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**COPING AND STRESS MANAGEMENT
TRAINING WITH SPECIAL FOCUS ON
WOMEN WITH BREAST CANCER**

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Coping and stress management training with special focus on women with breast cancer

THESIS FOR DOCTORAL DEGREE (Ph.D.)

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ABSTRACT

Background: People diagnosed with cancer are confronted with many stressors, such as worries about diagnosis and prognosis, demanding treatments, treatment decisions, and disruption of ordinary life functions and roles. Compared to other types of cancer, breast cancer affects relatively young women, half of them of working ages. Knowledge of effective strategies to cope with breast cancer, as well as development of interventions strengthening stress management skills among women with breast cancer, are important in order to decrease individual suffering and facilitate the transition back into everyday life, including work.

Aims: The general aim of this thesis was to generate more knowledge regarding psychological and social aspects of being diagnosed with breast cancer. More specifically, the aims were to examine sickness absence and disability pension after diagnosis, how different ways of coping with breast cancer are linked to health outcomes, and ways to promote mental health after diagnosis.

Methods: *Study I:* All 3547 women in Sweden aged 20-65 with a first breast cancer diagnosis in 2005 and a matched comparison group were followed by register linkage regarding annual levels of diagnosis-specific sickness absence and disability pension through 2010. Associations with disease-related and sociodemographic factors were estimated using logistic regression. *Study II:* 78 studies were included in a meta-analysis of associations between different strategies to cope with a breast cancer diagnosis and health outcomes. The influence of potential moderators was also studied. *Study III:* People with cancer (76% with breast cancer) were randomized to a mindfulness-based stress management training program (n=32) or a wait-list control condition (n=39). Effects on psychological processes and mental health outcomes after six months were analyzed. *Study IV:* University students participating in a feasibility study of an Internet-based version of the mindfulness-based stress management training program were randomized to the intervention (n=46) or an active control condition (n=44). Completion rate, participant experiences, and post-intervention effects on mental health were assessed.

Results: *Study I:* Sickness absence, mainly due to breast cancer, increased markedly in the first year after breast cancer diagnosis, however, it approached the levels of breast cancer-free women five years later. Pre-diagnosis sickness absence and advanced cancer stage were associated with higher risk of sickness absence and disability pension, as were lower education and being born outside of Sweden. *Study II:* Adaptive coping, such as acceptance and positive reappraisal, was associated with better mental health in women with breast cancer. These associations were strongest among individuals under current treatment and women assessed soon after diagnosis. *Study III:* No significant effect of the mindfulness-based stress management training program on mental health outcomes was found at the six-month follow-up. However, a positive effect on self-reported mindfulness was observed. *Study IV:* The Internet-based mindfulness-based stress management training program was experienced as usable and acceptable and had potential for increasing psychological well-being for those completing it. However, only 39% of the participants completed the program.

Conclusions: Among women diagnosed with breast cancer, levels of sickness absence were back to the same levels as before diagnosis in a few years. Adaptive coping was associated with better mental health among women with breast cancer, especially during

treatment and in newly diagnosed women. Despite increase in mindfulness at six-month follow-up after a mindfulness-based stress management training program, no statistically significant improvement in mental health was found. More knowledge is needed on the underlying mechanisms and moderating factors for achieving long-term benefits of this kind of training. The Internet could be a promising way to disseminate programs and tools facilitating mindfulness training, but if retention and compliance is important, additional modification of the assessed Internet-based mindfulness-based stress management training program is needed.

SAMMANFATTNING

Bakgrund: Personer som diagnostiserats med cancer utsätts för mycket stress och oro gällande diagnos och prognos, krävande behandlingar, behandlingsbeslut, och avbrott i det vanliga livets funktioner och roller. Jämfört med andra typer av cancer drabbar bröstcancer relativt unga kvinnor, hälften i arbetsför ålder. Kunskap om effektiva strategier för att hantera bröstcancer, samt om insatser som kan stärka förmågan att hantera stress bland kvinnor med bröstcancer, är viktig för att begränsa individuellt lidande och underlätta återgång till vardagslivet, inklusive arbetet.

Syfte: Det övergripande syftet med denna avhandling var att generera mer kunskap om psykologiska och sociala aspekter av att få en bröstcancerdiagnos. Mer specifikt var målet att undersöka sjukfrånvaro och förtidspension efter bröstcancerdiagnos, hur olika sätt att hantera bröstcancer är kopplat till hälsoutfall, och metoder att främja psykisk hälsa efter bröstcancerdiagnos.

Metoder: *Studie I:* Alla 3547 kvinnor i Sverige i åldern 20–65 som fick en första bröstcancerdiagnos år 2005 samt en matchad jämförelsegrupp följdes via registerdata till och med 2010 avseende årliga nivåer av diagnosspecifik sjukfrånvaro och förtidspension. Samband med sjukdomsrelaterade och sociodemografiska faktorer analyserades med hjälp av logistisk regression. *Studie II:* 78 artiklar ingick i en meta-analys om samband mellan olika copingstrategier för att hantera en bröstcancerdiagnos och hälsoutfall. Även olika faktorer påverkan på eventuella samband studerades. *Studie III:* Personer med cancer (76% hade bröstcancer) randomiserades till ett mindfulness-baserat stresshanteringsprogram (n=32) eller en väntelista-kontrollgrupp (n=39). Effekter på psykologiska processer och psykisk hälsa efter sex månader analyserades. *Studie IV:* Universitetsstudenter randomiserades i en förstudie av en Internet-baserad version av det mindfulness-baserade stresshanteringsprogrammet till interventionen (n=46) eller en aktiv kontrollgrupp (n=44). Slutförande av programmet, deltagarnas erfarenheter, samt effekter på psykisk hälsa bedömdes.

Resultat: *Studie I:* Sjukfrånvaro, främst till följd av bröstcancer, ökade markant under det första året efter diagnos, men närmade sig nivåer för kvinnor utan bröstcancer det femte året. Sjukfrånvaro innan bröstcancerdiagnos och avancerat cancerstadium var förknippat med högre risk för sjukfrånvaro och förtidspension, vilket även gällde lägre utbildning och att vara född utanför Sverige. *Studie II:* Adaptiv coping, såsom acceptans och positiv omvärdering, hade samband med bättre psykisk hälsa hos kvinnor med bröstcancer. Sambanden var starkast bland kvinnor som var under cancerbehandling och de som bedömts i nära anslutning till diagnostisering. *Studie III:* Ingen signifikant effekt på psykisk hälsa av det mindfulness-baserade stresshanteringsprogrammet sågs vid sex månaders uppföljning. Emellertid fanns en signifikant positiv effekt på självrapporterad mindfulness. *Studie IV:* Det internet-baserade mindfulness-baserade stresshanteringsprogrammet upplevdes som användarvänligt och acceptabelt. Det hade potential för att öka psykiskt välbefinnande för dem som slutförde det, vilket dock endast 39% av deltagarna gjorde.

Slutsatser: Sjukfrånvaronivåerna bland kvinnor med bröstcancer var nere på nivåer motsvarande dem före diagnos inom några år. Adaptiv coping var associerad med bättre psykisk hälsa bland kvinnor med bröstcancer, särskilt bland dem som genomgick cancerbehandling och bland nydiagnostiserade kvinnor. Trots ökad mindfulness vid sex

månaders uppföljning, efter ett mindfulness-baserat stresshanteringsprogram, sågs inga statistiskt signifikanta förbättringar av psykisk hälsa. Det behövs mer kunskap om bakomliggande mekanismer och modererande faktorer för att uppnå långsiktiga positiva effekter av mindfulness-baserade stresshanteringsprogram. Internet kan vara ett lovande sätt att sprida program och verktyg som underlättar mindfulnesssträning, men om fullföljande och efterlevnad av ett helt program är viktigt så behövs ytterligare modifiering av det studerade internet-baserade mindfulness-baserade programmet.

LIST OF SCIENTIFIC PAPERS

- I. Kvillemo P, Mittendorfer-Rutz E, Bränström R, Nilsson K, Alexanderson K. Sickness absence and disability pension following breast cancer diagnosis: a five-year nationwide cohort study. *Invited re-submission*
- II. Kvillemo P, Bränström R. Coping with breast cancer: a meta-analysis. *PloS One*. 2014 Nov 25;9(11):e112733
- III. Bränström R, Kvillemo P, Moskowitz JT. A randomized study of the effects of mindfulness training on psychological well-being and symptoms of stress in patients treated for cancer at 6-months follow-up. *International Journal of Behavioral Medicine* 2012;19(4):535-42
- IV. Kvillemo P, Brandberg Y, Bränström R. Feasibility and outcomes of an Internet-based mindfulness training program: a pilot randomized controlled trial. *JMIR Mental Health* 2016;3(3):e33

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LIST OF ABBREVIATIONS

CI	Confidence interval
DC	Disengagement coping
FFMQ	Five facets of mindfulness questionnaire
ICBT	Internet-based cognitive behavioral therapy
MANOVA	Multivariate analysis of variance
MANCOVA	Multivariate analysis of covariance
MBCR	Mindfulness-based cancer recovery
MBCT	Mindfulness-based cognitive therapy
MBSR	Mindfulness-based stress reduction
OR	Odds ratio
PCC	Primary control coping
SCC	Secondary control coping
WHO	World Health Organization

1 INTRODUCTION

Cancer poses a major threat to public health and the incidence rates have increased in most countries since 1990 (1). Due to early detection and better treatment, the proportion of breast cancer survivors has increased markedly during the past decades (2, 3). Being diagnosed with cancer can have profound psychological and social consequences and mental health concerns are common (4, 5). Patients treated for cancer commonly report symptoms of stress and decreased quality of life (6-8). In addition to demanding treatments, many patients diagnosed with cancer experience the disruption of ordinary life functions and roles (9-11). A better understanding of the consequences of different strategies to cope with various demands that patients face after a cancer diagnosis is important (12-14). There is also a need to develop effective and cost efficient interventions targeting stress and related symptoms after cancer diagnosis to facilitate transition back into everyday life and long-term health (11-13, 15).

1.1 The concept of health

Even if health is central to medical research, there is still no uniform definition of the concept. In parallel with medical advances and the detection of different forms of impairments, a number of definitions have been put forward (16, 17).

1.1.1 Medical or holistic approach

Discussing health and illness, Lennart Nordenfeldt (16) contrasts two quite different views on health. The first is a medical or biostatistical theory, formulated by Christopher Boorse (18), in which biological functioning and survival are crucial factors. Health is in this perspective a function of internal processes in the human body or mind and implies the absence of disease. The second view presented is derived from holistic theories, in which health instead is regarded as a function of a person's abilities to perform intentional actions and achieve goals. Health is in this perspective compatible with the presence of diseases, although the assumption is that a disease tends to reduce its bearer's health.

1.1.1.1 *Disease, illness, health concerns, and sickness absence*

The terms disease, illness, and sickness are sometimes used interchangeably to express varying health concerns, although they represent different realities (19). The term disease has in the literature on health been associated with biological and pathological processes (18-20), sometimes implying the assessment of a physician with a subsequent diagnosis (19). Illness on the other hand, has been referred to as a person's subjective sense of not feeling well, while experiencing physical or mental symptoms of poor health (19, 20). Finally, the term sickness, has been regarded as reflecting socially and culturally held conceptions of health (20) and the social role a person with different health concerns takes or is given in society (19). In this thesis, the term "health concern", is used to define subjectively experienced feelings of not feeling well (illness), as well as physical and mental (pathological) conditions diagnosed by a physician (disease). The term sickness absence is used when disease or illness has led to reduced work capacity and being absent from work, i.e., sickness absence.

1.1.2 Static or dynamic perspective

A holistic approach on health is reflected in the Constitution of The World Health Organization (WHO), adopted in 1946, in which health was defined as a state of complete physical, social and mental well-being, and not merely the absence of disease or infirmity (21). Although important for the now commonly accepted broad view of health, this definition has been criticized for defining health as a more or less unachievable state, implying that most people are unhealthy most of the time (17). In order to move away from a static formulation of health, Huber and colleagues (17) proposed a more dynamic concept, based on the capacity to cope, maintain and restore one's integrity, equilibrium, and sense of well-being, when confronted with different challenges. Applying this concept on physical as well as mental health, Huber and colleagues meant that a healthy organism is capable of maintaining physiological equilibrium despite changing circumstances, and recover from stress by enhancing the comprehensibility, manageability, and meaningfulness of a difficult situation. They also elaborated the concept in the social domain of health, stating that health can be regarded as a dynamic balance between the opportunities and limitations shifting through life. By successfully adapting to, for example a disease, people can be able to work or to participate in social activities and still feel healthy.

