

# When Breast Cancer Returns

Women's Experiences of Health, Illness and Adjustment  
During the Breast Cancer Trajectory

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## PERSEPHONE'S RETURN



*THE HANDS THAT HEAL* by Joyce Radtke

*After I was diagnosed with cancer, I became fascinated by the story of Persephone, the Greek goddess of eternal spring, of innocence. Abducted to the Underworld, Persephone ate the seeds of the pomegranate, symbol of fruition and creativity. Eventually, she was released, innocent no longer. I imagine that she felt she had a new chance to find her life again, to embrace the light. Like Persephone, I journeyed in the dark realms and used the seeds of creativity to find my way home. By imagining myself as the goddess of eternal spring, I was able to escape from the pain, the grieving, the dark and barren landscape the doctors painted for me. I have returned to the light, to living moments as they come and embracing every second I have.*

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## ABSTRACT

Although a recurrence of breast cancer is associated with significant distress, affecting health-related quality of life (HRQOL), little is known about women's experience during the recurrent breast cancer trajectory.

The primary aim of this thesis was to explore women's experiences of health, illness and adjustment to a recurrence of breast cancer. Both deductive and inductive methods were used. The first aim was to explore whether HRQOL factors predicted recurrence. The second aim was to explore distress, symptoms and HRQOL, over time in women with recurrent breast cancer. The third aim was to explore what major concerns these women experienced and how they deal with their situations living with recurrent breast cancer. The four papers included in this thesis are based on selected quantitative data (Papers I–III) and qualitative data (Paper IV).

Exploratory findings suggest that changes in physical well-being and nausea/vomiting may predict recurrence. Women with recurrent breast cancer experience multiple, concurrent, and persistent symptoms. Nearly ninety percent of the patients reported fatigue at the time of recurrence. Women with a strong sense of coherence reported a lower prevalence of symptoms and experienced lower levels of distress and better perceived adjustment to their illness, as well as perceived a better health and quality of life. Distress had a major impact on HRQOL. Over time, women adjusted to the many implications of a life-threatening illness through personal transition. By making sense of living with a threat to their lives, the women adjusted to their recurrence.

The findings highlight the major existential impact of a recurrence. Promoting health is possible, even in severe illness and in unchangeable and almost unbearable situations. Opportunities to manage adversity remain. Women may transcend their illness by finding new meaning through discovering or re-discovering significant values in life, and creating wellness by being in the present moment.

*Key words:* recurrent breast cancer, health, illness, adjustment, health-related quality of life, sense of coherence, distress, symptoms.

## ORIGINAL PAPERS

The thesis is based on the following papers, referenced in the text by Roman numerals I–IV:

- I           Kenne Sarenmalm, E., Odén, A., Öhlén, J., Gaston-Johansson, F., Holmberg, S., & Bernhard, J., Changes in health-related quality of life predict recurrent breast cancer. (Submitted for publication).
  
- II           Kenne Sarenmalm, E., Öhlén, J., Jonsson, T., & Gaston-Johansson, F., (2007). Coping with recurrent breast cancer - predictors of distressing symptoms and health-related quality of life. *Journal of Pain and Symptom Management* 34(1): 24-39.
  
- III          Kenne Sarenmalm, E., Öhlén, J., Odén, A., & Gaston-Johansson, F., (2007). Experience and predictors of symptoms, distress and health-related quality of life over time in women with recurrent breast cancer. *Psycho-Oncology*. 2007 Sep 20; [Epub ahead of print].
  
- IV          Kenne Sarenmalm, E., Thorén-Jönsson, A-L., Gaston-Johansson, F., & Öhlén, J., Making sense of living under the shadow of death – Adjusting to a recurrent breast cancer illness. (Submitted for publication).

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**PAPERS I-IV**

## ABBREVIATIONS

EORTC	European Organization for Research and Treatment of Cancer
EORTC QLQ; C-30	European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire; Breast Cancer
GDI	Global Distress Index
GT	Grounded Theory
HAD	Hospital Anxiety Depression Scale
HRQOL	Health Related Quality of Life
IBCSG	International Breast Cancer Study Group
IBCSG-QoL	International Breast Cancer Study Group Quality of Life Core Questionnaire
MSAS	Memorial Symptom Assessment Scale
MSAS-PHYS	Memorial Symptom Assessment Scale, Physical Scale
MSAS-PSYCH	Memorial Symptom Assessment Scale, Psychological Scale
SOC	Sense of Coherence
TMSAS	Total Memorial Symptom Assessment Scale
QOL	Quality of Life



## INTRODUCTION

The return of breast cancer is frequently associated with significant distress (Okamura et al., 2000; Andersen et al., 2005), and the recurrent breast cancer is perceived as much more distressing than the initial breast cancer (Northouse et al., 1995). Although a recurrent breast cancer will be treated, these women are challenged with a threat to their lives, along with further demanding treatments and debilitating side-effects. Apart from the emotional impact, women are faced with major concerns about their future and family, as well as feelings about why the cancer developed, and they also often perceive that there has been a delay in diagnosis and difficulties in communicating with their doctors (Turner et al., 2005). The recurrence of breast cancer generates significant impairments in physical, functional and emotional well-being in women and their family members (Northouse et al., 2002), and couples who are facing the woman's recurrent breast cancer work actively to balance their lives trying to manage the women's everyday illness, surviving, healing and preparing for her death (Lewis & Deal, 1995). For a significant proportion of women the recurrence is an emotionally traumatic event, and particularly in women with past life stressors and lack of social support (Koopman et al., 1998; Butler et al., 1999). The recurrence of breast cancer has a significant impact on health-related quality of life (Bull et al., 1999; Chie et al., 1999; Thornton et al., 2005; Lidgren et al., 2007), and is also associated with various distressing symptoms (Hanson Frost et al., 2000; Okamura et al., 2000; Kissane et al., 2004; Ell et al., 2005; Okamura et al., 2005; Burgess et al., 2005; Turner et al., 2005; Grabsch et al., 2006).

For women who experience recurrence, adjustment to the new diagnosis means adjusting to the prospect of a far more limited and uncertain future than they hoped for, and most women with recurrent breast cancer have to manage living with a persistent life-threatening illness for the rest of their lives (Rowland & Massie, 1998). While recurrent breast cancer is a major stressor for any woman, there is a great variability in women's emotional responses and adjustment to the illness (Spencer et al., 1998). A growing area of interest is the personal growth and transformation of individuals as they adjust to a life-threatening illness, indicating that cancer may be viewed as a psychosocial transitional event which alters an individual's presumptive world view, with the potential to engender both positive and negative outcomes (Andrykowski et al., 1996; Cordova et al., 2001). Although previous research shows that patients with recurrent cancer experience a wide array of concerns and psychosocial problems, there are few empirical studies focusing on women's experiences during the recurrent breast cancer illness trajectory.

Despite advances in the understanding of the psychosocial impact of cancer, suggesting that cancer should be regarded as a bio-psychosocial illness, care is still mostly bio-medically focused (Bultz & Carlsson, 2006). Because of the limitations imposed on quantity of life by the return of the disease, maintaining their quality of life is essential to women with recurrent breast cancer. While a great deal of attention has been directed to the psychosocial aspects of initial breast cancer, less has been paid to the psychosocial aspects of recurrent breast cancer. The health-related quality of life and distress experiences and their interrelations with physical symptoms are complex, clinically challenging problems. These circumstances may have psychosocial implications, and given the frequency of recurrence, further research attention is needed (Carlson et al., 2000). To date, however, there has been little research on experiences of health, illness and adjustment in women with recurrent breast cancer.

## BACKGROUND

In this thesis, distinctions are made between health, illness and disease. In accordance with Kleinman et al., (1978) health is not viewed as the absence of illness and illness is not identical with disease. Illness is regarded as the human experience of loss or dysfunction, whereas disease is the manifestation of aberration at the tissue, cellular, or organ levels (Benner & Wrubel, 1989). This definition of disease is necessary to analyzing certain phenomena for the purposes of diagnosis, prognosis and therapy (Engelhart, 1981), and it is essentially a bio-medical concept related to organic pathology, while it does not encompass social, psychological and behavioral aspects of illness (Fitzpatrick, 1984). Illness differs from disease, and may be more positively influenced by a meaningful sense of hope, or by fear, despair and meaning-making processes. Disease may also alter the experience of illness, in the case of recurrent breast cancer, for instance, owing to the direct impact of neuroendocrine and other bodily changes (Benner & Wrubel, 1989).

### ***Recurrent breast cancer disease and treatment***

Breast cancer is the most common invasive cancer disease among women in Europe (Ferlay et al., 2007). Each year, more than 330 000 women are diagnosed with breast cancer and 90 000 die of breast cancer per year in the European Union. Breast cancer incidence increases with age, and 65% of breast cancer patients are 55 or older (European Parliamentary Group on Breast Cancer, 2007). With its high incidence and relatively good prognosis, breast cancer is the most prevalent cancer among women, with an estimated 4.4 million women alive who had breast cancer diagnosed within the last 5 years (Parkin et al., 2005). Although, the prognosis for breast cancer generally is rather good, with estimated average survival rates being 73%, and 57% in developing countries (Parkin et al., 2005), the duration of individual survival varies greatly, even after account is taken of disease stage and treatment. A decline in breast cancer mortality has been reported, as a result of earlier detection and improved treatment. However, this decline was observed in younger women, and because Europe has an ageing population, the number of deaths from breast cancer in Europe is still rising (Ferlay et al., 2007). Despite improved survival rates in recent years, women with a history of breast cancer are at risk of recurrence for the rest of their lives (Burstein & Winer, 2000).

The clinical course of breast cancer may vary depending on hormone receptor status. Women with ER-negative tumors have higher rates of recurrence during the first two years of follow-up, but not thereafter, with a similar trend observed for breast cancer deaths. Women with ER-negative tumors have significantly higher rates of recurrence in the viscera and soft tissues, while women with ER-positive tumors have higher rates of recurrence involving bone (Hess et al., 2003).

Breast cancer may reoccur locally in the breast or scar, regionally via lymph nodes, or systemically through distant metastases. The most common sites of distant metastases are bone, followed by local recurrence, lung, liver, and brain (Elder et al., 2006). Although local recurrences may be cured, they are indicators of a poor prognosis (Fortin et al., 1999), with potential to metastasize (Engel et al., 2003). Most recurrences in the breast are diagnosed within 5 years of initial diagnosis, with a peak rate of recurrence during the second year following diagnosis, but a recurrence may occur 5 to 10 years after initial diagnosis, and even later recurrences are not uncommon (Saphner et al., 1996; Burstein & Winer, 2000; Elder et al., 2006).

While early recurrence (2-5 years) probably represents a relapse of the residual breast cancer disease, late recurrence (>5 years) is suggested to represent a new primary breast tumor (Galper et al., 2005).

Once metastases appear, the potential for cure is limited. Depending on site of recurrence and tumor factors 5-year survival rate after a recurrence is 20% and the median survival time for patients with metastatic breast cancer varies from 12-24 months (Gonzalez-Angulo et al., 2007). Patients with bone metastases have the best prognosis, with a median survival of approximately 2 years (Elder et al., 2006). Trends in survival for patients with recurrent breast cancer seem to be slightly improving, particularly in patient with a more recent initial diagnosis. Other predictors of longer survival are longer disease-free interval, smaller primary tumor size, lower stage of disease, fewer involved lymph nodes, non-visceral dominant site of recurrence, and positive estrogen receptor status of primary tumor (Giordano et al., 2004). Furthermore, compared to ductal primaries, patients with lobular histology seem to have worse prognosis (Galper et al., 2005).

While a number of treatment approaches have been used to manage recurrent breast cancer, complete remission cannot be achieved in most cases (Greenlee et al., 2000), and the goals for treatment are generally palliative (Chung & Carlsson, 2003). Treatment options in recurrent breast cancer are surgery and radiation therapy, as well as systemic therapy including chemotherapy, endocrine and biological therapy. Chemotherapy is indicated for patients with tumors unresponsive to hormonal therapy or more aggressive disease and metastases (Crown et al., 2002). Endocrine therapy is indicated for patients with hormone-receptor positive tumors (Carlson & Henderson, 2003). Biological therapy such as Trastuzumab (Herceptin) is used to treat recurrent breast cancer that is Her2-positive (Nishimura et al., 2008). Bisphosphonates and radiotherapy are used for the treatment and prevention of bone pain and fracture in women with bony metastases (Coleman, 2005). Contrary to initial breast cancer, there are no consistent treatment guidelines regarding women with recurrent breast cancer, and improvements are required, including the development of uniform global guidelines and recommendations for specific patient groups (Wardley, 2007). Thus survival is variable, and in the care of women with recurrent breast cancer the primary goal is to prolong survival and improve quality of life (Chung & Carlson, 2003).

