</th>
<th>Mycket nyta</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oro i samband med sjukdomen</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Oro i samband med provresultat och behandling</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Nedstämndhet</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Att klara av negativa tankar</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Praktiska problem</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Problem i kontakten med anhöriga</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Problem i kontakten med vänner</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Problem i kontakten med andra (arbetskamrater, grannar et c.)</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Kontakten med sjukvården</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Att få och bearbeta information om sjukdom och behandling</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Trygghet i vården</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Planering av dagliga aktiviteter</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Annat, nämligen</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>
13. Har du några andra synpunkter på samtalen med sjuksköterskan? Vi är mycket intresserade av dina synpunkter eftersom detta är en av de första gångerna denna typ av tidiga samtal provas.
Appendix B
DAGBOK

Formulär för daglig självregistrering

---

Instruktioner

Jag har dig att byta i en sida i denna "dagboken" varje dag vid dig sluka under de följande redaerna. Varje "dagbokssida" har sju rader, och du får attka att sluka tre varje vecka.

Två av dem har det kvar dig under dagen, och att kryss som motsvarar det på var och en av de des inga "Mycket gott - mycket bra". "Mycket aktiv - mycket passar" och "Mycket lugn - mycket aktiv".

Längst ner på sidan finns några rader där du kan skriva ner om något skönt, som påverkat din sinnesrörelse, hur hårt under dagen. Om ingenting särskilt har hänt under dagen, kan du skriva "numera" noget.

Om du tycker att det är svårt att kryssa "dagboken", under något eller vissa perioder, kan du gå och se till meg på helgrenshösten.

Tack för din medverkan

---

Sätt ett kryssa varje vecka för att bekräfta hur du har sluka dig under dagen som gått.
A doctoral dissertation from the Faculty of Medicine, Uppsala University, is usually a summary of a number of papers. A few copies of the complete dissertation are kept at major Swedish research libraries, while the summary alone is distributed internationally through the series Digital Comprehensive Summaries of Uppsala Dissertations from the Faculty of Medicine. (Prior to January, 2005, the series was published under the title “Comprehensive Summaries of Uppsala Dissertations from the Faculty of Medicine”.)