1.1.3 Classifying health concerns and measuring health

The International Statistical Classification of Diseases and Related Health Problems (ICD 10) (22) is used for classification of diagnoses. In addition to classifying and diagnosing physical and mental health concerns, the increase or decrease of symptoms related to poor health and various manifestations of good health are regularly monitored in the care of patients diagnosed with cancer. In order to measure states and changes in health, several self-report scales have been developed, reflecting different aspects, e.g., anxiety and depressive symptoms (23), perceived stress (24), positive state of mind (25), and quality of life (26). The term quality of life is often used in connection to cancer care, e.g., when assessing effects of cancer treatment or actions taken to relieve side effects (27). Quality of life has no uniform definition, but is often associated with experiences of satisfaction in life (27). Self-report scales are used in both clinical and nonclinical settings (27, 28).

1.2 Coping with stress

Being able to handle demanding or stressful situations is central for the maintenance of health (29). A lot of research has been carried out in order to understand the impact of stress on the human body and mind, as well as how people evaluate demanding situations as a basis for subsequent coping efforts.

1.2.1 The concept of stress

The origin of the concept of stress can be traced back to 1865 when Claude Bernard noted that the maintenance of life is critically dependent on keeping our internal state constant in a changing environment. Hans Selye (30) later defined stress in terms of a nonspecific response of the body to any demand upon it. Selye referred to the actual or perceived threat to an organism as a "stressor" and the response to the stressor a "stress response". More contemporary views on stress do not consider the stressor and the stress response as separable entities, rather as a phenomena interacting in a system with ongoing physical, cognitive and emotional processes, where individual psychological characteristics play a central role (31). Stress has been found to have a negative impact on health (32). Difficult situations, such as the loss of a loved one, unemployment, or

being diagnosed with a deadly disease, can result in complaints such as perceived stress, fearfulness, guilt, anger, anxiety and depression (32-37). Stress may also increase the risk of behavioral problems, for example sleep disturbance and substance abuse (38, 39). Biological and psychological processes are intertwined at the onset of stress. In healthy individuals, an acute stress response typically does not imply a negative impact on the individual, but may even be experienced as positive (32). This was noted by Seyle who referred to pleasant stress as “eustress” and negative or pathogenic stress as “distress”(40). In this thesis, the term stress is used to define the negative aspects of stress that can lead to poor health.

1.2.2 Appraisal and coping

In 1966, Richard S. Lazarus (41) presented a theory where psychological stress was a central concept, emphasizing a subjective approach in which a person’s evaluation of a situation is central for stress and related emotions. Continuing within this theoretical framework, Lazarus and Susanne Folkman some years later launched the stress appraisal and coping model, built on the concepts of cognitive appraisal and coping (42). The model suggests that the outcome or consequences of a stressful situation/event, or “stressor”, depends on both the individual’s evaluation of the stressor (primary appraisal) and an evaluation of available coping resources and options (secondary appraisal) (42). Primary appraisal refers to an individual’s evaluation of an event or a situation as threatening, stressful, challenging, positive, or irrelevant. Secondary appraisal, refers to what is perceived to be possible to do to manage the stressor. Given the two types of appraisals, different coping efforts are thought to follow that lead to various outcomes. Thus, the model implies that the response to an event or situation is dependent on the individual’s perception of the situation/event as threatening or challenging, and the individual’s perceived ability to handle or cope with the potential demands that the threat or challenge imposes (29). Factors influencing appraisal are linked to both the social and cultural environment and to personal characteristics (31).

1.2.2.1 Coping strategies

Coping strategies refer to the thoughts and actions people use to manage experience of stress, manage the problem causing the perceived stress, and sustain positive well-being (43). Many attempts have been made to measure various strategies to handle challenges, i.e., coping strategies (44). In order to structure and describe different types of coping strategies, researchers sometimes use groupings into *higher* and *lower order* categorizations (44). Higher order coping categorizations are thought to describe and bring together the common traits of several different lower order coping strategies. Commonly used higher-order coping categorizations are: problem-focused vs. emotion-focused coping, avoidance vs. approach coping, active vs. passive coping, cognitive vs. behavioral coping, and engagement vs. disengagement coping (44). In studies linking various forms of coping strategies with different health outcomes, more engagement forms of coping, aiming to eliminate, reduce, manage or adapt to stressors or their emotional consequences, have in general been found to be related to better health than more disengagement forms of coping, aiming to avoid, ignore, or withdraw from stressors or their emotional consequences (45-47). Examples of engagement types of (lower order) coping categories are seeking social support, taking action, and planning for managing the situation, trying to see something beneficial in the situation, or “actively” accepting the circumstances. Examples of disengagement forms of coping categories are distancing from the stressor, refusing to believe that the situation has occurred or withdrawal from social situations. In figure 2, higher and lower order

coping strategies relevant for Study II are presented, built on the higher order coping categories engagement vs. disengagement. In the grouping of engagement forms of coping, a distinction is made between primary control coping strategies (PCC) aiming to change the stressor or related emotions, and secondary control coping (SCC) aiming to facilitate adaptation to stress.

The choice of coping strategy may to some extent be stable over time (48), i.e., dispositional coping. Research, however, suggests that changes in coping in relation to stressful events may occur due to external factors, the nature of the stressor, as well as physical and mental states in the individual, despite a predisposition for certain strategies (14, 49, 50). Coping has been extensively researched among women with breast cancer, but studies still present divergent results with regard to associations between different coping strategies and physical and mental health (51). Engagement forms of coping have, e.g., been reported as being both positively (52) and negatively (53) related to better health, and studies on moderating factors is therefore warranted in order to clarify when the use of different strategies may be beneficial.

1.2.2.2 Coping with mental and work related demands after breast cancer diagnosis

Being diagnosed with breast cancer often lead to stress connected to uncertainty about prognosis and lack of control over how life will unfold (54), in parallel with the experience of more controllable stressors related to daily life, functions and roles. An approach connecting working life with coping and health concerns was put forward by Kristenson in 1991 (55), discussing sickness absence in terms of a coping behavior. Depending on how the individual perceive work in relation to his or her health condition, sickness absence can be viewed as both a form of withdrawal (disengagement coping) and an active choice aimed at keeping or restoring health and work capacity (engagement coping). In order to examine the relationship between coping behavior and sickness absence among women with breast cancer, Johnsson et al. (56) compared sicklisted women with working women regarding differences in the use of coping strategies. The authors assessed women treated with chemotherapy and women not treated with chemotherapy separately at six months and ten months after surgery. No significant differences in coping strategies between working and sicklisted women treated with chemotherapy was observed at six months post-surgery, but after ten months, women who worked used coping in the form of change of values (engagement coping) to a larger extent than those sick listed. In the group of women not treated with chemotherapy, working women used less fatalistic coping (disengagement coping) compared to those still fulltime sick listed at both time points.

1.3 Being diagnosed with breast cancer

In the following paragraphs, different aspects of being diagnosed with breast cancer are outlined. Every woman has her own unique experiences related to the diagnosis, and the description can only mirror a general knowledge of physical, psychological, and social aspects.

1.3.1 Incidence, prevalence and survival

In 2012, about 14.1 million new cases of cancer were diagnosed world wide and 1.7 million women were diagnosed with breast cancer. This number constitutes an increase of the incidence rate for breast cancer by more than 20% since 2008 (57). In Sweden, about 9 000 women are diagnosed with breast cancer each year, half of them before the

age of 65 (58-60). Breast cancer is uncommon before 35–40 years of age, after which the incidence increases with age (58). The survival rates for women with breast cancer have improved markedly over the last decades due to improvements in screening and treatments (2, 3, 61). The five-year survival rate in Sweden rose from 65% in the mid-1960s to 89% for 2004–2010. Today about 90 000 women in Sweden are living with a breast cancer diagnosis (58).

1.3.2 Classification and prognosis

In order to assess the severity and prognosis of cancer, different staging systems have evolved as the research on cancer has progressed. The most widely used cancer staging system, “TNM Classification of Malignant Tumors” (TNM), forms the basis for the grouping of breast cancer in different stages (0-IV) (62, 63). In this system, letter T describes the size of the primary tumor and whether it has invaded nearby tissue, N describes regional lymph nodes that are involved, and M describes distant metastasis, i.e., the spread of cancer from one part of the body to another. By combining information on T, N and M, breast cancer is grouped into stages reflecting the tumor advancement, represented by the Roman numerals 0, I, II, III and IV and the letters A, B and C. Stage 0 means that abnormal cells are in the lining of a breast duct but have not invaded nearby breast tissue or spread outside the duct. In stage IA, the breast tumor is no more than two centimeters across, and the cancer has not spread to the lymph nodes. In stage IB, the tumor is no more than two centimeters across, but cancer cells are found in lymph nodes. Stage IIA means that the cancer has spread to axillary lymph nodes, and in stage IIB, the tumor is 2-5 centimeters across, and the cancer has spread to axillary lymph nodes, or the tumor is larger than five centimeters across, but without spreading to axillary lymph nodes. In stage IIIA the cancer has spread to axillary nodes, or has been spread to lymph nodes behind the breastbone. In stage IIIB, the tumor has grown into the chest wall or the skin of the breast, and in stage IIIC, the tumor has spread to lymph nodes behind the breastbone and to axillary lymph nodes, or to lymph nodes above or below the collarbone. Stage IV means that cancer cells from the tumor have spread to other parts of the body, such as the lungs, liver, bones, or brain (64). At this last stage, the disease is largely incurable (65).

1.3.3 Treatment

The choice of breast cancer treatment and the duration depends on the characteristics of the tumor. The primary treatment for stage I-II breast cancer is surgery. In order to decrease the size of the tumor, chemotherapy, and sometimes targeted therapy with specific antibodies, can be given before surgery. Chemotherapy is recommended before surgery when treating stage III breast cancer (59). Chemotherapy and/or radiation, and/or hormone therapy are often given after surgery to prevent recurrence. Chemotherapy is in most cases given during five months after surgery, but can be recommended up to one year if the risk of recurrence is high. The length of radiation is usually four to six weeks. Hormone therapy is often given during five years after diagnosis, but extended treatment can be given in certain cases. If needed, targeted therapy is also given. When the cancer has reached stadium IV, the treatment is primarily palliative, in order to prolong life and prevent pain and suffering (59, 65, 66).

1.3.3.1 Short-term treatment side-effects

A number of side effects associated with the period of breast cancer treatment can cause substantial mental and physical strain (64, 67-70). Surgery can imply removing part of the breast or the whole breast, which can cause pain and tenderness in the

surgical area. If the axillary lymph nodes are removed, the flow of lymph fluid is slowed and fluid may build up in the arm, and impaired upper extremity movement occur (67). Chemotherapy can harm normal cells that divide rapidly, for example in the hair follicles, the blood and the gastrointestinal tract, leading to alopecia, lower levels of healthy blood cells with subsequent infections, fatigue, poor appetite, nausea, vomiting, diarrhea and muscle pain. Adverse effects of cognitive functions in the area of learning, memory, and processing speed have also been observed (71). Radiation therapy affects cells in the part of the body that is treated. The skin can become dry, tender, and itchy. It is also common to become tired during radiation therapy, especially in the later weeks of treatment. Hormone therapy may cause menopausal symptoms like hot flashes, vaginal discharge, and nausea. Research on side effects of hormone therapy indicate that some drugs can have adverse effects on cognitive functions as well (69). Possible side effects of targeted therapy include nausea, vomiting, and diarrhea, heart damage, heart failure, and breathing problems.

1.3.3.2 Long-term treatment side-effects

Most of the side-effects from cancer treatment are connected to the period of treatment, however, some effects arising during or after treatment may persist during several years (72). A substantial number of women who undergo axillary lymph node surgery continue to experience pain or physical discomfort during the first year after treatment, and some even for longer time. Upper-body limitations regarding pushing, lifting and reaching have also been reported from a substantial number of women in the first year (67). Cognitive side effects and menopausal symptoms from treatment may also be prevalent after completed chemotherapy and during possible hormone treatment (66, 69, 72). Fatigue is another long-term side-effect which is reported by some women up to 5-10 years after treatment (73).