### ***Theoretical perspective***

This thesis uses a salutogenic perspective based on the work of Anton Antonovsky (1979, 1987). Salutogenesis derives from *Latin*. salus=health; *Greek*. genesis=the origin of, and the salutogenic perspective is an orientation to health and illness as a complement the traditional pathogenic perspective. While pathogenesis is concerned with the origin of disease (pathos), salutogenesis focuses on resources directed towards maintaining or improving health (Antonovsky, 1979). Instead of focusing on singular pathogenic factors, from a holistic point of view on health and illness the salutogenic orientation focuses on conditions fostering and promoting an individual's well-being. Salutogenesis is a dynamic, flexible approach with a focus on ability and capacity to cope, as well as a major life orientation, focused on problem solving (Lindström & Eriksson, 2005). The key to health is seen as the individual's coping resources, not the absence of disease. The capacity to use resources to promote health is referred as a sense of coherence, which is a combination of the individual's ability to comprehend, understand and find meaning in stressful situations. The essential features of health and illness are intuitively viewed as health being

associated with well-being and ability, and illness with suffering and disability (Nordenfelt, 1987).

Experiences of health and illness, growth and loss, as they are lived, are central to nursing care (Benner & Wrubel, 1989). While there are many diseases, there is only one “health” – as perceived by the sufferer of the illness (Engelhardt, 1981). In my view, the needs and outcomes of patients would be better appreciated and understood if attention were paid to the patient’s conceptualization of the problem i.e. of his or her health (Hillier & Kelleher, 1996). For many women, recurrent breast cancer is an incurable and a progressive disease, with physical symptoms depending on the location of the metastases. And yet, in many cases these women will live for years or even decades with their illness. In this thesis, recurrence is viewed as “living” with cancer, as women adjust to live with disabilities and illness. The focus is on living rather than dying (Benner & Wrubel, 1989).

### ***Concepts integrated in this thesis***

The main concepts: health, illness, and adjustment, were chosen from a holistic existential nursing approach. Ever since Florence Nightingale wrote the first textbook for nurses, *Notes on Nursing* in 1859, health has been the overriding goal of nursing. To help individuals adjust with the experience of illness and suffering, and, if necessary, to facilitate meaning and hope in such experiences is also regarded as a purpose in nursing (Travelbee, 1971). In the following section, the concepts of health, illness and adjustment are described.

#### **Health**

In a salutogenic perspective, the individual is not categorized as being either “diseased” or “non-diseased”, instead the individual’s functioning may be plotted anywhere along a continuum from the pole of health to the pole of illness. Health is described by Antonovsky (1979, 1987) as a continuous and coherent process, moving between total health and ill health. According to Antonovsky, individuals may experience health even when they have been diagnosed with disease. Being healthy or being ill is not regarded as a static condition, but a constant flow.

Literally, health means “wholeness” and to heal means “to make whole”. To be whole is to be healthy, and to be healthy is to be whole (Kass, 1981, p 15). This conception of health as wholeness entails the integration of capabilities and capacities, the crucial point being that health is something over and above the absence of disease. Indeed, a high level of health may be compatible with some degree of disease, injury or impairment (Whitbeck, 1981). A simple formulation is that a person is healthy if he feels well and can function in his social context (Nordenfelt, 1987).

Health is one important aspect of quality of life. Quality of life is widely used as a health indicator, and is defined as “the individuals’ perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. It is a broad ranging concept affected in a complex way by the person’s physical health, psychological state, and level of independence, social relationships, and their relationships to salient features of their environment” (WHOQOL Group 1995). Health-related quality of life (HRQOL) is another broad concept, incorporating all aspects of the individual’s evaluation of his or her functioning in a wide range of areas. However, instead of measuring

health, most HRQOL instruments measure deviations away from a state of health, and really measure ill health, or the absence of illness and disease (Bowling, 2001). Although seldom explicitly defined in trials, there seems to be acceptance that HRQOL of life is a “multi-dimensional concept that encompasses the physical, emotional and social components associated with an illness or treatment” (Revicki, 1989).

During the past decade, HRQOL assessments, mostly made by patient self-reporting in questionnaires, have come increasingly into use in clinical trials (Gunnars et al., 2001). In cancer quality of life research, HRQOL generally includes the subjective perception of symptoms of disease and treatment side effects, including physical, emotional, social and cognitive functions (Leplege & Hunt, 1997). HRQOL is defined as “the state of well-being that is a composite of two components: the ability to perform everyday activities that reflect physical, psychological, and social well-being; and patient satisfaction with levels of functioning and control of the disease” (Gotay et al., 1992).

HRQOL is considered an important endpoint, particularly in cancer trials, traditionally including physical, emotional, social and cognitive functioning as well as symptoms of disease and treatment side effects (Kong & Gandhi, 1997). HRQOL data provides valuable information about treatment side effects, enabling patients to make informed choices regarding treatment options (Bottomley & Aronson, 2007). The most extensive early work on HRQOL focuses on breast cancer (Fallowfield & Hall, 1991). HRQOL is an important outcome measure and plays an essential role in understanding the impact of breast cancer diagnosis and treatment. The management of breast cancer is constantly evolving, introducing new treatment with improved outcomes and mortality, and highlights the significance of including quality of life assessment in clinical trials.

## Illness

The salutogenic perspective views illness as the opposite of health (Antonovsky, 1979, 1987). According to this perception of health and illness, an individual’s position and direction of movement along this continuum are determined by opposing forces of physical and psychological stressors and the coping resources of the individual. A stressor is defined as “a demand made by the internal or external environment of an organism that upsets its homeostasis” (Antonovsky, 1979, p.72.). Whether or not a given stimulus is a stressor for any given individual depends on the meaning of the stimulus to the person experiencing it and on the available homeostasis-restoring resources. There are three types of stressors: catastrophes, life events and daily hassles. The importance for the consequences of stressful life events of severe or terminal illness is the subjective meaning of the event, rather than its objective character. Antonovsky (1979) describes the response to a stressor as tension, which may be accompanied either by positive and negative effects, or both. Furthermore, Antonovsky makes a clear distinction between tension and stress, denoting stress as a contributing factor to pathogenesis. Although tension can be salutogenic, it can also lead to stress.

Illness is conceptualized as an experience of changes in bodily processes, and the appraisal of these processes as serious or requiring treatment (Kleinman, 1988). Furthermore, illness has a particular meaning to the person, in fact, illness is the disease understood in terms of its meaning for the person (Benner & Wrubel, 1989). Also, each illness has its own temporal nature. A common cancer illness trajectory entails a reasonably predictable decline in physical health over a period of time spanning weeks, months or years (Lynn & Adamsson, 2003). Physical,

psychological, social and spiritual needs are likely to vary according to the illness trajectory patients are following (Murray et al., 2005). Suffering is a part of the illness experience, a part of the human world of meaning (Benner & Wrubel, 1989).

Symptoms are a patient's experience of perceived indicators of change in normal functioning, and each symptom is a multidimensional experience (Lentz et al., 1997). Symptoms take on meanings related to the implications of impending illness, and belong to the lived experience of illness, rather than being a precise map of the underlying disease (Benner & Wrubel, 1989). Although symptoms may occur alone or in isolation from one another, patients often experience multiple symptoms simultaneously (Lentz et al., 1997). Symptoms are multiplicative in nature and may act for the occurrence of other symptoms, and the meaning the individual places in the experience of a symptom may influence his or her perception of a symptom regardless of its severity or frequency (Armstrong, 2003). Symptom experience includes the individual's perception of the symptom, evaluation of its meaning, and subsequent response (Dodd et al., 2001a). A symptom is also never experienced in isolation and will always be understood in terms of past and current life (Benner & Wrubel, 1989), and influencing factors are the nature of the symptom itself and lifetime experiences (Ryan & Zerwic, 2003).

Portenoy and colleagues (1994) describe symptoms as multidimensional phenomena, with frequency, severity and distress considered to be different dimensions of the symptom experience (Portenoy et al., 1994). Symptom distress is defined by Lentz et al (1997, p.16) as "the degree to which the person is bothered by the symptom", and distress, quality, timing and intensity are considered to be different dimensions of the symptom experience. Rhodes and Watson (1987) has defined symptom distress as "the degree or amount of physical or mental upset, anguish or suffering experienced from a specific symptom" (p. 243), and distinguished between the frequency of a symptoms occurrence and the distress caused by it (Rhodes et al., 2000). McCorkle (1987) defined symptom distress as "the level of distress from a specific symptom being experienced" (p.248). Studies regarding the symptom experience in lung cancer patients indicate that the symptom dimensions of occurrence, intensity and distress are conceptualized as differently (Tishelman et al., 2005; Broberger et al., 2005).

In addition to a dimension of a symptom, distress is conceptualized as a general multi-factorial unpleasant experience of psychological, emotional, social or spiritual nature that may interfere with the ability to cope effectively with cancer, its physical symptoms and its treatment. Distress is elucidated as existing along a continuum, ranging from common normal feelings of vulnerability, sadness and fears to problems that can become disabling, such as depression, anxiety, panic, social isolation, existential and spiritual crises (NCCN, 2003). According to this conceptualization, symptoms are regarded as one of several possible causes of distress, denoting social and existential issues (Godell, 2005). In this way distress, not the symptoms alone that trigger action. Finally the ability to cope with symptoms is viewed as an outcome of distress. Across the illness trajectory, patients with cancer experience a variety of distress as a result of disease and treatment side effects that may have a significant impact on quality of life (Dodd et al., 2001b; Miaskowski et al., 2007).

## Adjustment

In the salutogenic perspective, there is a direct relationship between coping capacity and the movement towards the health end of the health/illness continuum. According to Antonovsky (1979, 1987), the key to good health is coping moderated by "generalized resistance resources"

such as wealth, social support, ego strength and coping strategies. These resources are viewed as leading to life experiences that promote the development of a sense of coherence, which is a prerequisite for the coping capacity of an individual (Antonovsky, 1993).

Sense of coherence (SOC) is defined as a relatively stable and generalized orientation to one's world "a global orientation that expresses the extent to which one has a pervasive, enduring though dynamic feeling of confidence that (1) the stimuli deriving from one's internal and external environments in the course of living are structured, predictable and explicable; (2) the resources are available to one to meet the demands posed by these stimuli; and (3) these demands are challenges, worthy of investment and engagement" (Antonovsky 1987). Sense of coherence comprises three components, comprehensibility, manageability and meaningfulness. Lindström and Eriksson (2006) view these key components of SOC with comprehensibility being the cognitive component, manageability the behavioral component, and meaningfulness the motivational component. Sense of coherence is a global orientation about how individuals understand their lives and perceives themselves as understood by others, feel they able to manage their situation, and perceive it as meaningful to find a reason to continue (Lindström and Eriksson, 2006).

A sense of coherence is necessary in the movement towards health, and individuals with strong sense of coherence are able to mobilize their resources to cope with distress. Unlike other coping theorists (Lazarus & Folkman, 1984), SOC is flexible and not constructed around a fixed set of mastering strategies (Antonovsky, 1993). Antonovsky (1990) describes SOC as a particular coping strategy but a general orientation toward life. Furthermore, there is not one coping strategy but many, and a person who copes well has a strong sense of coherence and is able to select the best way for him or herself of dealing with distress.

Adjustment is a significant concept in psychosocial oncology, referring to the ongoing process as the cancer patient tries to manage distress (Brennan, 2001). Factors that contribute to adjustment are disease-derived, personal and social (Holland, 2003; Carver, 2005). Brennan (2001) states that "adjustment to cancer refers to the psychological processes that occur over time as the individuals, and those in their social world, manage, learn from and adapt to the multitude of changes which have been precipitated by the illness and its treatment". Thus, adjustment to cancer is not merely the end point of coping with the global threat of cancer but, rather "an active psychosocial process which may include both positive and negative consequences for the individual", spanning from personal growth to psychological disorder (Brennan, 2001).

## ***State of knowledge***

In general, cancer has a tremendous impact on health-related quality of life, and distress is a common emotional response. Nearly one-third to one-half of patients diagnosed with cancer, depending on site, experience significant levels of distress. Patients with poorer prognoses and patients with greater symptom burdens show similar rates of distress (Zabora et al., 2001). Despite the prevalence of distress in cancer patients, only about ten percent receive any psychosocial therapy (Holland, 2004). The majority of cancer patients report that the recurrence of their cancer was much more upsetting than the initial diagnosis and that they felt less hopeful (Mahon et al., 1990). Health, illness and adjustment in women with recurrent breast cancer are described in the following section.