1.3.4 Mental health

An increasing number of studies focus on the mental health aspects of breast cancer, investigating different symptoms of stress (8, 74, 75). Commonly reported complaints in women with breast cancer are anxiety, depressive symptoms, sleep disturbance, fear of recurrence and lower quality of life (6, 67, 76-78). Mental health concerns are particularly prevalent at diagnosis, surgery and recurrence (78, 79). Approximately 30% of the women have been found to suffer from depressive symptoms immediately following treatment (80). The prevalence of major depression (81) has been estimated to be around 10-25% among women with breast cancer in the year after diagnosis (82). Mental health concerns affect some women more than others. Poor physical health, e.g., pain and fatigue, directly influences the mental health status (72) and may also be a reminder of the diagnosis, creating anxiety about possible cancer recurrence (67). Studies have shown that younger women have a higher risk of depression after breast cancer compared to older women (75, 83). This elevated risk may be connected to the earlier menopause transition and infertility caused by the cancer treatment (72). In general, treatments that lower the levels of estrogen may partly explain the elevated risk for depression in breast cancer survivors (82). Disruptions in family and marital relationships, concerns about caring for children, work-related difficulties, and insurance and economic issues may add to the burdens of younger survivors (72). Generally, low education, low income/poor financial status, as well as being unmarried, have shown to be significantly associated with depression in breast cancer survivors (75). In a Danish study, immigrated women, or women who were descendant

from an immigrant, were shown to have a higher risk of depressive symptoms 3–4 months after breast cancer diagnosis, compared to other women (84).

1.3.5 Work-related aspects

Compared to other types of cancer, breast cancer affects relatively young women, half of them of working age (60, 85). A breast cancer diagnosis and subsequent treatment is often associated with absence from work due to effects of demanding treatments, reducing the work capacity. National regulations specify the right to gain economic support when one has reduced work capacity, temporarily or permanently due to disease or injury. From a societal point of view, there are economic reasons for encouraging people to return to work as soon as possible after a period of disease or injury (86). From the patient's point of view, there are also benefits to return to work, including the regaining of social connection, a professional identity, and the promotion of health (9, 10).

1.3.5.1 Swedish rules on sickness absence and disability pension

In Sweden, all individuals ≥ 16 years of age with income from work or unemployment benefit are entitled to sickness absence benefit if unable to work due to disease or injury (87). After a first qualifying day, employers pay sick pay for the first 14 days of a sick-leave spell, thereafter sickness benefit is paid by the Social Insurance Agency. Self-employed usually have several qualifying days. A physician certificate is required after seven days of self-certification. Sickness absence can be for full-time (100%) or part-time (25, 50 and 75%) of ordinary working hours. Further, residents in Sweden aged 19–64 years, who due to disease or injury permanently have lost their work capacity at least to 25% of ordinary working hours, can be granted disability pension from the Social Insurance Agency. Disability pension can be granted for 25, 50, 75 or 100% of ordinary working hours. Sickness benefits cover 80% of lost income, up to a certain level and disability pension covers 64% of lost income up to a certain level. In order to promote return to work, the Swedish government launched new rules for sickness absence in 2008, implying stricter assessment related to sickness absence and disability pension. Provision of sickness absence benefit was for most individuals limited to one year, instead of being unlimited, which was previously the case (88).

1.3.5.2 Breast cancer-specific guidelines for sickness absence duration

In order to assist physicians and Social Insurance officers when making decisions on sickness absence, the Swedish National Board of Health and Welfare implemented general as well as diagnosis-specific sick-leave guidelines or recommendations for the maximum time of sickness absence in 2007 (66, 89). According to the guidelines for breast cancer, sick leave for up to three weeks after breast conserving surgery with less lymph node procedures and no additional therapy is recommended. When larger lymph node procedure and/or mastectomy with no additional therapy are carried out, sick leave up to six weeks can be justified. Job modification as well as partial sick leave should be considered in these cases. During post-operative chemotherapy, usually five months, women's work capacity is in most cases reduced according to the guidelines. Some women are, however, able to work between the treatment occasions. Adaptation of work tasks as well as partial sick leave and successive return to work are options during this period. If pre-operative chemotherapy has been given, a longer sick-leave period is often required. During radiation therapy without complications, the work capacity is often good. Hormone- or targeted therapy also often implies work capacity, at least part time, according to the guidelines.

1.3.5.3 Work after breast cancer diagnosis

A number of international studies examining return to work among women with breast cancer show that a large majority of those working at the time of diagnosis are working full-or part-time within two years after diagnosis (85, 90-92). Most studies on return to work among women with breast cancer have follow-up periods shorter than three years and many of them focus only on the first year post-diagnosis, which means that the knowledge regarding longer periods after diagnosis is limited (93). A recent nationwide population-based cohort study of 26 120 women in the Netherlands with matched control sample, however, shed more light on the very long-term consequences of breast cancer, showing a higher risk of being granted disability benefits up to 10 years post diagnosis (94).

This research area involves a number of outcome measures depending on research questions and available data sources. Outcome measures used are for example prevalence of sickness absence (94, 95), duration of sickness absence (85, 96), proportion who have returned to work (91, 97, 98), and change in working time (99, 100). Several studies also focus on changes in employment status (94, 101, 102). Moreover, due to differences in social insurance arrangements between countries, there is a great variability between countries with regard to length and rate of return to work. Such differences must be considered when comparisons of country specific data are carried out (90, 93, 103, 104). In a recent systematic review on return to work among breast cancer survivors in Europe, North America, and Asia, the authors found that the prevalence of return to work varied from 43% to 93% within one year of diagnosis (93). Studies from Sweden indicate that breast cancer is associated with higher sickness absence three years post-diagnosis (95) and a higher risk of at least part time sickness absence or disability pension even after five years (105). To date, however, knowledge is lacking on long-term patterns of sickness absence and disability pension, including sickness absence and disability pension due to mental diagnoses, as well as different physical diagnoses, and detailed information on pre-diagnosis sickness absence and disability pension.

1.3.5.4 Factors associated with return to work

The capacity and ability to work during or after a period of disease is influenced by physical, as well as mental, socio-demographic, and work related factors (86, 91, 93, 106-111). Regarding mental factors, depression has been found to influence cancer survivors' work resumption negatively (93). Among physical or disease-related factors, tumor stage has been found to influence return to work, implying that women with early stage breast cancer are more likely to return to work compared to women with advanced tumor stage (90, 91, 112). This may possibly be because of the association between tumor stage and treatment (105, 106). Chemotherapy has been found to increase the risk of sickness absence (95, 105), decrease working time (92) and be negatively associated with return to work (90, 93).

A number of sociodemographic factors are associated with return to work. Younger age has been shown to be associated with higher sickness absence duration (113, 114), while older age is associated with no return to work (91, 101, 103, 112, 114). Low-income is associated with not resuming the job after breast cancer (93) and low education has been found to increase the risk of sickness absence and longer absence from work (101, 103, 105). Marital status is often not found to be associated with return to work (90, 91, 112), which is also the case for having children at home (90, 91, 93,

106), at least if there are two parents present. Regarding work-related factors, pre-diagnosis sickness absence has been shown to be associated with higher risk of sickness absence up to five years after diagnosis (95, 105). Part time employment pre-diagnosis has been shown to be negatively associated with return to work , (112), as have factors, such as blue-collar or manual work, work with high demands and a non-supportive supervisor (90, 91, 115).

1.4 Rehabilitation and stress management training

According to WHO, rehabilitation is "the use of all means aimed at reducing the impact of disabling and handicapping conditions and at enabling people with disabilities to achieve optimal social integration" (116).

1.4.1 Cancer rehabilitation

Cancer rehabilitation promotes the regaining of abilities that may have been changed in connection to the disease and subsequent treatment and provides means to reduce the impact of possible disabling conditions (117). The Swedish national program for cancer rehabilitation (117) explicitly includes physical, mental, social, as well as existential aspects in the concept of cancer rehabilitation. According to the program, rehabilitation is relevant during the whole disease process, from the time around diagnosis, during treatment, and after treatment (117). Since work is an important aspects of social integration, some cancer rehabilitation interventions are explicitly focused on employment and return to work, i.e., vocational rehabilitation (12).

1.4.1.1 Effects of different rehabilitation interventions for women with breast cancer

There is a number of rehabilitation interventions developed and used among women with breast cancer, however, the evidence of efficacy for most of them is still unclear. A recent review (13) of systematic reviews on the effects of different rehabilitation methods for post-operative women with breast cancer assessed six categories of interventions: 1) physical therapy, 2) physical exercise, 3) psychosocial interventions, 4) nutritional interventions, 5) complementary (alternative) interventions, e.g., yoga and acupuncture, and 6) combined interventions, e.g., counselling and exercise. Evidence for narrowly-focused exercise rehabilitation in improving physical symptoms, particularly for shoulder mobility and lymphedema, was found, but inconclusive results for methods to improve psychosocial, cognitive, and occupational outcomes. Despite a lack of clear evidence of mental health effects of physical exercise in the review, a growing number of studies show beneficial effects of physical exercise regarding, e.g., quality of life, depression, and fatigue in women with breast cancer (118, 119).

In a systematic review from 2011(120), the authors assessed 18 randomized controlled trials (RCT) regarding the effects of interventions for rehabilitation of women with breast cancer. The interventions were focused on psycho-education, social support, and cognitive behavioral therapy (CBT). Cognitive-behavioral therapy refers to a class of interventions focusing on strategies to change general beliefs about the world, the self, and the future, which are giving rise to specific and automatic thoughts in particular situations. Through the changing of maladaptive cognitions, a change in emotional distress and problematic behaviors is assumed to occur (121). The authors concluded that limited documentation exists on the efficacy of psycho-education and social support interventions, but found that there might be benefits on the quality of life from cognitive behavioral therapy given after primary breast cancer treatment.

1.4.2 Stress management training in rehabilitation

Mental health concerns in women with breast cancer appear to be mediated through thoughts about illness and prognosis, with cognitive intrusions by thought of recurrence, death and disability (120). These aspects of stress have been the rationale for the use of interventions with a psychological approach, among them stress management training. Stress management training is in this thesis defined as interventions aimed at alleviating stress and related mental health concerns (42, 122). Apart from worrying about prognosis, there may be other factors creating elevated stress at different time points in the disease trajectory, e.g., the returning to roles and functions of ordinary life, including work, making the managing of stress an important aspect of rehabilitation.

1.4.3 Mindfulness in stress management training

Mindfulness-based interventions are today widely spread and used both within health care, in rehabilitation (including vocational), and in the general population. Although research supports the view that mindfulness training can reduce stress related symptoms and increase well-being, knowledge on in which situations and for whom mindfulness training is suitable and beneficial is still not clear.

1.4.3.1 The concept of mindfulness

The concept of mindfulness is firmly rooted in Buddhist psychology and has not been clearly translated into contemporary research psychology. An operational working definition of mindfulness was put forward by Jon Kabat-Zin, who developed the program for mindfulness based stress reduction (MBSR) in the late seventies. Kabat-Zin defined mindfulness as: “the awareness that emerges through paying attention on purpose, in the present moment, and nonjudgmentally to the unfolding of experience moment by moment” (123). In 2007, Brown et al. (124) found that the psychological literature revealed considerable variance regarding descriptions of the nature of mindfulness. Discussing the nature of the concept, the authors concluded that different schools of thought emphasized certain characteristics of mindfulness more than others, and that the ways in which mindfulness-based interventions actually work to a large extent was still unknown. In recent years, however, studies on pathways of the effects of mindfulness training have been carried out and some suggestions have been put forward (125-127), as outlined in section 1.4.2.4.

1.4.3.2 Mindfulness-based interventions for better health

Mindfulness meditation is increasingly well regarded for its therapeutic efficacy in a broad range of conditions and settings and have become increasingly used in psychosocial care for cancer survivors (127, 128). The most common mindfulness based program, Mindfulness based stress reduction (MBSR), involves the practice of sustained attention on the breath, the body and sensory input, in order to attain a state of mindfulness. Central exercises are sitting meditation, mindful yoga, and body scan. The program also contains psycho-educational material about stress and behavioral exercises like activity scheduling. The program is carried out during eight weeks with weekly common sessions in which participants can share experiences and practice together, combined with daily practicing at home. The content of an Internet-based mindfulness-based stress management training program is outlined in Table 3. MBSR was originally developed to improve the lives of people with chronic diseases, but has become increasingly recognized as an effective program in the treatment of elevated stress and anxiety. This development is a part of the so called third wave of behavioral

therapy in which a number of treatments have appeared, sharing common characteristics like mindfulness, acceptance and cognitive defusion (129, 130). Examples of applications of mindfulness in different therapies are Mindfulness-Based Cognitive Therapy (MBCT) (131), Dialectical Behavior Therapy (DBT) (132) and Acceptance and Commitment Therapy (ACT) (133). In order to adapt MBSR to cancer survivors, a program named Mindfulness-based cancer recovery (MBCR), was developed (54). MBCR has somewhat shorter weekly sessions compared to the original MBSR and includes specific material on coping with cancer.

1.4.3.3 Effects of mindfulness training

The effects of mindfulness-based interventions on anxiety and depression are well-documented, as highlighted in three meta-analyses. One of them included nine randomized controlled trials, assessing the benefits of MBSR in women with breast cancer (134). The authors compared MBSR with standard or usual care and found that those receiving MBSR had a significant improvement with regard to depression, anxiety and stress, compared with women in control conditions. MBSR did also show some effect on quality of life (Mean difference (MD), -1.16 ; 95% confidence interval (CI), -2.21 to -0.12 ; $p=0.03$). The second meta-analysis included nine studies among women with breast cancer (two randomized controlled trials, one quasi-experimental case-control study and six one-group, pre-intervention and post-intervention studies) (135). The estimated Cohen's d effect size (95% CI) on stress was 0.710 (0.511 - 0.909), on depression 0.575 (0.429 - 0.722) and on anxiety 0.733 (0.450 - 1.017). The third meta-analysis included 31 mindfulness based randomized clinical trials with active controls carried out in different study-populations (136). The authors found that mindfulness meditation programs had moderate evidence of improved anxiety with the Cohen's d effect size (95% CI) 0.38 (0.12 - 0.64) at 8 weeks and 0.22 (0.02 - 0.43) at 3-6 months, and of depression 0.30 (0.00 - 0.59) at 8 weeks and 0.23 (0.05 - 0.42) at 3-6 months, indicating a declining effect in the longer run. In the same review, the authors concluded that there was low strength of evidence for improvement in stress and mental health related quality of life, suggesting that stronger study designs are needed in order to determine the effects of meditation programs in improving the positive dimensions of mental health. Promising results regarding improvement of sleep and decreased fatigue after participation in mindfulness-based interventions have also been shown in some studies among women with breast cancer (137-139).

The support for long-term positive effects of mindfulness training is not as evident as the short time effects outlined above, although some studies have shown improvements up to one year post-intervention (138, 140-142). Several reasons for the lack of evidence regarding long-term benefits have been suggested. Firstly, there are problems with attrition in long-term studies, making the detection of long-term effects complicated (27). Secondly, absence of long-term effects may be due to decreased meditation practice after course completion. The amount of formal practice as well as the use of informal practice has been shown to be related to beneficial effects of mindfulness (143, 144). Thirdly, there may be positive effects from group support and sharing of experiences, as well as attention from a professional/therapist during a course period, influencing mental health in the short term, but not after program completion (145).

Although less reported, there are also possible adverse effects of mindfulness meditation. Case reports of negative effects of mindfulness meditation, such as feelings of anxiety and derealization, was put forward by Lustyk et al. in 2009 (146). After

reviewing the literature on mindfulness in relation to psychosis up to June 2013, Shonin et al. (147) concluded that there is some small-scale clinical evidence suggesting that meditation techniques with integrated mindfulness components may induce psychotic episodes. The authors further stated that the evidence stems from case reports with low participant numbers (including single cases) and relates to individuals that have engaged in intensive meditation retreats (138).

1.4.3.4 Suggested mechanisms behind effects of mindfulness training

The mechanisms by which mindfulness training affects mental conditions have received quite a lot of attention in the last decade, but are not yet fully explored. A great deal of research on possible pathways has focused on the reduction of negative emotions. In recent years, however, positive psychological processes initiated by mindfulness training have gained an increased interest (126).

Building on the working definition of mindfulness (123), Shapiro et al. (125) suggest that intention (on purpose), attention, and attitude (nonjudgmentally) are fundamental internal behaviors which enable individuals to initiate a shift in perspective, termed *reperceiving*, in relation to thoughts and emotions. *Reperceiving* is akin to the concept of *decentering*, which means a shifting of cognitive sets that enables alternate appraisals of life events (127). *Reperceiving* may further lead to additional mechanisms that in turn contribute to positive outcomes for the individual (125). The authors highlight four such mechanisms: 1) self-regulation and self-management, 2) emotional, cognitive and behavioral flexibility, 3) values clarification, and 4) exposure. Through *reperceiving*, the individual doesn't have to be controlled by, e.g., anxiety or fear, but can instead use them as information while being able to attend to the emotion, and choose to self-regulate in ways that promote greater health. *Reperceiving* further enables development of the capacity to observe the ever-changing inner experience and thereby see more clearly the mental-emotional content, which in turn fosters greater cognitive-behavioral flexibility and less automaticity or reactivity. When being able to separate from own values and reflect upon them with greater objectivity, there is an opportunity to rediscover and choose values. Last but not least, *reperceiving* enables individuals to experience even very strong emotions with less reactivity, which serves as a counter to the tendency to avoid or deny difficult emotional states. Through this exposure the individual learns that emotions, thoughts or body sensations are not so overwhelming or frightening (125).

Connecting *decentering* with the concepts of appraisal and coping, Garland et al. (127) proposed a hypothetical causal model arguing that mindfulness promotes the use of the coping strategy "positive reappraisal" and ultimately a better health. Positive reappraisal is described as an adaptive coping strategy by which stressful events are reconstrued, i.e., revalued as benign, valuable, or beneficial. The causal chain in the model begins with a stressor stimulus which leads to a primary appraisal, followed by a secondary appraisal. In this phase, mindfulness brings *decentering*, enabling an attentional flexibility and broadened awareness, attributing new meaning to the stressor. Positive reappraisal, i.e., the revaluation of the stressor as benign, valuable, or beneficial, then leads to positive emotions, such as compassion, trust, confidence, and equanimity, which reduce stress and in turn influence subsequent appraisal processes.

The theory of a causal chain from stimulus to mindfulness and finally to coping and mental health gained empirically support in a study by Weinstein et al. (50). Using a

laboratory-based, longitudinal, and daily diary design, and four different but related studies, the authors found that individuals (college students) who demonstrated higher awareness in the present moment, i.e., higher trait mindfulness, made more benign stress appraisals compared to individuals who reported lower trait of mindfulness and that more adaptive stress responses and coping partially or fully mediated the relation between mindfulness and well-being. The mindful individuals reported less frequent use of avoidant coping strategies, and higher use of approach coping, i.e., direct action, acceptance, and cognitive reinterpretation and growth (finding the good in the threat, or use the situation to develop as a person). Mindfulness was found to predict approach coping strategies in individuals' lives on a day-to-day level, but interestingly, the authors found that this was not the case when the stress stimulus consisted of laboratory-based social threat or academic performance threat. Discussing these findings, the authors suggest that acceptance and positive interpretation and growth may be less relevant in connection to this kind of threats, compared to a day-to-day context, in which both threat and harm experiences could be expected to occur. Summarizing results from the four studies, the authors meant that mindfulness appears to foster more effective stress processing through cognitive appraisal and coping, but particular forms of coping strategy use may vary from one situation to another (50). According to previous research, the choice of a relevant coping strategy in a particular situation, i.e., trying to solve problems that are controllable while trying to adapt to problems that are not controllable, is also assumed to be associated with better health (48).

1.4.3.5 Mindfulness training and work capacity

To date very few studies have investigated the effects of mindfulness or mindfulness training on work capacity or return to work (148-150). A recent Norwegian prospective cohort study with 74 persons on long-term sickness absence due to different diagnoses is one example. The participants in this study completed a 4- or 6-week multidisciplinary vocational rehabilitation program with mindfulness training as one component. The authors found that enhanced mindfulness over the course of the program significantly predicted a higher self-reported work capacity (148). In another study of the same program, the authors found that mindfulness may enhance return to work through (increased) quality of life, and also that mindfulness significantly predicted return to work for highly educated individuals (151). More research, with well-designed studies, is however needed in order to conclude about the effects of mindfulness training on return to work.

1.4.4 Internet-based interventions

There is an increasing number of interventions delivered online, encompassing a diversity of conditions (152, 153). The program content of Internet-based interventions is often similar to face-to-face interventions, but adapted to an Internet environment with a website and a platform from which texts, audio files, films, and other facilitating material can be read and downloaded. Advantages of health-related Internet use include reduced barriers such as location, time and cost, and also decreased stigma that might be associated with some face to face consultations (154-157). Internet-based interventions are cost-efficient and can be implemented in a large group of persons at the same time. Emerging evidence on the effectiveness of health promoting Internet - based interventions, including mindfulness-based programs, has shown the potential efficacy of such interventions to improve outcomes in a number of health concerns (15, 158-160). Effects of specific mindfulness-based programs delivered online are promising with regard to the improvement of mental health outcomes such as perceived

stress, anxiety and depression (161-165). Few studies on Internet-based programs among cancer patients have been carried out and to the best of my knowledge, none has so far evaluated an Internet-based mindfulness-based program among women with breast cancer exclusively. However, a recent randomized controlled trial among individuals with different cancer diagnoses (47% with breast cancer) assessed psychological and mental health outcomes, feasibility and efficacy of an MBCR program, delivered online (166). Significant post-intervention improvements were shown and moderate Cohen's d effect sizes in the MBCR group relative to controls for total scores of mood disturbance ($d=0.44$, $p=0.049$), stress symptoms ($d=0.49$, $p=0.021$), spirituality ($d=0.37$, $p=0.040$), and mindfully acting with awareness ($d = 0.50$, $p = 0.026$). Internet-based programs, however, present other challenges for users than face to face-, or group-based interventions, and often involves high attrition (drop-out rates) and low levels of full adherence (167-169).

1.4.4.1 Challenges in Internet-based interventions

Program content and design, as well as degree of guidance and support, varies a lot between different Internet-based interventions. Participation can involve interaction with other participants, as well as with a therapist or instructor, or be more of a self-help application not involving anyone but the user. The latter implies very low costs for dissemination. The characteristics of the target group or users are a crucial factor for a successful implementation, regardless of program design. Many of these characteristics are common with those important in face-to-face interventions.

In a systematic review on adherence in Internet-based interventions for anxiety and depression based on 23 studies, Christensen et al. (167) found a number of self-reported reasons for dropout connected to the users. Time constraints, lack of motivation, technical or computer-access problems, depressive episodes or physical health concerns, lack of face-to-face contact, preference for taking medication, perceived lack of treatment effectiveness, improvement in condition, and burden of the program, were mentioned in one or more of the included studies. When exploring promoting factors for successful implementation of Internet-based programs in the general public, using qualitative methodology, Brouwer et al. (170) found that preexisting personal motivation to change a health behavior was an important factor for users to successfully complete the programs.

In the same study, some program related factors were highlighted as important, i.e., professional appearance, and texts that are easy to understand. Giving tailored feedback, reliable information, having easily navigated systems and the possibility to monitor personal progress, were further noted as important factors in a questionnaire study among experts from Internet intervention research and practice, e-marketing/e-commerce, web-design, and technical website development (171). In a recent Swedish study investigating the impact of both enriched treatment material presentation and increased frequency and quality of support on participants' adherence to a relaxation Internet-based cognitive therapy (ICBT) program, the authors found that the presentation of the treatment content in a rich, multimedia-based environment did not seem to improve adherence to the treatment program online or to prescribed exercises (169). However, frequent high-quality support using motivational techniques increased adherence to the program, but did not increase adherence to prescribed homework assignments. In an expert review on Internet-based psychological treatments (ICBT) for depression, examining different levels of contact between therapists and client in relation to outcomes, the authors found evidence for a strong

correlation between the degree of support and outcome, i.e., guided internet-based psychological treatments was found to be more effective than unguided treatments (172). In a recent Swedish study among participants from the general population with self-reported stress symptoms, the authors further found that symptom improvement after treatment was predicted by treatment credibility and therapeutic bond (173).

1.4.4.2 Experiences of mindfulness-based programs delivered via the Internet

Although there are several studies that have explored experiences of Internet-based interventions among users, few have investigated participants' experiences of mindfulness-based programs more in depth, and knowledge on how such programs are perceived in different groups of users is lacking to a large extent. Results from three studies are briefly described below, two using questionnaires and one using interviews.