### **Health**

Health-related quality of life in women with recurrent breast cancer has increasingly been used to assess disease and treatment outcomes, with the aim of relieving symptoms and if possible, of prolonging life without unwarranted toxicity (Osoba, 1995). Recurrent breast cancer has a significant impact on HRQOL (Bull, 1999; Chie et al., 1999), with the lowest scores reported by patients with distant metastases (Thornton et al., 2005). Although women with recurrence report good mood, low stress, and good quality of interpersonal relationships, they experienced more vulnerability (Oh et al., 2004). Reductions in HRQOL are mainly attributable to pain and discomfort as well as anxiety and depression (Lidgren et al., 2007). In a study by Bull and colleagues (1999) quality of life was measured prior to recurrence, after the diagnosis of recurrence, and at follow up 6 months later. Overall quality of life, general health status, emotional, physical and social functioning were all poorer immediately following the diagnosis of recurrence than they had been prior to the recurrence. After treatment completion, most areas of HRQOL return to levels equivalent to HRQOL levels in disease-free survivors (Lee et al., 2007). In the year after a recurrence of breast cancer, while physical health and functioning showed no improvement, stress declined and quality of life and mood improved (Yang et al., 2008).

An area of increasing interest is the relationship between HRQOL scores and prognosis. The majority of studies examining the associations between HRQOL variables and disease progression demonstrate contradictory findings. Previous research provides evidence that HRQOL has no prognostic value in patients with early stage breast cancer at the beginning of adjuvant therapy (Efficace et al., 2004a), and HRQOL and psychosocial status at diagnosis and 1 year later have also been found not to be associated with clinical outcome (Goodwin et al., 2004). The prognostic significance of HRQOL factors in adjuvant therapy setting is minimal or obscured by the side effects of chemotherapy, but there is strong prognostic significance after disease recurrence (Coates et al., 2000). Previous research identifies HRQOL factors as predictors of clinical outcome in patients with advanced or metastatic breast cancer. Coates and colleagues (1992) identified a good physical well-being as an independent predictor of survival. Better physical well-being and appetite in premenopausal patients and better physical well-being, mood, appetite, and coping in postmenopausal women predicted longer survival in patients with metastatic breast cancer (Coates et al., 2000). Appetite loss was found to be a significant prognostic factor for survival in women with metastatic breast cancer (Efficace et al., 2004b).

## Illness

During the illness trajectory, women with recurrent breast cancer are faced with various distressing symptoms such as fatigue, pain, anxiety and depression (Hanson Frost et al., 2000; Turner et al., 2005; Mayer & Burnstein, 2007; Okamura et al., 2000; Okamura et al., 2005). Tasmuth and colleagues (1995) found that 30-50% of the patients reported pain, paraesthesias and strange sensations. Patients treated with both radiotherapy and chemotherapy reported the highest incidence of pain. Breast cancer related pain also includes pain related to bone metastases and pain related to local surgery for recurrence (Coleman, 1997; Caffo et al., 2003; Riccio et al., 2007). Pain is also interrelated with other symptoms, such as fatigue (Burrows et al., 1998; Stone et al., 2000), and sleep disorders (Cleeland et al., 1996; Engstrom et al., 1999).

Recurrent breast cancer is often associated with various distressing symptoms depending on disease progression and demanding treatments. Women with recurrent breast cancer experience more difficulties in terms of health perceptions, physical function, somatization, impact on life, and medical interactions, than women with newly diagnosed or stable breast cancer, (Hanson Frost et al., 2000). Psychological disorders such as anxiety and depression are also reported (Ell et al., 2005; Burgess et al. 2005; Turner et al., 2005; Grabsch et al., 2006). Hjerl and colleagues (2002) found that breast cancer patients have an increased incidence of anxiety and depression after a breast cancer diagnosis, and preoperative depression was associated with a significantly higher risk of mortality in late-stage breast cancer patients (Hjerl et al., 2003). High levels of psychological morbidity were reported by 56.7% of women younger than 55 years, as compared with 34.5% of women over 55 (Turner et al., 2005). After completed chemotherapy, 10% of women had a major depressive disorder (Morasso et al., 2001). A study by Okamura and colleagues (2000) indicates that 42% of women with recurrent breast met the criteria for major depressive disorder (7%), or adjustment disorder (35%). Anxiety and depression are reported in women with recurrent breast cancer (Burgess et al., 2005; Okamura et al., 2005; Ell et al., 2005). Younger, more educated, and married women reported higher levels of symptom distress after surgical treatment (Kenefick, 2006). During first cycle of chemotherapy higher symptom distress scores was associated with fatigue and insomnia (Boehmke & Brown, 2005).

Distress rates are high and similar in women with both early and advanced stages of breast cancer, but the causes of distress are different. Women with metastases report more dissatisfaction with body image, and problems with lymphoedema and hot flushes (Kissane et al., 2004). In a prospective study Andersen and colleagues (2005) show that although women with recurrent breast cancer report higher levels of distress than disease-free women, their levels of distress were equivalent to their distress experience at the initial diagnosis. Distress and pain are found to increase significantly in the terminal phase of the disease (Butler et al., 2003). Furthermore, low distress levels, little fatigue and lack of anxiety predicts disease-free and overall survival, even after controlling for biological factors (Groenvold et al., 2007).

## Adjustment

Adjustment to breast cancer has been described as a series of phases related to the disease and its treatment, in women in early-stage breast cancer (Carver et al., 1998) pre-treatment (Cimprich, 1999), during treatment (Hoskins, 1997), post-treatment (Cohen et al., 2000), and during long-time survival (Tomich & Helgeson, 2002). Considerable interest has been directed to social

support and adjustment. Social support was not associated with mood disturbances or pain in women with metastatic breast cancer (Koopman et al., 1998). Couples facing breast cancer reported decreased marital and family functioning, uncertainty, and adjustment problems associated with the illness (Northouse et al., 1998). Furthermore, previous research indicates that 35% of patients with recurrent breast cancer suffer from adjustment disorder (Okamura et al., 2000).

Previous research illustrates the profound and precipitous emotional transformation women experience after a diagnosis of breast cancer (Boehmke & Dickerson, 2006). The women tend to redefine their lives through integrating the meaning of breast cancer (Öhlen & Holm, 2006). The impact of breast cancer is experienced in every aspect of a woman's daily life (Loveys & Klaich 1991), including their views of themselves and their relationships (Arman et al., 2002a).

A number of studies address different coping styles in women with breast cancer (Ray et al., 1982; Burgess et al., 1988; Stanton & Snider, 1993; Shapiro et al., 1997; Culver et al., 2002; Stanton et al., 2002; Classen et al., 1996), Petticraw and colleagues (2002) found no association between coping styles and cancer survival or recurrence in a meta-analysis of 37 studies. Despite the extensive research into coping responses, the answer to question of how coping affects disease outcome remains unclear.

## RATIONALE

The general rationale underpinning this thesis is that it is important to describe women's experiences of health, illness and adjustment throughout a recurrent breast cancer trajectory. Women with recurrent breast cancer are faced with many demanding challenges different from those faced at initial diagnosis and treatment. While recurrent breast cancer is an incurable disease in most cases, some women will live for years or even decades with their illness. The goals of treatment of recurrent breast cancer are optimal palliation and prolongation of life with maximal health-related quality of life. Women with recurrent breast cancer are not only challenged in terms of coping with changes in health and progressive experiences of illness, they also have to comprehend, manage and enhance meaning in life while living with a persistent threat, as well as creating new ways of interacting with families and significant others. This thesis reflects three foci of psychosocial responses to a recurrence of breast cancer.

The first focus is HRQOL in women before a recurrence of their breast cancer. In recent years there has been increasing interest in studying HRQOL factors as predictors of disease-free and overall survival in women with breast cancer. Although recent research supports the hypothesis that HRQOL independently predicts survival in breast cancer patients with advanced (Coates, et al. 1992) and metastatic disease (Coates et al., 2000; Efficace et al., 2004b), there is still insufficient knowledge about the underlying mechanisms. Recent studies provide evidence that HRQOL has no prognostic value in patients with early stage breast cancer at the beginning of adjuvant therapy (Efficace et al. 2004a), and HRQOL and psychosocial status at diagnosis and 1 year have also been found not to be associated with clinical outcome (Goodwin et al., 2004). To my knowledge, there are no studies addressing whether changes in HRQOL may predict recurrence.

The second focus is distress, symptoms and HRQOL in women after a recurrence of breast cancer. Previous psychosocial research in breast cancer has mostly been focused on screening, initial diagnosis and early treatment (Spiegel, 1997; Dow & Lafferty, 2000; Chie et al., 1999). Despite the prevalence of cancer-related symptoms such as fatigue, pain and depression and their impact on HRQOL, the interaction between these symptoms remains unexplored (Carr et al., 2002), even in breast cancer. Previous research on symptoms in cancer patients has mainly addressed one single and primary symptom, but more recent studies have addressed constellations of interacting symptoms or symptom cluster (Given et al., 2001; Francoeur, 2005; Barsewick et al., 2006). There is also a need for further knowledge and understanding of the variables influencing or mediating the level of symptom distress experienced by the cancer patient, and further research is needed to define the differences between distressing symptoms and symptom distress (McClement et al., 1997). Furthermore, there is limited knowledge as to whether personal or disease-derived factors predict distressing symptoms and HRQOL in women with recurrent breast cancer. There are no studies addressing the occurrence of distressing symptoms and the consequences in relation to HRQOL in postmenopausal women with recurrent breast cancer.

The third focus is how women deal with the diverse dimensions of living with a recurrence of breast cancer. Previous research illustrates different dimensions of living with newly diagnosed breast cancer (Landmark et al., 2001), the transformation following a diagnosis of breast cancer (Boehmke & Dickerson, 2006), and incorporating the meaning of breast cancer in one's life (Öhlen & Holm, 2006; Bertero & Chamberlain, 2007), as well as creating new meaning and behaviors (Nelson, 1996; Coward, 1990; Coward & Kahn, 2005). Women with recurrent breast cancer experience an increased awareness of the relationship between life and death, and an increased openness to their own needs and desires, which may be an important resource for health (Arman & Rehnsfeldt, 2002b). Recurrent breast cancer has an extensive emotional impact, but there is no research exploring how women adjust to an incurable breast cancer illness.

## **AIMS**

The primary aim of this thesis was to explore women's experiences of health, illness and adjustment during the recurrent breast cancer trajectory.

### ***Specific aims***

#### *Paper I*

The aim of this study was to explore whether changes of symptoms (tiredness, hot flushes, nausea/vomiting and arm impairment) and global quality of life domains (social support, physical well-being, mood, perceived adjustment and health status) may predict breast cancer recurrence.

#### *Paper II*

The aim of this study was to explore predictors of health-related quality of life (HRQOL) in postmenopausal women diagnosed with recurrent breast cancer and to:

- describe the occurrence of distressing symptoms, coping capacity, and HRQOL,
- analyze correlations among concurrent symptoms and HRQOL,
- identify which factors predict distressing symptoms and HRQOL.

#### *Paper III*

The aim of this study was to explore the experience and predictors of symptoms, distress and health-related quality of life over time in postmenopausal women with recurrent breast cancer and to:

- examine symptoms (frequency, severity and distress), and HRQOL,
- determine how cancer-related symptoms (fatigue, pain and depression) predict distress and HRQOL.

#### *Paper IV*

The aim of this study was to explore what major concerns women with recurrent breast cancer experience and how they deal with their situations.

# METHOD

## *Design*

When addressing complex phenomena such as illness, which cannot be described using a single methodological strategy, a mixed-methods design is suggested (Morse, 2005). A mixed-methods design is a combination of deductive and inductive research methods. In this thesis the core component is quantitative, with a supplementary qualitative component.

The deductive research component (Papers I–III) aimed to explore experiences and predictors of HRQOL throughout the recurrent breast cancer illness. For these studies a longitudinal, predictive and explorative (Paper I), and a longitudinal, correlational and predictive (Papers II–III) design were chosen.

The inductive research component (Paper IV) aimed to reveal and understand what major concerns women with recurrent breast cancer experience and how they deal with their situations. A grounded theory design, as described by Glaser and Strauss (1967) and Glaser (1978) was chosen.

## ***Deductive research component***

### Participants

#### *Paper I*

Participants were the Swedish sample of 146 participants in The International Breast Cancer Study Group Trial 12-93 (n=69) and trial 14-93 (n=77). Eligible patients in IBCSG trials 12-93 and 14-93 were postmenopausal women, 70 years old or younger, diagnosed with primary breast cancer and positive lymph nodes. In trial 12-93, 12 patients and in trial 14-93, 32 patients were diagnosed with early recurrence (n=44). Of the total sample, six patients also participated in studies II – IV.

#### *Papers II – III*

Participants were 56 consecutive postmenopausal women (>55 years), newly diagnosed with local, regional, or distant recurrent breast cancer. Further inclusion criteria were that the participants had been informed and aware of diagnosis of their disease, and mentally and physically able to participate.

### Procedure

#### *Paper I*

Data was collected by a review of the IBCSG Quality of Life Core Questionnaire (IBCSG QoL) assessments included in medical records. HRQOL was assessed according to the IBCSG protocol at randomization, 3, 6, 9, 12, 18 months, and at annual follow-ups for 72 months.