In one randomized controlled trial among self-selected people in the US, participants were asked to complete a questionnaire about overall feedback on a self-directed stress management program (ISM) based on mindfulness principles (165). About 25% of those who completed the baseline questionnaire responded. Of those who gave feedback, 45% found the overall program to be very or extremely helpful, 35% somewhat helpful, and 19% little or not at all helpful. The most common reason for leaving the program was that the participant was too busy. The second most common reason for termination was technical or access problems.

In an American study (174) involving participants with a lifetime history including at least one major depressive episode, the current program aimed at reducing residual depressive symptoms and preventing relapse. The program was mindfulness-based (MBCT) and included a variety of web-based learning modalities, including group leader guidance, interactive exercises, as well as the possibility to contact the leader by phone or e-mail. Interviews with the participants after program completion revealed a lot of positive experiences like appreciation of the modular e-learning format outlining key concepts, videos of group leaders speaking, and audio recordings of guided meditations. Some participants lacked an instructor or group when meditating. Reasons reported for not completing the recommended home practice were time constraints and lack of motivation. Lack of support during the program was expressed but also appreciation of the flexibility of completing weekly sessions according to the participants' own schedule.

Finally, cancer patients' satisfaction with a guided mindfulness-based online program including online class sessions with an instructor, contact with other participants and support within an online environment, as well as meditation recordings and videos for daily home practice, was assessed through post-intervention questionnaires (166). Five persons (16.66%) left the program before completion and post-assessment. The mean amount of reported home meditation and yoga practice was 150 minutes per week, which did not include the weekly class practice or six extra hours of retreat time. The results showed that 100% of the participants were satisfied with the program (49% satisfied that the program met their expectations, and 51% positively surprised by the program, which exceeded expectations). Of the 51 participants who completed "program recommendation data", 48 would recommend the program to other cancer survivors with no hesitation, whereas three participants indicated that they would recommend the program with reservation. Reservations were a) requirement of adequate space around the computer for yoga and meditation, b) requirement of quiet space to meditate, and c) an interest in exploring mindfulness.

1.5 Summary and need for further knowledge

During the last decades, research on psychological and social aspects of breast cancer has been highlighted, but there is still limited knowledge on work-related consequences of a breast cancer diagnosis and how to promote long-term mental health among women diagnosed with breast cancer.

1.5.1 Sickness absence and disability pension

To date, knowledge on diagnosis-specific sickness absence and disability pension (including due to mental diagnoses) in women with breast cancer is lacking, and knowledge on sickness absence and disability pension in a long-term perspective is limited. Accordingly, there is a need for well-designed population-based studies to identify risk factors for short and long-term diagnosis-specific sickness absence and disability pension over a number of years.

1.5.2 Coping with breast cancer

The understanding of psychological processes in relation to stressful situations like breast cancer and how different ways of coping with breast cancer may affect health is limited due to divergent results from a growing number of studies. In order to make progress in this particular area of research, there is a continuous need to summarize existing knowledge, calling for systematic reviews including meta-analyses.

1.5.3 Sustained effect of mindfulness training

Mindfulness training has proven to give short-term positive effects on mental health in women with breast cancer, i.e., immediately after program completion, while the detection of long-term effects is rare. The mechanisms underlying positive effects of mindfulness training are not yet fully understood, although quite extensive research on psychological processes in general and some in connection to mindfulness training in particular, has been carried out. Therefore, well-designed studies on longer-term effects of mindfulness training are warranted in order to understand when and for whom mindfulness training is suitable, and what factors are important in order to achieve sustained positive effects on mental health.

1.5.4 Internet-based mindfulness training programs

In parallel with research on mindfulness and its beneficial effects, the possibility to disseminate health promoting and treatment programs via the Internet has emerged, offering new opportunities for cost-effective research and clinical practice. The promising results of Internet-based programs for improving mental health in different populations calls for research on the possibility to disseminate mindfulness-based stress management training programs to women with breast cancer who are prevented to participate in face-to-face programs.

2 GENERAL AND SPECIFIC AIMS

2.1 General aim

The general aim of this thesis was to generate more knowledge regarding psychological and social aspects of being diagnosed with breast cancer. More specifically, the aims were to examine sickness absence and disability pension after diagnosis, how different ways of coping with breast cancer are linked to health outcomes, and ways to promote mental health after diagnosis.

2.2 Specific aims

2.2.1 Study I

To explore long-term diagnosis-specific levels of sickness absence and disability pension among women with breast cancer, and possible associations between sickness absence and disability pension and disease-related and socio-demographic factors.

2.2.2 Study II

To examine the associations between different types of coping and health outcomes among women with breast cancer and to explore potential moderating factors.

2.2.3 Study III

To examine longer-term effects of a mindfulness-based stress management training program on psychological processes and mental health among people with a cancer diagnosis.

2.2.4 Study IV

To explore the feasibility, usability, acceptability and effects on mental health of an Internet-based mindfulness-based stress management training program.

3 DESCRIPTION OF STUDY I-IV

This thesis is based on the findings from four studies (I-IV) described in Table 1.

Table 1 Overview of study I-IV.

	Study I	Study II	Study III	Study IV
Aim	To explore long-term diagnosis-specific levels of sickness absence and disability pension among women with breast cancer, and possible associations between sickness absence and disability pension and disease-related and socio-demographic factors	To examine the associations between different types of coping and health outcomes among women with breast cancer and to explore potential moderating factors	To examine longer-term effects of a mindfulness-based stress management training program on psychological processes and mental health among people with a cancer diagnosis	To explore the feasibility, usability, acceptability and effects on mental health of an Internet-based mindfulness-based stress management training program
Design	Prospective registry-based cohort study with baseline data at 31 December 2004 and follow-up until 31 December 2010	Meta-analysis	Two-armed randomized controlled trial	Pilot randomized controlled trial and feasibility study
Population/ material	All women in Sweden, 20-65 years of age, with a first breast cancer diagnosis in 2005 (n=3547) and a matched comparison group (n=14 188)	78 studies published before May 2013, including 11 948 women diagnosed with breast cancer, with sample mean age 46,8-61,8 years	71 persons with a cancer diagnosis (76% with breast cancer), 30-65 years of age	76 university students in Stockholm, Sweden, 18-45 years of age
Data Sources	-Swedish Cancer Register -The Cause of Death Register -LISA ¹ -MiDAS ²	Articles identified by use of search engines in PubMed and PsycINFO databases	Self-report questionnaires	-Self-report questionnaires -Telephone interviews
Analyses	-Descriptive -Logistic regression models	-Random effects meta-analysis model -Fixed effect meta-analysis model for sub-group analyses -Trim-and-fill procedure for test of publication bias	-Descriptive statistics -Inferential (pre-intervention and at six month follow-up)	-Descriptive statistics -Inferential (pre- and post-intervention) -Content analysis
Main outcome	-Annual number of net-days with sickness absence or disability pension - Rates of women on sickness absence or disability pension -Associations of disease-related and socio-demographic factors with sickness absence and disability pension	Correlations between different coping strategies and mental and physical states, respectively	Change in perceived stress, symptoms of anxiety, symptoms of depression, posttraumatic stress symptoms, positive states of mind, coping efficacy, and mindfulness	-Change in psychological well-being and symptoms of depression. -Satisfaction with the program -Categories of participant's expressed experiences

¹ Longitudinal integration database for health insurance and labor market studies, held by Statistics Sweden

² Micro-data for analyses of social insurance, held by the National Social Insurance Agency

3.1 Study I

Study I is a prospective population-based cohort study, exploring sickness absence and disability pension after a breast cancer diagnosis.

3.1.1 Methods

3.1.1.1 Data from nationwide registers

Data from four nationwide registers, linked by the use of the personal identity numbers (PIN) attributed to all Swedish inhabitants, was used.

The Swedish Cancer Register, held by The National Board of Health and Welfare, covers the whole Swedish population (175). It is compulsory for every health care provider to report newly detected cancer cases to the registry. A report has to be sent for every cancer case diagnosed at clinical-, morphological-, other laboratory examinations as well as cases diagnosed at autopsy. Data on all cases of breast cancer (in women) in 2005, date, type, and T, N, and M classifications was used.

The Longitudinal Integration Database for Health Insurance and Labour Market Studies (LISA) is updated annually by Statistics Sweden (176) and includes all individuals aged 16 years and older who were registered as living in Sweden on 31 December for the respective years. The database contains information on social-demographics and social insurance measures. Information on socio-demographic factors at baseline 31 December 2004 (and on emigration 2006–2010) was used.

The Cause of Death Register is held by the National Board of Health and Welfare (177), recording all deceased individuals, regardless of whether the death occurred in Sweden or abroad. Data on date of deaths in the cohort during 2005–2010 was used.

The database called Micro Data for Analysis of the Social Insurance (MiDAS) is held by the National Social Insurance Agency and includes annual data from the year 1994 and onwards, covering detailed information on sickness absence benefits and disability pension (178). Information on date, grade (full or part time), and main diagnosis of sickness absence and disability pension with benefits from the National Social Insurance Agency in 2003–2010 was used. The register does not include information on most sickness absence spells ≤ 14 days, nor on secondary diagnoses.

3.1.1.2 Descriptive statistics

The annual number and percentages of women ($n=3547$) with breast cancer on sickness absence and disability pension, as well as the mean number of net-days with sickness absence and disability pension due to different diagnoses in accordance with ICD-10 (22): 1) mental diagnoses (F00-F99), 2) breast cancer (C50), 3) other diagnoses, i.e., all remaining ICD-codes, most of them musculoskeletal (M00-M99), and 4) missing, was calculated. Net-days were obtained by transforming part-time days into net days (e.g., two days on half-time sickness absence/disability pension was counted as one net day). The period assessed started two years before date of diagnosis (T_0) and ended five years after date of diagnosis (2003–2010). The results were compared to the corresponding figures for a comparison group of women with no record of breast cancer ($n=14\ 188$), matched on age, education-, type of living area-, and birth country categories. Matched women were assigned a T_0 time point corresponding to that of the woman she was matched to. In the calculations, women at risk of sickness absence and disability

pension were included, i.e., not those who had died, emigrated, or turned 65 years of age.

3.1.1.3 Logistic regression

Univariable and multivariable logistic regression were used to estimate odds ratios (OR) with 95% confidence intervals (CI) between the covariates pre-diagnosis sickness absence, cancer stage, age, educational level, family situation, birth region, type of living area and sickness absence (>30 days) in the third and fifth year post-diagnosis, as well as the receiving of disability pension during follow-up. Women older than 62 years in December 2004 were excluded from the analysis of sickness absence in the third year, due to possible transition into old-age pension. In the same way women >60 years in December 2004 were excluded in the corresponding analyses in the fifth year. Women who died or emigrated prior to these time points respectively, were also excluded in the analyses, as were women on full-time disability pension during the respective year. In the analysis of disability pension, women who had disability pension at time of diagnosis, as well as those who emigrated or died without first having experienced the event, were excluded, leaving 2640 women.

3.1.2 Main findings

During the twelve months following diagnosis, 71% of the women with breast cancer had sickness absence, most of them due to breast cancer. The corresponding proportion on sickness absence for breast cancer-free women was 17%. During the two years pre-diagnosis, this proportion was around 19% in both groups. In the second year post-diagnosis, 40% of the women with breast cancer had at least some sickness absence and in the fifth year the percentage was 19%. For the comparison group, the corresponding proportion was 11% in the fifth year. A higher proportion of women with breast cancer, compared to breast cancer-free women, had at least some sickness absence during follow-up and in the fifth year, the estimated difference was 7.7 percentage units (95% CI 6.1–9.3). In the two years before diagnosis, the proportion of women on disability pension was about 20% in both groups and this proportion remained relatively constant for the comparison group. In the third year post-diagnosis, women with breast cancer had 2.3 percentage units (95% CI 0.7–4.0) higher proportion on disability pension compared to breast cancer-free women. In the fifth year, the level was 3.8 percentage units higher (95% CI 2.0–5.6). There was no higher level of sickness absence due to mental diagnoses during follow-up, and none or just a minimally elevated level of disability pension due to mental diagnoses.

Figure 1 illustrates mean numbers of sickness absence and disability pension net-days in the different diagnostic categories for each group respectively.

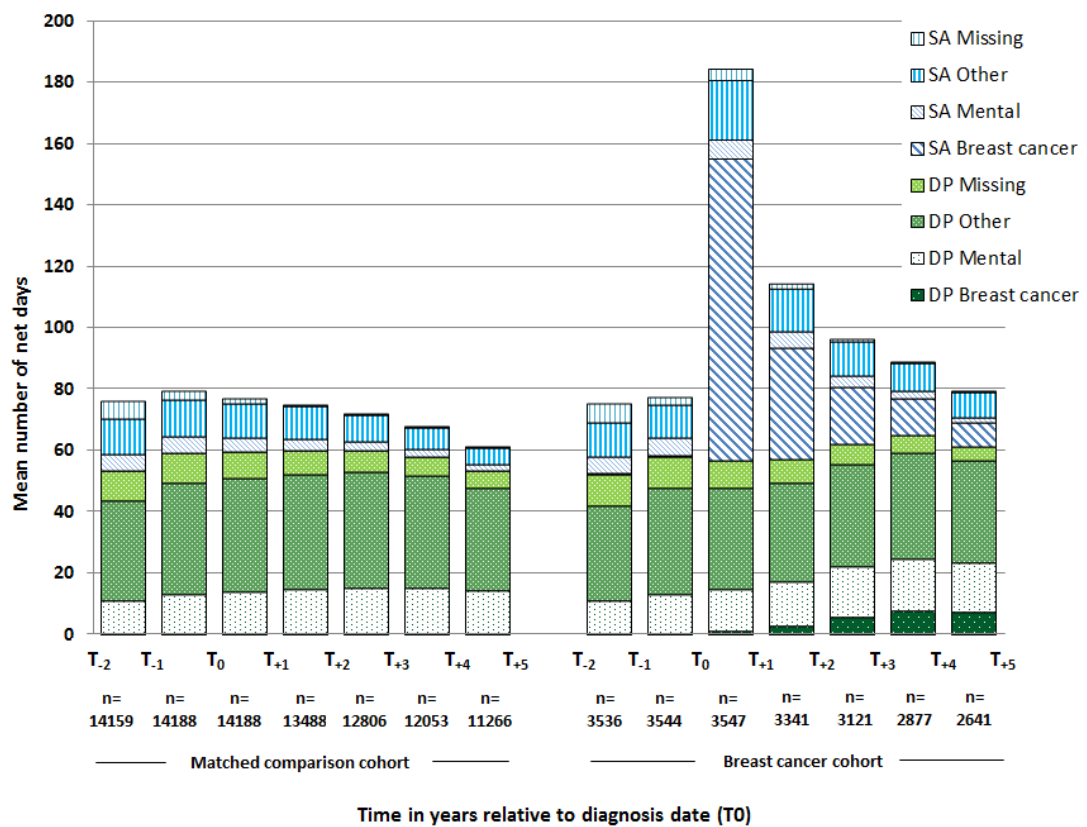


Figure 1. Mean number of sickness absence and disability pension net days per year intervals from date of diagnosis for the women in the breast cancer cohort.

The results from the regression analyses are displayed in Table 2 (adjusted estimates). Women with stage II–IV had higher ORs of being sickness absent both in the third and fifth year, as compared to women with stage T0N0M0 + Stage 0+I. A strong association was found between pre-diagnosis sickness absence >90 days and sickness absence post-diagnosis, in particular in the third year. In the fifth year, younger women (aged ≤35–45) were more likely to have sickness absence, as compared to women aged 46–50. Other factors associated with higher ORs of sickness absence were high school, as compared to college/university in the fifth year, and being born outside Sweden, as compared to natives in the third year. The strongest association for being granted disability pension was found for long-term pre-diagnosis sickness absence. Also, women with advanced cancer stages were more likely to be granted disability pension, compared to those with early stage breast cancer. Women born outside Sweden were twice as likely to be granted disability pension, even when adjusting for cancer stage. Women with education below university level were also almost twice as likely to be granted disability pension, compared to those with university education, even when adjusting for other variables. Age 56–60 was associated with a higher risk of disability pension, while age ≥61 was associated with a lower disability pension risk as compared to age 46–50. For additional statistics, see Study I.

Table2. Adjusted Odds Ratios (ORs) with 95% Confidence Intervals (CI) for being sickness absent (SA) >30 days during the third year (T₊₂-T₊₃; n=2746) and the fifth year (T₊₄-T₊₅; n=2322) after breast cancer diagnosis and for being granted disability pension (DP) during the five-year follow-up period among those not on disability pension at T₀ (n=2640). In the adjusted models, all covariates were included.

Variable and category	SA >30 days T ₊₂ -T ₊₃		SA >30 days T ₊₄ -T ₊₅		Granted DP T ₀ -T ₊₅	
	N (%)	Adj. OR (95% CI)	N (%)	Adj. OR (95% CI)	N (%)	Adj. OR (95% CI)
Age						
≤35	37/108 (34.3)	1.36 (0.86-2.15)	23/97 (23.7)	2.53 (1.44-4.44)	9/94 (9.6)	0.90 (0.40-2.04)
36-45	144/527 (27.3)	1.06 (0.8-1.41)	89/507 (17.6)	1.77 (1.21-2.59)	52/502 (10.4)	0.95 (0.59-1.55)
46-50	135/526 (25.7)	1	52/494 (10.5)	1	42/475 (8.8)	1
51-55	128/558 (22.9)	0.90 (0.67-1.21)	62/527 (11.8)	1.19 (0.79-1.78)	60/506 (11.9)	1.21 (0.75-1.94)
56-60	166/696 (23.9)	0.93 (0.69-1.25)	58/697 (8.3)	0.78 (0.5-1.20)	112/624 (17.9)	2.21 (1.41-3.48)
61-62	31/331 (9.4)	0.27 (0.17-0.43)			25/439 (5.7)	0.48 (0.26-0.88)
Educational lev.						
Element. school	97/419 (23.2)	1.14 (0.86-1.52)	35/328 (10.7)	1.09 (0.72-1.67)	58/414 (14.0)	1.89 (1.26-2.84)
High school	307/1245 (24.7)	1.17 (0.96-1.43)	150/1057 (14.2)	1.41 (1.07-1.87)	158/1181 (13.4)	1.76 (1.28-2.41)
College/Univ.	237/1082 (21.9)	1	99/937 (10.6)	1	84/1045 (8.0)	1
Family situation						
Married/cohab., no children	172/814 (21.1)	1	64/596 (10.7)	1	100/799 (12.5)	1
Married/cohab., children	237/963 (24.6)	0.93 (0.71-1.22)	120/912 (13.2)	0.84 (0.57-1.23)	92/908 (10.1)	0.97 (0.65-1.46)
Single, no childr.	161/700 (23.0)	1.01 (0.78-1.31)	63/568 (11.1)	0.86 (0.58-1.26)	83/679 (12.2)	1.12 (0.78-1.61)
Single, children	71/269 (26.4)	0.94 (0.65-1.35)	37/246 (15.0)	0.89 (0.54-1.46)	25/254 (9.8)	0.70 (0.39-1.24)
Type of liv.ar.						
More rural area	182/740 (24.6)	1.09 (0.87-1.38)	69/621 (11.1)	0.84 (0.61-1.18)	73/705 (10.4)	0.80 (0.56-1.14)
Medium cities	214/914 (23.4)	1.03 (0.83-1.29)	101/768 (13.2)	1.06 (0.79-1.43)	108/865 (12.5)	1.06 (0.77-1.46)
Larger cities	245/1092 (22.4)	1	114/933 (12.2)	1	119/1070 (11.1)	1
Country of birth						
Sweden	533/2383 (22.4)	1	241/2018 (11.9)	1	240/2301 (10.4)	1
Other	108/363 (29.8)	1.40 (1.08-1.81)	43/304 (14.1)	1.11 (0.77-1.60)	60/339 (17.7)	2.05 (1.43-2.95)
Cancer stage group						
TONOM0+St. 0+I	185/1105 (16.7)	1	69/938 (7.4)	1	102/1094 (9.3)	1
Missing all TNM	160/622 (25.7)	1.76 (1.37-2.25)	82/531 (15.4)	2.3 (1.63-3.24)	59/580 (10.2)	1.16 (0.79-1.71)
Stage II	242/901 (26.9)	1.77 (1.42-2.22)	109/773 (14.1)	1.94 (1.4-2.68)	121/866 (14.0)	1.98 (1.43-2.73)
Stage III+IV	54/118 (45.8)	4.29 (2.84-6.50)	24/80 (30.0)	4.76 (2.73-8.31)	18/100 (18.0)	3.69 (2.02-6.74)
SA days T₁-T₀						
0	444/2219 (20.0)	1	210/1897 (11.1)	1	147/2149 (6.8)	1
>0-30	70/213 (32.9)	1.90 (1.39-2.60)	26/179 (14.5)	1.34 (0.85-2.10)	28/194 (14.4)	2.28 (1.45-3.56)
>30-90	57/143 (39.9)	2.74 (1.90-3.94)	19/109 (17.4)	1.65 (0.97-2.81)	30/121 (24.8)	4.39 (2.75-7.01)
>90-180	27/79 (34.2)	2.24 (1.37-3.68)	15/61 (24.6)	2.89 (1.55-5.39)	22/72 (30.6)	6.45 (3.67-11.34)
>180	43/92 (46.7)	4.15 (2.66-6.47)	14/76 (18.4)	1.78 (0.96-3.30)	73/104 (70.2)	44.02 (26.88-72.1)

3.2 Study II

Study II is a meta-analysis examining the associations between different types of coping and health related outcomes.

3.2.1 Methods

3.2.1.1 Search and selection of articles

Literature searches were conducted in the PubMed and PsycINFO databases for studies published before May, 2013. Keywords used were: “Breast Cancer” or “Breast Neoplasm” and “Coping”. Limits were “English language”, “Human subjects”, “Published 1860–2010”, “Peer-reviewed journal”, and “Above 18 years”. After removing of duplicates, 1196 articles remained and were screened with regard to the following inclusion criteria: (a) published in peer-reviewed scientific journals; (b) written in English; c) women diagnosed with breast cancer; (d) participant 18 years or older; (e) from the United States, Canada, Europe, or Australia/New Zealand; (f) coping measured quantitatively; (g) sample size larger than $n=30$; and (h) at least one quantitatively measured psychological state or aspect of physical health. After exclusion of 742 articles, the remaining 454 were read in full text and 78 finally included.

3.2.1.2 Extraction, classification and operationalization of data

Cross-sectional and prospective bivariate correlation coefficients for coping and health related variables were obtained from each article. If correlations were not included in the article, the primary author was contacted to ask whether there was relevant data that could be obtained.

Two approaches were adopted to classify different coping categories. The first was to use a lower-order classification based on specific subscales from the Ways of Coping scales and COPE, a procedure that was adopted in a previous meta-analysis of coping effectiveness by Moskowitz et al. (46). The second approach was to use a higher-order classification based on factors previously described by Connor-Smith et al. (179) and Compas et al. (180). The higher order categories used are engagement vs. disengagement, with the engagement category divided into primary control coping (PCC) and secondary control coping (SCC), respectively. Some lower-order coping categories were not easily categorized into the higher-order categories, and were therefore left out from the analyses of higher-order coping. The lower-order subcategories of coping included in each higher-order category are presented in Figure 2. Lower-order categories left out from the higher-order categorization are in the figure displayed as “Miscellaneous Coping strategies”.

Mental and physical health outcomes measures were categorized into 1) positive affect, e.g., positive mood, meaning in life, 2) negative affect, e.g., depression, perceived stress, and 3) aspects of physical health, e.g., fatigue, somatic symptoms. If correlations between coping and more than one health-related variable of each kind were presented, and no summary measure was presented, an average for the correlations for that category was calculated and used.

Potential moderators assessed in sub-group analyses were cancer stage, current treatment, time since diagnosis, and coping measure. Categorization of each moderator was done to facilitate the analysis as follows: cancer stage (0–II/0–IV), current treatment (yes/no), time since diagnosis (≤ 6 months/ >6 months), coping measure

(cancer-specific/dispositional). Too few studies among women with later stage breast cancer were identified, and thus studies were categorized into stage 0–II and 0–IV.