*Papers II – III*

Participants were recruited from two surgical and two oncology centers. Potential participants were identified by the specialist nurse with expertise in breast cancer. Eligibility was determined by consultation with the attending physician and by chart review. Eligible patients were approached and informed about the aims of the study. Patients, who agreed to participate, gave their signed, informed consent. Baseline data was collected at the time of confirmation of a recurrence, and follow-up data was collected 1, 3, and 6 months after recurrence. Questionnaires were sent to participants by ordinary post to be filled out at home and returned by post.

**Measurements and instruments**

Background data was collected through chart review and interviews. Socio-demographic characteristics were age, marital status, living situation, employment status, children, occupation and educational level. Clinical characteristics investigated were type of treatment, tumor characteristics, and co-morbidity.

In this thesis five instruments were used, shown in Table 1.

Table 1. Instruments used in each study

<b>Concept</b>	<b>Item</b>	<b>Symptoms</b>	<b>Global indicators &amp; Subscales</b>	<b>Paper</b>	
<b>HRQOL</b>	International Breast Cancer Study Group Quality of Life Core Questionnaire (IBCSG QoL)	10	Appetite, Nausea Tiredness Hot flushes Restrictions in arm movement	Physical well-being Mood Perceived adjustment Support Health	I–II
	European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30)	30	Fatigue Pain Nausea/vomiting Dyspnoea Insomnia Appetite loss Constipation	Physical Cognitive Emotional Social Financial difficulties Global health-related quality of life	II–III
<b>Illness</b>	Memorial Symptom Assessment Scale (MSAS)	32	24 symptoms (frequency, severity, distress) 8 symptoms (severity, distress)	Global Symptom Distress Index Physical symptom Psychological symptoms Total Symptom Burden	II–III
	Hospital Anxiety and Depression (HAD)	14		Anxiety Depression	II–III
<b>Adjustment</b>	Sense of Coherence (SOC)	13		Comprehensibility Manageability Meaningfulness	II–III

### *International Breast Cancer Study Group Quality of Life Core Questionnaire*

Breast cancer specific quality of life was evaluated using the 10 item visual analogue scale of the International Breast Cancer Study Group Quality of Life Core Questionnaire (IBCSG QoL). Each indicator consists of a 100mm line anchored at both ends with words describing the two extremes of the item's content. The questionnaire includes global indicators for physical well-being, mood, coping (PACIS), perceived social support and subjective health estimation. In addition, indicators of symptoms of appetite, nausea, tiredness, hot flushes and restrictions in arm movement are included, covering possible specific disease and treatment-related effects (surgery, chemotherapy, endocrine and radiation therapy). Higher scores indicate a higher level of symptoms/problems. The reliability and validity of the questionnaire has been established in several studies (Hürny et al., 1993; Bernhard et al., 1999).

### *European Organization for Research and Treatment of Cancer Quality of Life Questionnaire*

HRQOL was measured using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30). The EORTC QLQ-C30 is a cancer-specific questionnaire, including 30 questions incorporating five function scales; (physical, role, cognitive, emotional and social), three symptom scales (fatigue, pain, nausea and vomiting), six single item scales (dyspnoea, insomnia, appetite loss, constipation, financial difficulties) and a global health and quality of life scale. The questionnaire consists of Lickert scales, coded 1 – 4, with the response alternatives: not at all, a little, quite a bit, and very much. Higher scores on the functional scales and the global health and quality of life scale represent a higher level of function, while higher scores on symptom scales indicate a higher level of symptoms. In accordance with the EORTC guidelines, the raw scores were transformed to 0 – 100 (Fayers et al., 1995). The EORTC QLQ-C30 questionnaire has been widely used (Bergman et al., 1992; Hammerlid & Taft 2001; Hammerlid et al., 2001) and good reliability and validity have been shown, with Cronbach's  $\alpha$  ranging between 0.71 and 0.93 (Aaronson et al., 1993; Borghede et al., 1997).

### *Memorial Symptom Assessment Scale*

Symptom experience (frequency, severity and distress) were measured using the Memorial Symptom Assessment Scale (MSAS), a multidimensional questionnaire consisting of 32 symptoms. For 24 symptoms the severity, frequency and distress associated with each symptom were evaluated. For 8 symptoms, only severity and distress were measured. The MSAS consists of two subscale scores: a physical symptom subscale (MSAS-PHYS) and a psychological subscale (MSAS-PSYCH). In addition, the MSAS generates the Total Symptom Burden Scale (TMSAS) and the Global Symptom Distress Index (GDI). TMSAS is calculated from the average scores of all 32 symptoms, and each symptom score is an average of its dimensions. The GDI is a 10 item measure of global distress, calculated on the frequency of four symptoms: feeling sad, worrying, feeling irritable, and feeling nervous, and distress associated with six symptoms: lack of appetite, lack of energy, pain, feeling drowsy, constipation, and dry mouth. The MSAS is proven to be a reliable and valid multidimensional measure of symptom experience in cancer populations (Portenoy et al., 1994; Tranmer et al., 2003).

### *Hospital Anxiety and Depression Scale*

Anxiety and depression were measured with the Hospital Anxiety and Depression Scale (HAD). HAD is a 14 item questionnaire consisting of two sub-scales, anxiety and depression. Each response is rated on a four-point scale. Subscale scores range from 0 to 21. Scores of 0-7 indicate

“normal”, 8-10 “borderline” and scores of > 11 or more on either sub-scale is considered to represent those who are at risk of psychological morbidity (Zigmond & Snaith, 1983). The HAD Scale is widely used in cancer populations, with well established validity and reliability (Herrmann, 1997). The internal consistency of reliability for the Swedish version of HAD is satisfactory, with Cronbach’s alpha >0.80; higher for anxiety than depression (Sullivan et al., 1993).

#### *Sense of Coherence*

Personal coping resources were evaluated using the Sense of Coherence scale (SOC). The sense of coherence is a global orientation through which the person views the world and his or her own life as comprehensible, manageable and meaningful. Individuals with a strong sense of coherence are able to mobilize their resources to cope with distress. The SOC short version scale consists of 13 items on a 7-point Lickert-scale. The SOC scale evaluates perceived comprehensibility (5 items), manageability (4 items) and meaningfulness (4 items). A higher score represents a stronger sense of coherence. The reliability and validity of the SOC scale has been proven in many studies and different languages (Antonovsky, 1993; Langius et al., 1992.; Gilbar, 1998; Thomé & Hallberg, 2004; Eriksson, 2005) with a Cronbach’s  $\alpha$  range of 0.74 to 0.93.

#### Statistical analyses

Descriptive statistics were used to summarize socio-demographic and clinical characteristics (Papers I–III). Descriptive statistics were also used to describe symptoms, coping, distress and health-related quality of life (Papers II–III).

Pearson’s correlation coefficient was calculated to determine the strength of relationships between selected variables. A p-value = <0.05 was considered significant (Papers I–III). A paired t-test was used to compare baseline and follow-up scores and to investigate significant changes over time (Paper III). Poisson regression analysis was used to calculate the hazard function of recurrence, depending on time since primary diagnosis and HRQOL variables. The HRQOL variables were included in the analysis one by one, and considered to be time-dependent covariates, as the scores of one assessment was continuously replaced with the scores of the next assessment. Changes since preceding assessment divided by time (change per time unit) was thereafter examined as time-dependent covariates. Only selected variables that provided a statistically significant contribution were included in the prediction model (Paper I). A stepwise multiple regression procedure was used to determine regression equations for predicting the dependent variables. The stepwise procedure selected variables that provided statistically significant contributions to the prediction model (p<0.05) (Paper II). Logistic regression was used to estimate the probability of drop-out, depending on global distress at baseline, while linear regression was used to determine regression equations for predicting distress and health-related quality of life. Only selected variables that provided a statistically significant contributions were included in the prediction model (p<0.05) (Paper III).

Data was analyzed using SPSS (Statistical Package for Social Sciences, version 14.0 for Windows), except for Poisson regression (Papers I–III).

### ***Inductive research component***

Grounded theory was chosen as it is a qualitative method tailored to explore processes, actions and meaning, and it is a systematic method of comparative analysis and a strategic method of generating theory grounded in data (Glaser & Strauss, 1967). The goal of grounded theory is to generate a theory that “accounts for a pattern of behavior which is relevant and problematic for those involved” (Glaser, 1978, p.93). Grounded theory is distinguished from other qualitative methods in that data collection and analysis occur simultaneously, and that data analysis sets the direction for further data collection. Theory generation occurs around a core category, accounting for most of the variation in a pattern of behavior. Thus the result of a grounded theory study based on Glaser and Strauss (1967) and Glaser (1978) may generate substantial theory that explains the studied area (Hallberg, 2006).

### **Participants**

From the sample of 56 postmenopausal women newly diagnosed with a recurrence of breast cancer, twenty women were asked to participate in interviews concerning their major concerns and how they were dealing with their situations. These twenty women were purposefully selected in order to provide a wide range of variation of socio-demographic and clinical factors. Potential participants were approached and informed about the study, and all agreed to participate. Written informed consent was obtained before enrolment, and confidentiality and anonymity were assured. Participants were advised that they could withdraw from the study at any time. Respect was shown to the participant’s condition, and the interview was discontinued if the participant was too ill or disabled to go on.

Repeated interviews were performed with the aim of exploring processes over time. Two to five repeated interviews were conducted with twelve participants, and continued until a pattern of categories was reached. These repeated interviews were performed 2 weeks to 24 months after the recurrence of their breast cancer. Six of the participants were also interviewed in a late stage of their disease. With the purpose of selectively collecting data for supporting emerging theory development, single additional interviews were performed. These interviews were conducted with eight participants between 3 and 6 months after the recurrence of their breast cancer.

### **Procedure**

Qualitative inquiry with grounded theory methodology was used to simultaneously collect and analyze data. Thus, the phases of data collection and analysis overlapped. Data was collected from 40 in-depth interviews. All interviews were conducted by the first author, and the interviews lasted between 90 and 150 minutes, and took place in settings including participants’ homes and hospital wards. Interviews were audio-taped, with the exception of two cases. One participant refused tape-recording, and another preferred a telephone interview. In these cases, field notes were made. The interviews were transcribed verbatim. The introductory question was “Would you please tell me about your experiences of being diagnosed with breast cancer?” followed by “Would you please tell me about your experience of being diagnosed with recurrent breast

cancer?”. After these initial questions the interviews continued with of a series of open-ended questions designed to explore the experiences of difficulties, challenges and strategies.

## Data analysis

The constant comparative analysis method according to Glaser and Strauss (1967) and Glaser (1978) was used to identify similarities and differences across data. Open inductive coding was performed, combining analytical procedures of explicit coding and constant comparison. Focused coding was used to cluster continually reappearing codes into subcategories. Significant subcategories were thereafter clustered into categories. Glaser and Strauss (1967) describe categories as conceptual elements of theory, and a higher level of abstraction is achieved through the process of constant comparison. A core category, central to the data, was identified and determined the emerging theoretical framework. Focused data analysis occurred concurrently with further data collection, and continued during the writing of the final research report. Theoretical sampling was used in order to describe and refine categories, their properties, and relationships, which were achieved by going back to previously collected data, and conducting additional interviews. This procedure was continued until saturation was reached. Saturation was considered satisfactory when no additional data were being found to further develop the properties and relationships of the category. When no new data were added to the collected data, the data was considered to have reached the saturation point, and data collection was concluded. With the aim of strengthening dependability, analyses were performed to explore the degree to which data changed over time.

## ***Ethical considerations***

The studies included in this thesis follow the ethical principles of The World Medical Association of Declaration of Helsinki (WMA, 2004) regulations regarding research involving human research subjects.

All participants received written and verbal information about the study. Written informed consent was obtained from participants before enrolment. Participants were guaranteed confidentiality and anonymity in presentation of study results. Participants were also advised that they could withdraw from the study at any time, without having to explain the reason for withdrawal.

Participants were contacted by phone, and were asked about their current health status and general condition at every follow-up, before questionnaires (Papers II–III) were sent out and before interviews (Paper IV). Respect was shown to the participant’s condition, and participation was discontinued if the participant was too ill or disabled to go on. Guided by the principles of beneficence, with aim of doing good and doing no harm, respect was also shown to the integrity and vulnerability of severely ill participants.

Ethical approval of the studies included in this thesis were obtained from the Ethical Research Committee, University of Gothenburg, Sweden (Gbg Dnr Ö 049-02, Supplement 447-02, 112-04; Ö 580-02, KI 03-496; M2 170-04). Approval was also obtained from medical directors of each participating hospital. Permission to use IBCSG data was granted by IBCSG, Scientific Committee.