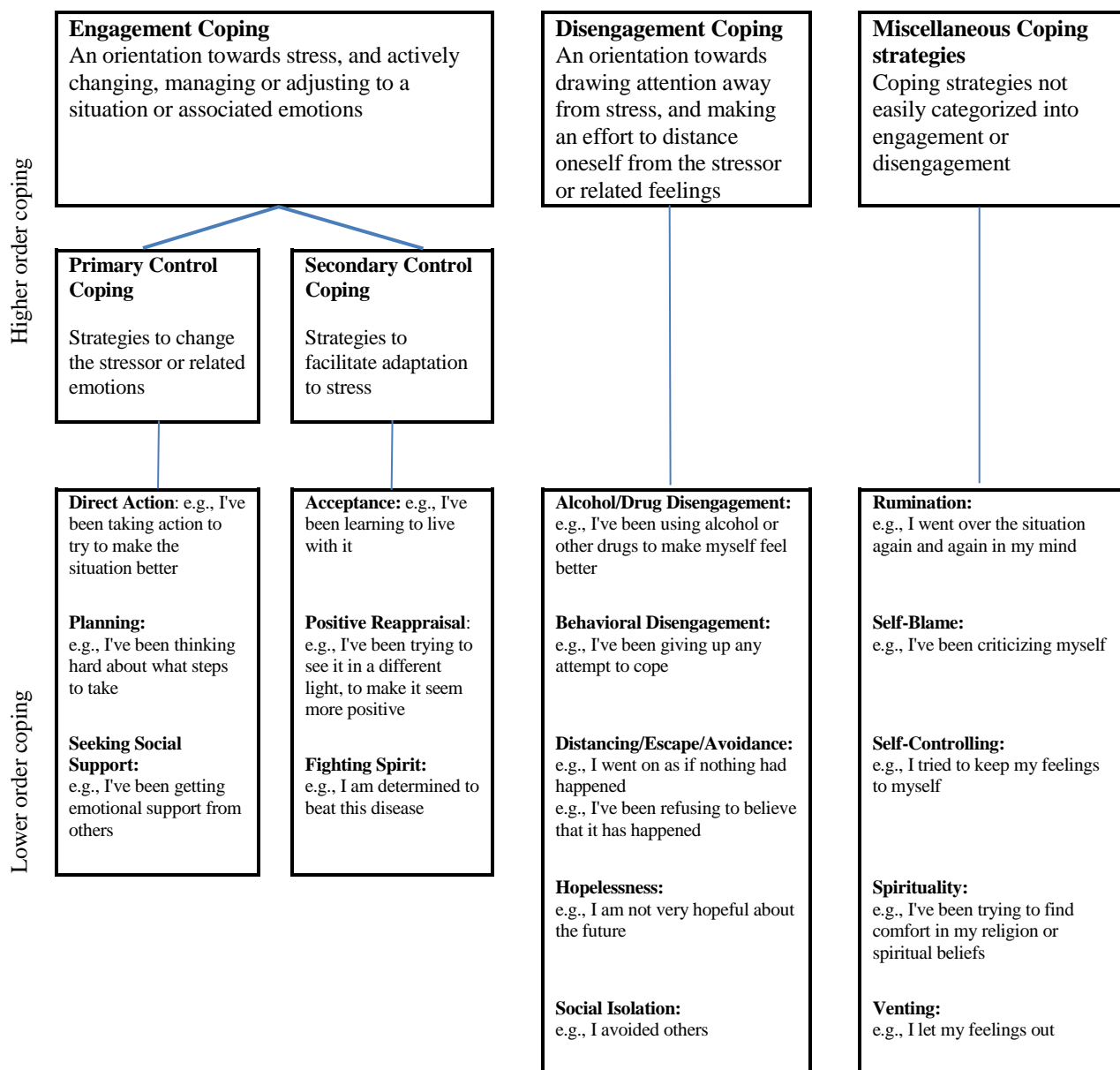


Figure 2. Coping hierarchy and coping categories included in the meta-analysis.

3.2.1.3 Statistical analyses

A random effects model was used for the main analyses (181). In order to deal with the problem of the large number of tests, the threshold for significance was set to $p \leq 0.01$. Publication bias was tested and corrected for using the trim-and-fill procedure described by Duval and Tweedie (182). The potential moderating influences of situational and measurement factors were assessed by comparing effect sizes from the operationalized sub-groups, using the fixed effect model. Heterogeneity between studies was assessed using the Q statistic. In order not to miss the option of finding moderating influence of selected factors, the threshold for significance for the Q -statistic was set to $p \leq 0.1$.

3.2.2 Main findings

The results showed that efforts to facilitate adaptation to stress, such as acceptance and positive reappraisal, were related to better mental health, while disengagement and avoidance types of coping were associated with poorer mental and physical health. The clearest associations were observed between SSC strategies and outcomes regarding positive and negative affect, respectively. Physical health was weakly and negatively related to DC strategies. Effect sizes were mostly small to medium. Results from subgroup analyses showed interactions with all the selected moderators, but most frequently with current treatment and time since diagnosis. A prominent example was the difference in effect of higher order SCC on positive affect among women undergoing treatment ($r=0.47, p<0.001$) compared to those not undergoing treatment ($r=0.10, p=0.008$; interaction $p=0.01$). A clear difference was also observed for the effect of higher order DC on negative affect between women undergoing treatment ($r=0.41, p<0.001$) and those who were not ($r=0.14, p<0.001$; interaction $p<0.001$). Time since diagnosis appeared to influence the association between higher order SCC in the way that it was more strongly associated with higher positive affect among newly diagnosed women ($r=0.36, p<0.001$) compared to women with a longer disease history ($r=0.12, p<0.001$; interaction $p<0.001$) and also, however less prominent, more strongly associated with lower negative affect among newly diagnosed women than among women with a longer disease history. Few interactions were found for cancer stage and type of coping measure. However, higher order DC was more strongly related to lower positive affect in the mixed cancer-stage group ($r=0.29, p<0.001$) than in the early-stage group ($r=0.13, p<0.001$; interaction $p<0.001$) and for the lower order DC-category hopelessness, the corresponding association was even stronger ($r=0.44, p<0.001$; interaction $p<0.001$). For additional statistics, see Study II.

3.3 Study III

Study III is a randomized controlled trial examining the effects of an eight week mindfulness-based stress management training program after six months. Participants were 71 self-selected persons with a cancer diagnosis (54 women with breast cancer), informed in advance about the intervention content and without screening for mental health problems. The intervention ($n=32$) was a modified version of the program developed by Jon Kabat-Zinn (183). Participants in the control condition ($n=39$) were randomized to a wait-list control condition and received the same program as the intervention group after six months.

3.3.1 Methods

3.3.1.1 Self-reported data

Established scales were used to measure the effect of the intervention:

Perceived Stress Scale (PSS) – a ten-item scale measuring perception of stressful experiences during the past month (24).

Hospital Anxiety and Depression Scale – a 14-item scale measuring anxiety and depression in nonpsychiatric populations (23). Two separate subscales are included measuring anxiety and depression, respectively.

Impact of Event Scale Revised – a 22-item scale measuring common posttraumatic stress symptoms and the impact of stressful life (184). Three subscales are included: intrusive thinking related to the traumatic event (IES-intrusion), avoidant behavior

(IES-avoidance), and emotional arousal (IES-hyperarousal). In the current study, the respondents were instructed to relate to their cancer diagnosis as their stressful event.

Positive States of Minds (PSOM) – a six-item scale measuring different positive emotional and cognitive experiences (25, 184).

Coping Self-Efficacy Scale – a 26-item measure of people's confidence in performing coping behaviors when faced with life challenges (185).

Five Facet Mindfulness Questionnaire (FFMQ) – a self-report measure of mindfulness (186). Five subscales are included: observing, describing, acting with awareness, nonjudging of inner experience, and nonreactivity to inner experience.

The internal consistency for different scales and sub scales in the sample was fair to good, showing Cronbach's $\alpha = 0.77-0.91$ (27). In order to assess meditation practice during the past three months, the participants were also asked to indicate the frequency with one of five response alternatives (never, at a few occasions, about once a month, about once a week, several times a week).

3.3.1.2 Statistical analyses

In order to answer the question of whether there was an effect of the intervention after six months, a multivariate analysis of covariance (MANCOVA) with baseline values and six-month follow-up values on mental health outcomes and coping self-efficacy was carried out. A corresponding analysis was made for the subscales of the mindfulness scale used. Imputation of missing values at six-month follow-up was made according to the last observation carried forward method (LOCF), also named last value carried forward (LVCF) (27). The method means that missing values at one time point are replaced by the last value obtained for each study participant. In this trial, there were data available from baseline as well as from post-assessment at three months follow-up, which mean that some (most) missing data was replaced by baseline values and some by post-assessment values. The information on meditation practice was used in a subsequent analysis comparing change scores of the outcome variables from baseline to six-month follow-up between those who continued to meditate regularly, i.e. several times a week, and the wait-list control group, using independent sample *t*-test. The information on practicing was also used to assess correlations between frequency of meditation practice and outcome variables using Spearman's rho correlation statistics.

3.3.2 Main findings

A significant effect on mindfulness was shown at six-month follow-up, with the intervention group showing higher mindfulness compared to the control group. No effect on other outcomes was shown. In univariate tests, there were, however, noteworthy trends of greater reduction in perceived stress ($p=0.06$) and anxiety ($p=0.09$) in the intervention group as compared to the control group. According to responses, 38% of the participants in the intervention group continued to meditate regularly (several times a week) after the eight weeks program period. When compared to the control group, those who continued to meditate regularly showed a significant reduction in post-traumatic avoidance symptoms. No other significant intervention effects were, however, found in this group. No significant correlation between frequency of meditation practice and change in mindfulness or mental health outcomes between baseline and the six-month follow-up was shown either.

3.4 Study IV

Study IV is a pilot randomized controlled trial exploring the feasibility, usability, acceptability, and outcomes of an eight-week Internet-based mindfulness-based stress management training program, carried out among 76 self-selected university students in Stockholm county. The participants were randomized to either an intervention consisting of an Internet-based, modified version of the group-based mindfulness program (MBSR) developed by Jon Kabat-Zinn (1983), or a control condition consisting of a four-week expressive writing program. The participants were not informed about whether they were assigned to the intervention group or the active control group. No further blinding of group assignment was made.

3.4.1 Mindfulness-based stress management training program

The program content of the intervention is outlined in Table 3. The exercises were made available on an Internet-based platform, to which participants were given access by logging in with an individual password. Along with texts assessing the topic of each weekly lecture, audio-files in different lengths were provided to guide the formal exercises. The participants were encouraged to practice 30–45 minutes a day, 6–7 days per week. The participants could make contact with the study coordinator through the program platform by sending an e-mail, or by making a phone call.

Table 3 Mindfulness-based stress management training program content.

Module	Topic of lecture	Formal exercises	Informal exercises
Week 1	Mindfulness - benefits to quality of life and health	Introduction of: - Mindful breathing - Body Scan Meditation	Introduction of: - Deliberate awareness of routine activities and events, e.g.: waking up, eating, taking a shower, driving, interpersonal communications
Week 2	Cultivation of mindful attitudes	Continued practice	Continued practice
Week 3	The desire to keep or avoid	Introduction of: - Lying yoga Continued practice	Introduction of: - 3-minutes meditation: Step One: Becoming aware Step 2: Gathering and focusing attention Step 3: Expanding attention Continued practice
Week 4	Mindfulness and stress	Continued practice	Continued practice
Week 5	Relations and social context	Introduction of: - Standing yoga - Sitting meditation - Walking meditation Continued practice	Continued practice
Week 6	Automatic thoughts	Continued practice	Introduction of: - STOP: A Short Mindfulness practice-enabling distancing from instant feelings Continued practice
Week 7	Sleep and Mindfulness	Encouragement to train without audio files and experiment with different combinations of exercises	Introduction of: - Short exercise to facilitate falling asleep Continued practice
Week 8	No lecture	Encouragement to again use audio files and choose preferred exercises	Continued practice

3.4.2 Control condition

Participants randomized to the active control condition took part in an Internet-based expressive writing program in which they were asked to write about stressor-related emotions and thoughts for 20 minutes on four occasions spread out over approximately four weeks. This procedure is drawn from the work by Pennebaker and colleagues who began to study expressive writing in college students in the mid-1980s. Studies have shown varying results in different study populations. Frattaroli et al. (187) found a relatively small overall effect from 146 randomized controlled studies of experimental disclosure. Results from a study among young adults (n=116) indicate that for people who already tend to manage emotions through expression, expressive writing may be beneficial in reducing anxiety, but the study did not find a main effect on anxiety, depressive symptoms or physical symptoms (188). In Study IV, the standardized procedure by Pennebaker was complemented with an additional writing instruction that was to write for 10 minutes using a positive prompt following the first writing assignment. The exercises were made available on an Internet-based platform, to which participants were given access by logging in with an individual password. The participants could make contact with the study coordinator through the program platform by sending an e-mail, or by making a phone call.