## RESULTS

### *Paper I*

At the primary diagnosis of breast cancer the median age of patients was 60 years (mean 60 years, ranging from 45-73 years). Recurrence was reported in 55 patients, 19 patients from Trial 12-93 and 36 patients from Trial 14-93. Nineteen women were diagnosed with loco-regional recurrence and thirty-six had distant metastases. In Trial 12-93 the median time from primary diagnosis to recurrence was 57 months (ranging from 18-112 months), and in Trial 14-93 the median time was 36 months (ranging from 7-104 months). Data were available from 141 patients of the 146 eligible randomized participants in the IBCSG Trials 12-93 and 14-93.

According to the Poisson multivariable regression analysis, changes in physical well-being (p-value=0.0081), and nausea/vomiting (p-value=0.0026) together significantly predicted recurrence. A deteriorated physical well-being and improved nausea/vomiting were associated with increased risk of recurrence. The predictor was analyzed as a time dependent covariate, i.e. for every new measurement the previous calculated difference was replaced by a new difference, and a further analysis was performed to estimate the predictive ability of the variable. The results indicated that the predictive ability of the variable seemed to be strongest approximately 3 years after primary diagnosis.

A multivariate analysis was conducted including both physical well-being, and nausea and vomiting, and time since primary diagnosis. The analysis identified significant changes in physical well-being ( $\beta=0.00585$ ) and nausea/vomiting ( $\beta=-0.00784$ ). A time model was used to show when the predictive ability of physical well-being and nausea/vomiting had the highest predictive ability. A score of the coefficients of physical well-being and nausea/vomiting ( $Z$ ) was created. The model included  $Z$ ,  $Z \cdot$  (time since assessment) and  $Z \cdot^2$  (time since assessment)<sup>2</sup>. According to the time model, the predictive ability might be estimated as highest or best 0.93 years after assessment, indicating that deteriorated physical well-being and improved nausea/vomiting together may predict recurrence within 1 year. As expected, the extremes of  $\Delta$  physical well-being and  $\Delta$  nausea/vomiting per time unit occur early after the primary diagnosis of breast cancer.

A further exploration of the correlation between changes in physical well-being and nausea/vomiting as a predictor of recurrence demonstrated a small but significant association between changes in physical well-being, and changes in nausea and vomiting is ( $r = 0.31$ , 95% confidence interval: 0.24-0.37;  $p<0.05$ ). Although the correlation between the two variables was positive, their association with recurrence was opposite,  $\beta=0.00585$  for changes in physical well-being and  $\beta=-0.00784$  for changes in nausea and vomiting.

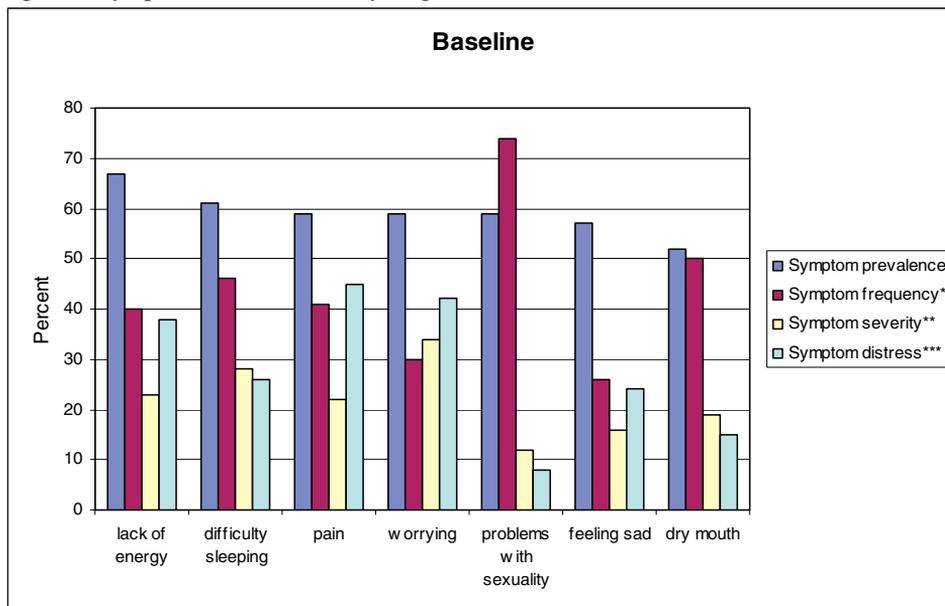
### *Paper II*

A total of 56 women were recruited from a consecutive sample of 65 eligible women. The nine non-participating women were excluded because of lack of strength ( $n=3$ ), being too anxious ( $n=2$ ), being too ill ( $n=1$ ), cognitive deficiency ( $n=1$ ) or refusal to participate ( $n=2$ ). Participants had a mean age of 65 years (range 55 to 79 years). At the initial breast cancer diagnosis, the

women had a mean age of 59 years (range 40 to 78 years). The mean time from the primary diagnosis to recurrence was 87 weeks (range 10 to 437 weeks). Twenty-nine participants had loco-regional recurrence, and 24 had distant metastases.

Women with recurrent breast cancer reported a wide variety of symptoms. At baseline a majority (65%) reported as many as 10-23 symptoms with an average of 14 symptoms. Twenty-one (35%) patients reported 0-10 symptoms with an average of 4 symptoms of illness. Highly prevalent symptoms reported were almost identical with symptoms included in the global distress score. In every assessment, feeling sad was most significantly associated with other symptoms. Symptom prevalence, frequency, severity and distress are outlined in Figure 1.

Figure 1. Symptoms in women newly diagnosed with recurrent breast cancer



\*Percentage Frequently to Almost Constantly; \*\* Percentage Severe to Very Severe; \*\*\* Percentage; Quite a Bit Distressing to Very Much Distressing

### Coping capacity

Coping capacity was measured in terms of sense of coherence. Patients with low sense of coherence reported higher scores of anxiety ( $r=-0.59$ ) and depression ( $r=-0.62$ ). Furthermore, a low sense of coherence also significantly correlated with worse perceived health ( $r=0.54$ ). The prevalence of perceived adjustment was calculated by dichotomizing the scores as less or equal to 10 (=having no or fewer symptoms/problem) and more than 10 (=having symptom/problem), and indicated that 61.1% of patients perceived themselves as having problems with adjustment.

### Sense of coherence predicts distressing symptoms

A stepwise regression model including coping capacity, measured as sense of coherence, socio-demographic variables and clinical factors were selected as independent variables. Dependent variables included were anxiety, depression, fatigue, mood, physical well-being, number of symptoms, total symptom burden, perceived health, and HRQOL. The regression model identified sense of coherence as the only statistically significant predictor of the symptom experienced.

### *Predictors of health-related quality of life*

Stepwise regression analyses were performed with anxiety, depression, fatigue, mood, physical well-being, total symptom burden, number of symptoms, global quality of life, and perceived health as the dependent variables. Independent variables were coping capacity, global distress, perceived adjustment, and socio-demographic and clinical factors. The only predictor of fatigue and of the total symptom burden was global distress. Perceived adjustment was the only predictor of perceived health.

## **Paper III**

Participants who experienced multiple symptoms at the time of recurrence also reported multiple symptoms at every follow up, with an increased number of symptoms at the 3 month follow-up assessment. Participants reporting few symptoms at baseline also experienced few symptoms at 6 month follow-up, but an increased number of symptoms at 3 month follow-up.

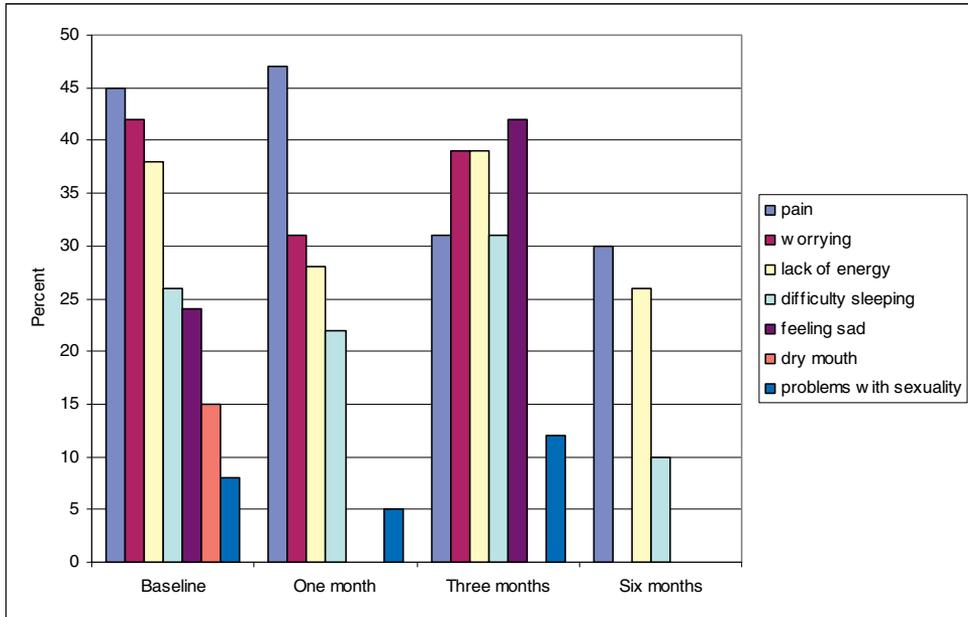
At the time of recurrence, 8 patients (14%) were categorized with anxiety and 6 patients (10%) with depression. Three patients (5%) scored 11 or higher on both subscales. With a threshold value of 8 or more, 16 patients (29%) would have been regarded having or possibly having anxiety and 12 patients (21%) with depression. Nine patients (16%) scored 8 or higher on both subscales. Eight (25%) patients reported both anxiety and depression. Twelve patients (37%) had a pre-history of anxiety and depression at baseline. Over time cases or doubtful cases of anxiety and depression changed. Anxiety decreased at one month follow up (18%), but increased at three-month follow up (32%), and declined at six month follow up (17%). Depression declined over time: one month follow up (16%), three month follow up (14%), and six month follow up (12%).

Except for three month follow-up assessment, the most distressing symptoms were pain, at baseline reported by 32 (59%) patients. Of these patients, 13 (40%) patients could be regarded as doubtful cases of anxiety, and 10 (31%) patients reported depression. Feeling sad was commonly reported as most distressing at three months follow up. Using a cut-off for symptoms evaluated as being “quite a bit or very much distressing”, highly distressing symptoms were investigated. The results suggest that 59% experienced highly distressing symptoms three months after recurrence as compared with 48% at six month follow up.

Fatigue, pain and depression were highly significantly correlated ( $p=0.01$ ) over time. Fatigue and depression were correlated at baseline and in every follow-up assessment. Fatigue and pain were correlated, with exception of at one month follow up. Finally, pain and depression were correlated at baseline and three month follow up. The partial correlation coefficients between distress and each of the variables mentioned, given for the two other variables, were 0.391, 0.420 and 0.509, respectively.

Patients who experienced 10 symptoms or more had higher co-morbidity, including a prehistory of depression as well as concurrent anxiety and depression, and reported higher levels of distress over time than patients who experienced few symptoms over time. At three-month follow up high levels of symptom burden and distress were reported. Socio-demographic and medical factors were not related to symptom prevalence or distress. Changes in symptom distress over time are illustrated in Figure 2.

Figure 2. Changes in symptom distress over time



The probability of dropout at the one-month follow up, attributable to global distress, was estimated by use of logistic regression analysis. There was a significant ( $p=0.02$ ) increase in the probability of dropping out with a higher value for global distress. The drop-outs were mainly due to death or deterioration of the breast cancer disease. Health-related quality of life changed over time, decreased at three-month follow-up, but improved at six-month follow up. Similar tendencies were reported for physical, role, emotional, and social function. Mean levels of fatigue, pain and insomnia improved over time.

#### *Predictors of distress and HRQOL over time*

A linear regression analysis identified fatigue, pain and depression as predicting distress at baseline and at three-month follow up. Fatigue and pain, but not depression, predicted distress at 1 month and at six-month follow up. Over time, distress predicted HRQOL.

### **Paper IV**

Participants ranged in age between 55 and 81. The median time from the primary diagnosis to recurrence was 68 weeks (range 4 to 236 weeks). At the time of recurrence, thirteen of the participants were married, five were divorced, one was widowed, and one was single. Twelve were working full or part time, one was a housewife, one was unemployed, four were disability pensioners, and two were retired. Three women had loco-regional recurrences, and seventeen had distant metastases.

Making sense of living under the shadow of death describes the process the women went through, when adjusting to a recurrence of breast cancer. The return of breast cancer was experienced as a devastating life-altering event, and women experienced a variety of emotions related to the uncertainty and unpredictable nature of recurrent breast cancer, and to the certainty of future negative outcomes throughout the recurrent breast cancer trajectory. Moving through a difficult and challenging time, struggling with losses and fears, women eased their distress by letting go of losses and reassessing important values in life. Women transcended their illness as they re-evaluated meanings and attitudes, and re-patterned relationships, and they created a sense of wellness.

We found that the core category, “making sense of living under the shadow of death”, was related to three additional categories: Confronting, entailing shifting expectations and shifting awareness, Struggling–Easing Distress, involving losing–fearing, letting go–being reassured, and Transcending, entailing re-evaluating, re-patterning relationships, and creating wellness. Each of these sub-processes influenced the others in an ongoing and interactive process. The dialectical pattern between the opposites of struggling with and easing distress was framed by confronting a recurrence and transcending a life-threatening illness.

Adjustment was impeded by additional changes in terms of further disease progression or treatment failure. These changes were experienced as non-stop changes, as being constantly affected by serious setbacks and disappointments, and being without time for recovery, resulting in an inability to cope. Adjustment was facilitated by motivating thoughts and emotions directed to a goal of managing the transition. Maintaining hope was described as crucial, and the women never wanted to be told that there was nothing more to be done. Although participants described hoping for different things, the most frequent hope was to survive, or if not, just to have more time to live. Participants viewed their illness as a challenge, a reminder, or an opportunity to change. They tried to find their inner strength, and to regard themselves as survivors, despite their poor prognosis.

# DISCUSSION

## *General discussion*

The main purpose of this thesis work was to explore women's experiences of health, illness and adjustment during their breast cancer trajectory. In order to gain deeper understanding, both deductive and inductive methods were used to explore women's experiences of changes in health before recurrence, their health and illness response over time after being diagnosed with a recurrence, and how they adjusted living with recurrent breast cancer.

In the following general discussion section, findings from both the deductive and inductive studies about women's experiences during the recurrent breast cancer trajectory are discussed in an attempt to describe the illness trajectory by comparing findings from the quantitative analyses (Papers I-III) with the qualitative analysis of women's experiences of living with recurrent breast cancer (Paper IV). Thereafter, the three primarily concepts used in this thesis: health, illness, and adjustment, are discussed from a salutogenic perspective. Finally, in the methodological discussion section, limitations and shortcomings are described.

### Health

Many of the women studied here experienced changes in their health before they were diagnosed with recurrence. They had been experiencing an increase in symptoms for a long time, and had repeatedly tried to make contact with the medical services, or even been through several medical examinations without any recurrence being found (Paper IV). The analysis of patient-estimated HRQOL variables such as symptoms (tiredness, hot flushes, nausea/vomiting, arm impairment) and global quality of life domains (support, physical well-being, mood, coping effort, health status), illustrates the finding that changes in terms of deterioration of physical well-being, and improvements in terms of nausea/vomiting were identified as significant predictors of recurrence (Paper I).

The finding in Paper I, suggesting that a change in improved nausea/vomiting level was predictive of outcome, might be related to chemotherapy treatment. It might be hypothesized that these findings reflect more severe underlying disease requiring chemotherapy, and that the improvement in nausea/vomiting levels was the result of completion of adjuvant chemotherapy. Patients who discontinued chemotherapy treatment prematurely owing to side effects such as severe nausea/vomiting might have contributed to this type of explanation. Previous research indicates that early termination of chemotherapy affects survival (Hershman et al., 2005). The most extreme changes in physical well-being, and nausea/vomiting were observed initially, and the majority of recurrences occurred within 3 years after primary diagnosis. Poisson regression analysis was used to predict recurrence depending on time since initial diagnosis and HRQOL variables. These findings then generated new hypotheses in relation to which further prospective investigation is required to determine the prognostic value of changes in HRQOL indicators (Paper I).

Although prognostic value of changes in HRQOL indicators requires further investigation it may be hypothesized that patient self-evaluated HRQOL reflects underlying systemic disease, not yet

diagnosed. This hypothesis raises questions about the role of an undetectable metastatic disease on the symptom experience of subjects. Analyses of bone marrow have revealed that disseminated cells are present in 20-40% of primary breast cancer patients with no clinical or histopathological signs of metastases. The presence of tumor cells in bone marrow is predicative of metastases in bone, lung, or liver (Pantel et al., 2003; Braun et al., 2003). Despite a growing body of research on the metastatic process, there is limited data available concerning the impact of micrometastases or tumor burden on physical well-being, nausea and vomiting. In the future, such data may have important clinical implications.

Many biomedical analyses have studied the time to an event (van Belle et al., 2004), for example for the prevention of fracture related to osteoporosis. Today treatment of osteoporosis is based on the 10-year probability of fracture, calculated using a set of risk variables (Kanis et al., 2007). Many of the risk variables were originally found in small samples, then verified by several studies and finally merged into a material based on of thousands of individuals, and used to obtain accurate estimates. Another example is the use of a new and expensive generation of anti-tumoral treatment for rare gastrointestinal stromal tumors. In order to identify patients at medium or high risk of recurrence, an advanced health-economic model has been developed (Simonsson et al., 2007).

The increasing incidence of breast cancer makes breast cancer an important public health problem (Ferlay et al., 2007). Although the majority of women will recover from their breast cancer, some women's breast cancer will return. Although recurrent breast cancer is sometimes also curable, in most cases it is considered incurable. This, in combination with new treatment options and the use of more and more expensive drugs, highlights the need for developing models to identify women who are at risk of recurrence early, and to determine who might actually benefit from specific expensive drugs.

HRQOL variables are important components in clinical trials, in assessing treatment side effects, and in the decision making processes of patients and physicians. There is a need for a deeper understanding of the subjective experience of global indicators such as physical well-being and for tools to distinguish, for example, general physical well-being from other more specific symptoms such as nausea and signs such as vomiting. Physical well-being is a multidimensional construct referring to symptoms (i.e., physical experience) and function (i.e., physical abilities and activity). Nausea and vomiting are different entities and differ in frequency, duration and severity. While the mechanisms of retching and vomiting are well delineated, the physiology of nausea remains unclear (Paper I).

## Illness

The return of breast cancer was experienced as a very stressful life event that altered the women's lives in many ways. Whether or not the women had suspected the recurrence, they all described themselves as totally unprepared for the trauma of being told about it. The recurrence of breast cancer generated emotional chaos, because the women were well aware of the possible consequences of the recurrence (Paper IV).

During the recurrent illness trajectory, women experienced multiple concurrent symptoms, and at the time of the diagnosis of recurrence the majority experienced a very high prevalence of symptoms (Paper II). These findings are in line with previous research reporting that women with advanced breast cancer experience a multitude of symptoms (Turner et al., 2005). Highly

prevalent symptoms at baseline remained six months after recurrence (Paper III). Study results also indicated stability of the symptom pattern over time, and women who experienced multiple symptoms at baseline also experienced multiple symptoms at every follow-up assessment. Three months after the diagnosis of recurrence of breast cancer seemed to be a particularly difficult time, with the highest symptom prevalence. Regardless of socio-demographic characteristics or disease and treatment-related factors, symptom burden and distress increased while health-related quality of life decreased 3 months after diagnosis of the recurrence (Paper III).

The findings also point out the interrelation of specific symptoms such as fatigue, pain, anxiety and depression. At the time of recurrence, half of the women experienced anxiety and/or depression. One third of these women had a past history of anxiety and/or depression. Most of the women who experienced pain also reported anxiety and depression, and had a pre-history of psychological disorder. The study findings highlight specific symptoms such as fatigue, pain and depression as significant contributors to distress (Paper II).

Women described how distressing symptoms such as pain caused anxiety, leading to sleep disturbances, which in turn led to a vicious circle of constant pain and anxiety, with increased fatigue as an outcome (Paper IV). Having sleeping problems is a common concern in women with metastatic breast cancer who also experience pain and depression (Koopman et al., 2002). Fatigue and psychological symptoms of depression or anxiety are commonly reported by women who have been treated for breast cancer (Bennett et al., 2004).

Although some participants reported increased fatigue as a foreboding symptom of disease relapse, all participants experienced more fatigue after being told that the breast cancer had returned (Paper IV). Fatigue was a highly prevalent symptom, and a nearly ninety percent of patients reported fatigue at the time of recurrence (Paper II). More than half of the patients experienced persistent fatigue 6 months after recurrence (Paper III). Furthermore, the study findings indicate fatigue more as a symptom of existential distress than as related to the disease and treatment. Even when fatigue was reported as a disease and treatment side effect, emotional responses such as depression and anxiety were perceived as major contributors to fatigue. Fatigue was described to be deeply associated with grieving (Paper IV). Findings also showed that fatigue seem to be most significantly associated with depression (Paper III).

One significant finding was the extent to which the recurrence contributed to distress. As expected women who reported multiple symptoms also experienced higher levels of distress which, in turn affected their health-related quality of life. Study findings underscore that some symptoms (i.e. pain and sadness) were more distressing than others, even when they were experienced as moderate in frequency and severity, while other symptoms that occur almost constantly and severely (i.e. problems with sexual interest and activity) did not cause distress (Paper II–III). In accordance with Butler et al. (2003), significantly higher levels of distress were found in progressive or terminally ill women, and a high value of global distress often preceded death or deterioration of the disease (Paper III).

Over time, health-related quality of life also changed significantly, with improved emotional and role functioning (Paper III). Although, previous research indicate improvements in distress over time in women with early stage breast cancer (Carver et al., 1993; Epping-Jordan et al., 1999) and because adjustment is associated with time elapsing since diagnosis (Dow et al., 1996; Gotay & Muraoka, 1998) it could be expected that a recurrence of breast cancer would persistently or increasingly affect distress and quality of life. Changes in symptom experience and quality of life may not only be due to changes in the disease or responses to treatment, but to patients' adaptation to their changed health and life situations, often referred as a response shift (Schwartz

& Sprangers, 1999; Sprangers & Schwartz, 1999). The aim was not directly to assess response shift, it is noteworthy that patients who experience persistent symptoms also experience decreased distress over time, suggesting not that a symptom does not disappear, but rather that the patient adapts to its presence. A response shift may be a natural way of adapting to changes in health, and women may evaluate distressing symptoms and health differently over the course of an illness trajectory.

## Adjustment

Confronting a recurrence of breast cancer was experienced as a life-threatening and life-altering event. All women in this study described awareness of the consequences of the breast cancer recurrence. Facing a life-threatening recurrent illness engendered significant existential distress over losses and fears. Women experienced multiple losses of important life values, and fears of uncertainty about the illness, as well as certainty of future negative outcomes affecting the adjustment to a recurrence of their breast cancer (Paper IV).

Fear of uncertainty about the future is reported as one of the most common problems for women with breast cancer (Ferrell et al., 1996; Pelusi, 1997; Mast, 1998; Sammarco, 2001; Wonghongkul et al., 2006). The experience of uncertainty in illness occurs when the individual is unable to determine the meaning of illness-related events (Mishel, 1988). Previous research into living with primary breast cancer highlights existential issues (Landmark et al., 2001; Davies & Sque, 2002; Richer & Ezer, 2002). Women experience profound and precipitous emotional transformations following a diagnosis of breast cancer (Boehmke et al., 2006), and as these women move through the illness they tend to redefine their lives through integrating the meaning of breast cancer into it (Öhlen & Holm, 2006). Our findings are congruent with previous research suggesting that the impact of breast cancer is experienced in every aspect of women's daily lives (Loveys & Klaich, 1991), including their views of themselves and their relationships (Arman et al., 2002a).

This thesis focuses on the main existential impact of a recurrence of breast cancer. While some women experienced distressing symptoms such as pain, nausea and dyspnoea related to disease and treatment, all participants experienced existential distress. Women experienced distress, spanning from worries and sadness to anxiety and depression, as they struggled with their losses and fears (Paper IV). A study of patients living with different types of cancer shows that patients feel they are left to their own resources during the rehabilitation phase, and that they feel physically and mentally drained and without the knowledge they need to tackle their new, difficult life situations. Furthermore, the patients live with the constant threat of new cancer cells being discovered (Saegrov & Halding, 2004). Although living with a recurrence of breast cancer involved the experience of having the disease, including symptoms related to changes in bodily state, coping with the illness had at least as serious implications in their lives. Women who experienced repeated exposure to additional changes such as disease progression or treatment disappointments, described not having time for recovery between disappointments, which severely impeded their ability to adjust. One major source of distress was the fearful and anxious waiting women were exposed to, was inflicted on them by the slowness of the medical services to a large extent (Paper IV).

Over time, women adjusted to their recurrent breast cancer illness, by making sense of living with the shadow of death, of living with a persistent, and in some cases imminent threat to their lives. These women faced the challenge of coping with the loss of health, which they had previously largely taken for granted, and of making sense of living with their illness in a world of healthy people. Making sense of life-threatening illness comprised dealing with these changes and

accepting that life would never be the same again. Having hope was perceived as essential. Furthermore, living with a life-threatening illness embraced making sense of disruption of the imagined future biography. Women transcended their illness by reevaluating their meanings and attitudes, and by finding new ways of interacting with others. Even if, in some cases, the consequences of a recurrent breast cancer illness were overwhelming, women made sense of living with a lifelong threat, and were able to cope with it in their everyday-lives. Women eased their distress by letting go of losses and rediscovering important values of life, and created well-being by living in and managing in the present. Choosing to accept the inevitable, they rediscovered important and precious life values in their everyday life (Paper IV).

The present findings highlight that the women adjusted not only to their recurrent breast cancer disease and its treatment but also to living with its ramifications. Over time, the women came to terms with living with their illness. Time is an important component of adjustment to recurrent cancer. Women who experienced repeated exposure to additional changes such disease progression or treatment disappointments, described not having time for recovery, which severely impeded their ability to cope. Although our findings indicate time as a healer, the process was not sequential and had no chronological time span (Paper IV).

This thesis clearly reveals that adjusting to a recurrence of breast cancer goes beyond coping with disease and treatment. Women with recurrent breast cancer have to face adjusting to living with a persistent threat to the rest of their lives. Making sense of living with a recurrent breast cancer illness encompassed not only changes in health and life expectations, but also change in attitudes and behavior, and in relationships (Paper IV). This finding is in line with previous research suggesting that adjustment to cancer is a personal transition more than merely a process of coping with the disease and its treatment (Brennan, 2001). Although women used different coping strategies to ease their distress, they adjusted through a personal transition to the many implications of a life-altering illness (Paper IV).

Life is always a journey of change and transition. While change is situational, transition is the process individuals go through as they cope with the change. Transition theory emanates from early research on bereavement, life events family crisis and depression by Parkes, Holmes and Rahe, Kübler Ross and others (Goodman et al., 2006). Transitions are processes that occur over time and that involve changes in identity, roles and relationships, abilities and behaviors (Schumacher and Meleis, 1994) Bridges (2006) suggests that transitions have three phases: endings, neutral zones, and beginnings. Every beginning starts with an ending. The neutral zone is “a psychological no-man’s land between the old reality and the new one” (p. 8) and is a time of confusion before “life” returns to some sense of normalcy. Beginnings are a phase of renewal. To be in a transition might be described as a journey through, usually to an unknown destination (Brammer 1991). A transition is broadly defined as “any event or non-event that results in changed relationships, routines, assumptions and roles” (Goodman et al., 2006 p. 33).

A transition is not so much a matter of change as of the individual’s own perception of the change, and a transition is a transition only if it is so defined by the person experiencing it. Transition is a central concept in nursing (Schumacher & Meleis, 1994; Meleis et al., 2000). Changes in health and illness create a process of transition that may produce alterations in the lives of individuals and their significant others. Transitions have important implications for well-being and health. Supporting people living through transitions is a key function of nursing (Meleis et al., 2000), and “the challenge for nurses and others involved in supporting those undergoing transition is to understand transition processes and to develop interventions which are effective in helping them to regain stability and a sense of well-being” (Schumacher & Meleis, 1994).

## Promoting health in women with recurrent breast cancer illness

The salutogenic orientation seeks to understand why individuals are located at or moving towards the positive end of the continuum of health and illness. Antonovsky (1979) denotes three aspects of health: health may affect the extent to which a person is exposed to stressors, health itself is a resistance resource and being on the healthy side may facilitate the acquisition of other resources. Antonovsky proposed that stressors result in tensions, and it is the individual's capability to deal with these tensions that determines whether the outcome will be salutary or pathological. Sense of coherence (SOC) is crucial to health, and the strength of SOC has direct psychological consequences and affects health status (Antonovsky 1987).

The findings in this thesis showed that sense of coherence, rather than socio-demographic characteristics or medical factors, was the only significant predictor of distressing symptoms such as anxiety, depression, fatigue, mood, physical well-being, total symptom burden, and number of symptoms (Paper II). However, distressing symptoms such as fatigue, pain and depression predicted distress at baseline and at three-months follow up. Fatigue and pain predicted distress at one-month and six-months follow up (Paper III). These results indicate fatigue, pain, and depression as important contributors to distress in women with recurrent breast cancer. Fatigue, pain and depression were also significantly independent of each other in their ability to predict distress. Furthermore, the findings also verified that tiredness, physical well-being, and mood disturbances all had significant impacts on perceived adjustment to illness and perceived health status. One important finding was the impact of distress and perceived adjustment had on health-related quality of life over time. Perceived adjustment was the only predictor of perceived health status (Paper II). Taken together, patients with stronger sense of coherence reported a fewer symptoms and reported lower levels of distress and better perceived adjustment to their illness, as well as better perceived general health status (Paper IV).

SOC captures a person's global subjective state in terms of coping with everyday life in relation to health and well-being. According to Antonovsky (1979) having a strong SOC means having a stable, long-lasting way of viewing the world as comprehensible, manageable and meaningful. The SOC does not describe coping strategies, but to factors that affect the ability to cope with stressors. Our findings demonstrate that sense of coherence was significantly associated with anxiety, depression, and perceived health status. Furthermore, the lower scores for SOC reflected higher scores for anxiety and depression and worse perceived health. These results are in line with previous research recognizing SOC as an important aspect of the coping resources required for adjustment to illness (Ekman et al., 2002; Nesbitt & Heidrich, 2000; Kattainen et al., 2006), cancer pain (Cohen et al., 2005) and perceived health and well-being after breast cancer surgery (Boman et al., 1999).

In a review, Flensburg-Madsen and colleagues (2005) conclude that SOC is a strong predictor of health measured by incorporating psychological aspects, including stress and behavior, while it seems to be a weaker predictor of health measured only in physical terms. This thesis showed that while some women experienced distressing symptoms such as pain, nausea and dyspnoea related to disease and treatment, they all experienced existential distress. This thesis illustrates that women experienced multiple distressing symptoms of distress, spanning from worries and sadness to anxiety and depression, as they struggled with their losses and fears (Paper IV). Furthermore, the most prevalent symptoms were virtually identical to the symptoms included in the subscale of global distress (GDI), indicating that while physical and psychological symptoms were sources of distress, existential issues concerning losses and fears were the major contributors to overall distress.

As described in the body of the thesis, the concept of sense of coherence consists of three components: comprehensibility, manageability, and meaningfulness. Comprehensibility refers to which extent to which the individual perceives a stressful event as comprehensible and understandable, and predictable. This component includes making cognitive sense of the stressful situation (Antonovsky, 1987; Lindström & Eriksson, 2005). To some participants a recurrence was a threat that became real, while others it was perceived as totally unintelligible and inconceivable. The women experienced the need to shift their expectations from curability to incurability, from disruption in health, to facing living with a persistent life-threatening illness. All the women were aware of the consequences of the return of their breast cancer (Paper IV).

Manageability refers to the resources the individual has at his or her disposal for dealing with the demands and challenges of a stressful event. Salutogenesis is a dynamic flexible approach and unlike other coping theories, the salutogenic orientation is non-normative, in the sense that it is not discussing adjustment in terms of “normal” adjustment or “maladjustment”. Although the women used various coping strategies, the central was their personal transition when challenged with making sense of living with a recurrent breast cancer illness, in other words their way of making the new situation manageable (Paper IV).

Meaningfulness is the motivational component of SOC, the extent the individual feels that life makes sense, and that difficulties and demands are viewed as challenges, worthy of investment and engagement (Antonovsky, 1979, 1987). Many women viewed the illness as a challenge, a reminder, or a chance to change. Hope is an essential aspect of the will to live. Having hope facilitated adjustment. Women described the importance of hope, motivating thoughts and emotions directed to a goal of managing the illness. They hoped that the treatment would help and, if not, that there were alternative treatments—but they never wanted to be told that there was nothing more to be done. Although the women described hopes of different kinds, the most frequent hope was to survive, or if not, just to have some more time to live. Participants described not giving up, finding inner strength, and viewing oneself as a survivor despite a poor prognosis (Paper IV).

In situations where it is impossible to avoid inescapable suffering, it is the person’s attitude towards the suffering, the manner and mode in which the individual copes with the illness that can enhance meaning-making processes in a “hopeless” situation. Even when a person has to confront an unchangeable situation and is left without ways of making the situation meaningful, he or she still has the opportunity to choose a manner of facing the adversity (Frankl, 1969). Frankl (1969) believed that people always reach out, either to another person or to a differently meaningful meaning. The will to achieve meaning could be defined as the basic striving of a human being to find sense and purpose. This meaning can be found in suffering, for example by transcending the moment to understand the fullest impact of the experience (Frankl, 1969).

Kellehear (2000) points out spirituality as a source of transcendence. Three different dimensions of spirituality can be described: situational, moral and biographical, and religious. Situational spirituality encompasses purpose, hope, meaning and affirmation. Moral and biographical spirituality comprise achieving peace and reconciliation, reunion with others, and forgiveness. Religious spirituality involves various aspects such as religious reconciliation, divine forgiveness and support, and religious rites or discussions. These dimensions of spirituality are evolving aspects of the human need to transcend, “to go beyond the immediacy of suffering and to find meaning in that experience”. These dimensions have the potential to be ways to achieve transcendence and promoting wellness (Kellehear, 2000 p.153).

Although recurrent breast cancer is often incurable, many of the women in our study could be expected to live years with their recurrent illness, which can therefore, in many respects be regarded as a chronic life-threatening illness. According to Kleinman (1988) the trajectory of chronic illness is so intimately intertwined with the development of a particular life that the illness becomes inseparable from the person's life history as a whole. Continuities and transformations, lead to the appreciation of the meaning in illness. A majority of the women in our study stated that life never ceased to have meaning, whatever difficulties they went through. Over time, the women adjusted by making sense of living with a life-threatening illness as they transcended it by re-evaluating their meanings and attitudes, and by finding new ways of interacting with others. Our results highlight how these women created wellness by living in and coping with the present. By choosing to accept the inevitable, the women re-discovered important and precious life values in their everyday lives (Paper IV). Thus, it is essential to encourage and affirm a sense of empowerment to transcend difficulties and challenges. Even in unchangeable and distressing situations, there are opportunities to manage adversity, through discovering or rediscovering significant meanings and values in life, and by creating wellness being in the present moment.

### ***Methodological discussion***

Measuring symptom experience and quality of life poses various methodological problems. Symptoms and quality of life are often measured using ordinal scales, such as VAS or other ranking scales. A scale is defined as ordinal if the characteristics of a phenomenon can be classified into equidistant categories and these categories can be ordered. As ordinal scales have no measure of equidistance, their results should be regarded as ordered qualitative data, which should be analyzed using non-parametric statistical methods (Svensson, 2003). This is a controversial issue, and although such variables are technically considered ordinal, in practice they are regarded as intervals (Hazard Munro, 1997). Despite this controversy, in most medical and nursing science ordinal data are analyzed using parametric methods. Hence, we used parametric methods such as Pearson's correlations and linear regression.

Two types of error, type I and type II errors can arise in statistical test (Burns & Grove, 2005). Type I errors occurs if the null hypothesis is rejected, when it is actually valid. In order to minimize the risk of type I error, only variables which provided a statistically significant contribution ( $p < 0.05$ ) were included in the final prediction model. Type II errors arise if the null hypothesis is invalid, but not rejected. The risk of type II errors is higher in small sample sizes. In order to controlling for type II error, we made calculations of power, see below:

#### *Paper I*

The Poisson regression model was used to predict a value of the dependent variable given known values of the independent variable in a limited sample. One major problem with multiple regression analysis is the inclusion of too many variables for the number of subjects. The effect size is defined as a function of power and the number of independent variables at a given level of alpha. We selected a power of 0.80, an alpha of 0.05, which gave a moderate effect size to determine appropriate sample size. Our study findings in Paper I are based on an explorative investigation. To replicate these findings a somewhat larger sample size than the present one is needed. Using an 11% larger sample, the power 80% (two-tailed test at the significance level 0.05) would be achieved. With current sample size, we calculated that a gradient of risk per standard deviation of 1.63 or more gives a power of at least 80%. For a fairly weak predictor, the

power was 80%. Our sample consisted of 55 recurrence events. Thus, the study was large enough to identify candidates for prediction and to reject many variables that are not predictors.

However, a final confirmation, or rejection of the candidates would have to be made using another material. The obvious reason that the results need to be confirmed is we tested 20 variables tested. Applying a Bonferroni correction, we should have to multiply the p-values with 20. A good strategy might be to use a small part of a material to generate hypotheses about predictors and the rest for confirmation, or rejection. In conclusion, the prognostic value of changes in HRQOL indicators requires further prospective investigation.

### *Paper II – III*

Linear regression was used to determine regression equations for predicting distress and health-related quality of life. A stepwise multiple regression procedure was used to determine regression equations for predicting the dependent variables. The stepwise procedure selected variables that provided a statistically significant contribution to the prediction model. Logistic regression analysis was used to estimate the probability of drop-out in relation to global distress at baseline. The study sample was 56 participants. With 56 participants the power when testing the correlation coefficient ( $H_0: r=0$  versus  $H_1: r$  differs from 0) is at least 80%, and at two-tailed test at the significance level 0.05, gave a true correlation coefficient of 0.357 ( $r$  square = 0.127). Thus the size is sufficient to assess significant correlation even if the coefficient is fairly low.

Data collection was based on a prospective and longitudinal design. The study was strengthened by the use of a consecutive sample, with inclusion of patients at the time of first recurrence, and with repeated assessments using validated measurements. Weaknesses include the fact that organizational problems with recruiting participants might have resulted in missing presumptive participants. No medical data about these non-participants were collected. The drop out rate over time is another limitation. In addition, one eligibility criterion was that participants had to be mentally and physically capable of participating, which might have excluded some severely ill patients. In these cases, the symptom distress burden might be even higher than reported in this study. Furthermore, the history of prior psychiatric disorders found in this study was determined by chart review, and then confirmed by the participants, but chart reviews has questionable validity and could have resulted in underestimating the prevalence of prior psychiatric disorders.

The Memorial Assessment Symptom Scale (MSAS) is designed to specifically measure symptoms in patients with cancer (Portenoy et al., 1994). The advantage of the MSAS is that it measures multiple symptoms, and symptom frequency, severity and distress. The MSAS generate physical (MSAS-PHYS) and psychological subscales (MSAS-PSYCH) as well as the Global Distress Index (GDI) and Total (TMSAS). The GDI is a short scale, consisting of selected symptoms, empirically tested and found to be distressing than others. These are used to measure global symptom distress (Portenoy et al., 1994). Measuring abstract phenomena like distress with a global distress index poses many challenges. A global index measures the total sum of several dimensions, and it is therefore difficult to identify what it really measures. A global measure is also difficult to interpret, but it is still important to explore its relationship and interactions with other health-related quality of life variables. The scores from both GDI and TMSAS are determined in relation to the number of symptoms, and the frequency, severity, or distress associated with each symptom. According to Portenoy and colleagues (1994) GDI is more clinically meaningful than TMSAS because of the high correlation between this measure and quality of life. Furthermore, the relationship between the symptom distress score and the clinical status of the patient is more likely to be interpreted appropriately using the GDI, because it is less influenced by the cumulative effect of many mild symptoms. Patients reporting many mild symptoms may have scores identical to patients with fewer, but more distressing symptoms

(Portenoy et al., 1994). Findings from these studies showed that symptoms highly prevalent (reported by >50% of the sample) in women with recurrent breast cancer were almost identical with the symptoms included in the GDI.

#### *Paper IV*

Grounded theory is used to explore processes, with the purpose of developing a substantive theory, and is based on symbolic interactionism, assuming that interaction is inherently dynamic and interpretative, addressing how people create, enact, and change meanings and actions (Charmaz, 2006). Our study findings illustrate the interpersonal changes women experienced as they learned new ways of interacting with others. However, the main finding is the existential focus of adjusting as an intrapersonal transition.

Although some participants were immigrants, only women who understood and spoke Swedish were included. Considering the existential nature of the adjustment process, further research addressing different ethnic groups is also needed.

Grounded theory is a method used to describe the world of the person or persons being studied, with the aim of developing a well integrated theory (Stern, 1994). Gathering data by repeated in-depths interviews gave us opportunities to attain a deeper understanding of the major concerns of the participants. Trustworthiness was achieved as theory was derived from the major concerns identified by the participants themselves, and related to ways in which they were dealing with their situations, and involved repeated interviews, checking back and revealing and refining the theory as it developed. Quotations were selected, aiming to illustrate the richness of the data and to give an insider's perspective of the world as experienced and described by women with recurrent breast cancer.

## **CLINICAL IMPLICATIONS AND FUTURE DIRECTIONS**

This thesis illustrates the many implications of breast cancer recurrence. Women with recurrent breast cancer suffer multiple symptoms, and some women suffer more than others. Adjusting to a variety of symptoms is a process influencing health-related quality of life. This thesis has several implications for nursing and for the care of women with recurrent breast cancer.

The goal of caring for women with recurrent breast cancer is palliation, with the aim of enhancing quality of life, throughout the illness trajectory (Chung and Carlson, 2003). This thesis highlights distress as an exceedingly important dimension in the symptom experience for women with recurrent breast cancer. Distress in patients must not go unrecognized or unrelieved. High quality of care must target distressing symptoms across the illness trajectory. This is particularly vital for patients where the symptom prevalence is expected to increase. Patients at increased risk of vulnerability to distress are women who experienced multiple, concurrent symptoms such as fatigue, pain and depression. Other risk factors are co-morbidity, prehistory of anxiety and depression, and progressive or terminal recurrent breast cancer disease. In clinical care, there is a need to implement screening for distress, and to offer psycho-social interventions to relieve the distress.

To help women adjust to recurrent breast cancer, it is important to routinely use multidimensional measurement to assess concurrent symptoms, rather than assessing individual symptoms. Symptoms are patients' perceptions of an abnormal physical or psychological state: symptoms are patients' responses to illness. Assessment is more than a measure of symptoms; it is a process

that should be built into the care of cancer patients from the diagnosis throughout the disease trajectory (NCCN, 2003). Using a multidimensional assessment tool, measuring prevalence, frequency, severity, and distress of concurrent symptoms facilitates the identification and palliation of symptoms in women with recurrent breast cancer.

Women with recurrent breast cancer suffer from multiple symptoms of illness. Some of these women suffer more than others. Adjusting to living with a life-threatening illness is a unique and individual process. Understanding different aspects of adjustment may enhance nurses' and other health care providers' ability to help women adjust to transitions following a recurrence of breast cancer. It is important that care is based on awareness of factors that facilitate or impede adjustment, so that individuals particularly vulnerable to distress associated with transitions may be identified, and so patients receive help in examining their own shortcomings and improving their potential resources for contributing to wellness. Psychosocial interventions aimed at reducing depression and anxiety, to increase the feeling of mastery of the situation and to facilitate active participation in medical treatments have been shown to be valuable (Hellbom et al., 1998). Supportive counselling, meeting individual patients' expectations and needs, is also known to be beneficial (Öhlen et al., 2005). In order to support women with recurrent breast cancer, psychosocial support or interventions could be offered. To support patients' adjustments to a life-altering illness it is important to recognize the extent to which the transition engenders existential distress. To help women with recurrent breast cancer relieve their suffering, it is essential for the medical professions to move beyond symptom control and to recognize existential distress.

Our findings suggest that is of major concern to reduce delays in care, minimizing waiting time for medical examinations, test results, and start of treatment. Other important ways of supporting patients might be to mediate comfort (Morse, 2001) and consolation (Norberg et al., 2001) and promote a feeling of inner space, which may enable patients to be reconciled and to alleviate suffering (Öhlen et al., 2002). It is also important to promote an atmosphere of ease (Edvardsson et al., 2005) by listening to patients stories, and to acknowledge the diversity of their needs (Thorne et al., 2005). Lastly, it is important to encourage a sense of empowerment to transcend difficulties and challenges. This thesis indicate that even in unchangeable and distressing situations, opportunities to manage adversity remain, by discovering or re-discovering significant values in life, and creating wellness by being in the present.

While symptom distress may define one dimension of a symptom (i.e. the extent to which a symptom is bothersome or problematic), distress itself is a multidimensional phenomenon, the total experience of trauma or a life-altering event. Distress is considered a condition, and not a diagnosis (Sellick & Edvardsson, 2007). There is a need to identify the relationship and difference between distressing symptoms and overall distress. Further research is needed to examine the incidence and impact of symptoms such as anxiety and depression as co-morbid conditions, occurring with but not necessarily due to recurrent breast cancer.

The increasing interest in psycho-social variables as prognostic factors requires consensus concerning HRQOL methodology. There is a need to determine the relationship between symptoms and general indicators. HRQOL is based on measuring loss of health, by assessing symptoms, physical and psychological well-being, functioning and health status, but only to a lesser extent to meaning and existential issues. Global indicators and symptom scales quantify functional impairment and disabilities. Having these measures make HRQOL a more useful tool. Existential issues become very prominent in relation to recurrent breast cancer. An intriguing issue is to deal with the problem of suffering, and its effect on HRQOL.

## CONCLUSIONS

Guided by a salutogenic perspective, this thesis describes health, illness and adjustment, as experienced and perceived by women during their breast cancer trajectory.

Several women described their experiences of changes in health before their recurrence, which forced them to repeatedly seek consultations with the medical services. Using HRQOL variables such as symptoms (tiredness, hot flushes, nausea/vomiting, arm impairment) and global quality of life domains (support, physical well-being, mood, coping effort, health status) we analyzed changes in health before a recurrence of breast cancer. Our findings suggest that changes in physical well-being and nausea/vomiting levels may be predictors of recurrence.

Women with recurrent breast cancer experience multiple, concurrent, and persistent symptoms. Nearly ninety percent of our patients reported fatigue at the time of recurrence. Although some participants reported increased fatigue as a foreboding symptom of disease relapse, all participants experienced increased fatigue after being told that the breast cancer had returned. Findings indicate that fatigue was more associated with existential distress than related to the disease and treatment. Women reported higher symptom burden and levels of distress as well as deteriorated quality of life three months after a recurrence. Distress and perceived adjustment had major impact on HRQOL. Significantly higher levels of distress were found in progressive or terminally ill women. Over time, HRQOL also significantly changed, with improved emotional and role functioning.

Sense of coherence predicted distressing symptoms more than socio-demographic characteristics or medical factors. Distress and perceived adjustment predicted HRQOL. Taken together, patients with stronger sense of coherence reported a lower prevalence of symptoms and experienced lower levels of distress and better perceived adjustment to their illness, and perceived a better health status and quality of life.

Women experienced distressing symptoms, spanning from worries and sadness to anxiety and depression, as they struggled with their losses and fears. While women used various coping strategies to ease their distress, they adjusted to the many implications of a life-threatening illness through a personal process of transition. Most of the women stated that life never ceased to have meaning, and whatever difficulties they went through, they adjusted to the changes in their health and lives. Over time, the women adjusted to their recurrent breast cancer illness by making sense of living with the shadow of death.

In conclusion, this thesis provides a contribution to a deeper understanding of the many facets of a recurrent breast cancer trajectory and how it is mirrored in the affected women's lives. This thesis highlights the major existential impact of a recurrence of breast cancer. Health is a core concept in nursing, along with elucidating meaning to help individuals move beyond their trauma and mobilize transcendence. Being regarded as a living rather than a dying person, and being received with empathy and compassion are essential to every person suffering from a serious illness. To live in the present, a person must have hope, as hope is an essential aspect of the will to live. Promoting health is possible, even in severe illness and in unchangeable and almost unbearable situations. Opportunities to manage adversity remain, as well as a movement toward health. Women may transcend their illness by finding new meaning through discovering or re-discovering significant values in life, and creating wellness by being in the present moment.

*Look to this day, for it is life...*

*For yesterday is but a dream,  
And tomorrow is only a vision.*

*But today, well lived,*

*Makes every yesterday a dream of happiness,  
And every tomorrow a vision of hope.*

– *Sanskrit proverb*

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**DISSERTATIONS FROM  
INSTITUTE OF HEALTH AND CARE SCIENCES,  
THE SAHLGRENSKA ACADEMY AT UNIVERSITY OF GOTHENBURG**

Doctoral dissertations

Skärsäter, I. (2002). The importance of social support for men and woman, suffering from major depression – a comparative and explorative study.

Ahlberg, K. (2004). Cancer-Related Fatigue – experience and outcomes.

Drevenhorn, E. (2006). Counseling patients with hypertension at health centres – a nursing perspective.

Olsson, L-E. (2006). Patients with acute hip fractures motivation, effectiveness and costs in two different care systems.

Berg, L. (2006). Vårdande relation i dagliga möten. En studie av samspelet mellan patienter med långvarig sjukdom och sjuksköterskor i medicinsk vård.

Knutsson, S. (2006). Barns delaktighet genom besök hos närstående som vårdas på en intensivvårdsavdelning.

Jakobsson, E. (2006). End-of-life care in a Swedish county – patterns of demographic and social condition, clinical problems and health care use.

Henoch, I. (2007). Dyspnea Experience and Quality of Life. among Persons with Lung Cancer in Palliative Care.

Sahlsten, M. (2007). Ömsesidighet i förhandling – Sjuksköterskors förutsättningar för och erfarenheter av att främja patientdelaktighet.

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Lindström, A-C. (2007). ”Något som inte längre är” – distriktssköterskors yrkesutövning på vårdcentral ur ett genusperspektiv.

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Patel, H. (2008). Patients with worsening Chronic Heart Failure – Symptoms and aspects of Care.

Larsson, I. (2008). Patient och medaktör. Studier av patientdelaktighet och hur sådan stimuleras och hindras.

#### Licentiate dissertations

Moene, M. (2006). Samtal inför ett kirurgiskt ingrepp.

Lindström, I. (2007). Patienters delaktighet – en studie om vård i livets slutskede.