3.4.3 Methods

3.4.3.1 Scales and questionnaires

For the assessment of effect, self-reported data were obtained by using two established scales:

Psychological Well-Being – a questionnaire measuring six dimensions: environmental mastery, self-acceptance, positive, relations with others, purpose in life, personal growth, and autonomy (189). The alpha coefficient (Cronbach's α) of the scale was 0.82 in the student sample.

The Center for Epidemiologic Studies Depression Scale – a 20-item scale measuring depression symptoms in nonpsychiatric populations (190). The alpha coefficient of the scale was 0.90 in the student sample.

After each week, the participants in the mindfulness intervention group were asked to answer questions about how many days they had practiced and how much time they had spent on average practicing formal and informal mindfulness training. At the post-assessment follow-up, the respondents were asked seven questions to evaluate their overall experiences of the programs, based on research into factors considered to be important for participation in Internet-based programs, e.g. how well the intervention is received and perceived by users (165, 167, 191).

3.4.3.2 Interviews

Interviews with eight participants were carried out shortly after program completion by the study coordinator, using a semi-structured interview-guide. The interview guide reflected issues that have previously been shown to influence participants' perceptions of Internet-based programs, e.g. if the program was easy to use (192), how it was perceived in terms of reliable information, professional appearance, as well as challenges in carrying out the exercises (84, 165, 170, 171, 193).

3.4.3.3 Statistical methods

In order to answer the question of whether there was an effect of the intervention on mental health, the difference between the groups on the contrast between baseline and follow-up was tested using multivariate repeated-measures analyses of variance (MANOVA) with baseline and follow-up scores as dependent variables. Time and group were entered as factors. Imputation of missing values at post-assessment follow-up was made according to the last observation carried forward method (LOCF/LVCF) (27). In addition to the MANOVA, analyses to examine pre- and post-intervention change for each dependent variable stratified by randomization condition were conducted, using paired sample *t*-test. Cohen’s *d* effect size for within group differences was calculated.

3.4.3.4 Content analysis of interviews

Qualitative content analysis was used to analyze the interview data (194). The analysis was to a large extent deductive, since the interview questions initially directed the analysis. Unexpected content was also taken into account in order to refine and extend the understanding of the material. The approach most closely resembling the current has been described as “Directed Content Analysis” (195). A team-based approach was used for developing codes and coding the narratives (196).

3.4.4 Main findings

Number and proportion of participants completing each course week is displayed in Table 4. Half of those who terminated the program before completion stated an explanation for leaving by e-mail to the study coordinator. Of these persons, nine mentioned lack of time, one had technical problems with the computer at home, and one referred to changed circumstances.

Table 4. Number and proportions of participants completing each weekly module.

Modules	Mindfulness training program (n=46)		Expressive writing program (n=44)	
	Number	Proportion	Number	Proportion
Week 1	28	60%	35	80%
Week 2	23	50%	32	73%
Week 3	21	46%	31	70%
Week 4	20	43%	31	70%
Week 5	19	41%	Program finished	
Week 6	19	41%		
Week 7	19	41%		
Week 8	18	39%		

The participants practiced on average 3.6 days per week.

No overall effect on the mental health outcomes was shown. Within-group comparisons showed that participants in the mindfulness training program had a statistically significant increase in psychological well-being over time with a small effect size. No statistically significant change over time appeared for depressive symptoms. Participants in the control condition did not report any statistically significant pre- and post-assessment changes on the two outcomes. Overall, the participants in the intervention group were satisfied with the program and appreciated

the flexibility of being able to practice at suitable time-points, as illustrated by a citation from one of those interviewed:

The advantage is that it has been great to be able to do it just when you feel like it, that you don't need to fit in with a time.

[Woman, 23 years] (197)

In line with the reasons expressed via e-mails from those who left the program, also those who carried on and completed the program found it time consuming and also somewhat stressful:

What I do think is that I have felt a little stress that there have been so many times when we've had, so to speak, . . . when it has been expected that you should do these exercises. It's been something that I thought, what can I say, was a bit stressful.

[Woman, 26 years] (197)

More frequent contact with the study coordinator was suggested as a way to improve program completion rate, for example, a phone call before the beginning of the program. All of the participants in the intervention group who completed the program stated that participating in the program was experienced as having been meaningful, however, challenging.

4 DISCUSSION

4.1 Summary of results

Sickness absence, mainly due to breast cancer, increased markedly in the first year after breast cancer diagnosis, however, it approached the levels of breast cancer-free women five years later. Pre-diagnosis sickness absence and advanced cancer stage were associated with higher risk of sickness absence and disability pension, as were lower education and being born outside of Sweden. Adaptive coping, such as acceptance and positive reappraisal, was associated with better mental health in women with breast cancer. These associations were strongest among individuals under current treatment and women assessed soon after diagnosis. No significant effect of the mindfulness-based stress management training program on mental health outcomes was found at six-month follow-up. However, a positive effect on self-reported mindfulness was observed. The Internet-based mindfulness-based stress management training program was experienced as usable and acceptable and had potential for increasing psychological well-being for those completing it. However, only 39% of the participants completed the program.

4.2 Methodological considerations

Methodological considerations regarding each of the studies are discussed below.

4.2.1 Prospective cohort study

4.2.1.1 *The register data*

The advantage of using data from nation-wide registers covering all individuals in a population, is the absence of selection bias, recall bias and dropouts, which are common problems when using survey-data, impairing the validity of studies (198). The assumption of high validity is based on the fact that the Swedish registers are regarded as having high quality and rigorous routines for reporting and coding information (177, 199-201), reducing the risk of misclassification and missing data. Misclassification can be non-differential (random) and differential (non-random) (202, 203). Non-differential misclassification regarding exposure variables (e.g., age, or country of birth) increases the similarity between the exposed and unexposed groups, and may result in a dilution of the true strength of a possible association between exposure and outcome. Non-differential misclassification regarding the outcome, i.e., sickness absence and disability pension, may result in a corresponding dilution of the strength of a possible association. Differential misclassification, on the other hand, may increase or decrease the similarity between the exposed and unexposed groups, thereby lead to either an overestimation or an underestimation of the strength of a possible association between exposure and outcome. Differential misclassification would occur if the misclassification of exposure (e.g., educational level or cancer-stage) would be unevenly distributed (non-random) between women who had sickness absence or disability pension, and those who had not. Similarly, it would occur if the misclassification of the outcome (sickness absence and disability pension) were unevenly distributed between those exposed and those unexposed. Some information on cancer stage was missing in the current study, which could also be a problem if it were unevenly distributed as described above. To investigate whether the lack of this information influenced the results in the regression analyses, all analyses were also run excluding individuals lacking such information. Similar results as for those presented

were obtained, indicating that lack of information regarding cancer stage did not bias the results. For some sickness absence and disability pension, information on diagnoses was missing, primarily for disability pension (displayed in Figure 1). This was a problem in the descriptive part of the analysis, i.e., in estimation of the mean number of diagnosis-specific sickness absence and disability pension net days per year intervals. The displayed “Missing” categories include diagnoses belonging to one or more of the other categories. Since the missing category is quite small regarding sickness absence, it is unlikely to considerably affect the conclusions drawn. Regarding disability pension, the missing category is larger, however, quite stable over time, and smaller at the end of the follow-up. Still, it is likely that the conclusions drawn would not be affected by the knowledge of what diagnoses were included in the missing disability pension category. Finally, we had no information on most sickness absence spells lasting for 14 days or less, which limits the possibility to assess shorter periods of sickness absence.

4.2.1.2 Statistical analysis

The logistic regression model is the most frequently used regression model for the analysis of data concerned with describing the relationship between a dichotomous dependent variable (e.g., sickness absence/disability pension) and one or more independent variables (e.g., type of living area, family situation) (204). Using the multivariate model enables controlling for (other) independent variables when examining the relationships between a dependent variable and several independent variables, some of which may be on different measurement scales, which is the case in the current study (e.g., age and country of birth, respectively). A strength of the study design was that women no longer at risk of sickness absence and disability pension due to death, turning 65, or emigration during follow-up, could be excluded from the denominator. This might, however, affect the risk estimates since those who are left out from the analyses may differ in relevant aspects from those remaining. A somewhat higher percentage of women with breast cancer compared to women in the comparison group also died during follow up, implying that the risk estimates in the regression analyses could be affected by selective mortality. However, sensitivity analyses with Cox regression, censoring for mortality during follow-up, revealed comparable findings.

In order to estimate associations between dependent and independent variables, confounders need to be accounted for. Confounders are variables that are associated with both the dependent and the independent variable, without being a part of a causal chain between them (202). Although, several potential confounders were taken into consideration, i.e., sociodemographic- and disease-related factors, there may have been confounding which was not considered. Another limitation is that we did not have information on cancer treatment. Cancer treatment can influence sickness absence after breast cancer, as well as attenuate statistical associations between cancer stage and sickness absence (95, 105).

4.2.2 Meta-analysis

Meta-analysis is a quantitative design used to assess previous research and obtain a more precise estimate of outcomes, than any individual study (205). The meta-analysis design is also suitable for the investigation of reasons for differences regarding effects between studies (181).

4.2.2.1 Search and selection

Searching in only two databases may have resulted in the exclusion of some relevant studies, although the assumption was that the selected databases cover most of the relevant studies with the specified inclusion criteria. Only studies from United States, Canada, Europe, and Australia/New Zealand were selected, which limits the generalizability to women in other countries. This choice was found to be reasonable with regard to the difficulties that can arise when trying to interpret findings from samples derived from very different cultural contexts.

4.2.2.2 Grouping of coping and health categories

The grouping of coping categories and outcome categories imply challenges regarding reliability and validity. What is actually measured? Calculation of mean scores for different health-related variables may further lead to lowered precision, and the mixing of quite different measures into one. This strategy can, on the other hand be considered fruitful with regard to the amount of measures used in the research field, creating a larger group of included studies with higher precision of estimated values.

4.2.2.3 Publication bias

Publication bias is a form of bias related to the assumption that the research literature is not totally representative for all the studies actually carried out. There are strong indications that studies with large effects sizes are more likely to be published than studies reporting lower effect sizes, making “missing studies” systematically different from those that are located (181). In this meta-analysis the trim-and-fill procedure described by Duval and Tweedie (182) was used to handle the problem with publication bias. An advantage of this approach is that it can obtain “the best estimate of the unbiased effect size”. A disadvantage is a strong dependence on the assumptions that a) large studies are likely to be published whether or not they obtain statistically significant results, b) some of the moderately sized studies are lost, and c) small studies run the highest risk of being lost (unpublished), creating a risk that one or two (small) studies with divergent results may influence the estimate disproportionately. A more radical way of handling the risk of publication bias is to restrict the meta-analysis to larger studies, which might be expected to be published regardless of their results (effect sizes). In the current study, this was partly done since only studies with sample size larger than $n=30$ were included, making the risk of influence of divergent results from small studies less prominent.

4.2.3 Randomized controlled trial

Randomized controlled trial design is considered superior to other study designs when studying intervention effects. The strength lies in the possibility to avoid influence of confounding factors by allocating individuals randomly to an intervention group or a control group. However, there are several limitations connected to this kind of studies too (206). Limitations in the current study include the lack of blinding and no active control group. Having to wait for an intervention can affect psychological processes and mental health outcomes in the wait-list control group. Moreover, participants in the intervention group knew from the program content that they were expected to become more “mindful” and also less stressed by participating in the program, which may have influenced the self-reported outcomes. Such a placebo effect (207) is not necessarily a problem but should be considered when interpreting the results.

4.2.3.1 *Self-reported data*

The effect of the program was measured by self-reported data at baseline and six-month follow-up. Self-reported measures can be regarded as a limitation due to the risk of response bias (208). As mentioned, participants in the intervention group knew that they were expected to become more “mindful” and less distressed by participating in the program, and if the reporting was exaggerated regarding improvements due to social desirable answering it can be a problem with regard to interpreting the results.

4.2.3.2 *Statistical methods*

In order to answer the question of whether there was an effect of the intervention after six months, a multivariate analysis of covariance (MANCOVA) with baseline values and six-month follow-up values on psychological and mental health outcomes was carried out. Advantages of the MANCOVA is the possibility to analyze multiple outcome variables (e.g., perceived stress, depression, anxiety, post-traumatic stress symptoms, positive states of mind, coping self-efficacy) at the same time without running the risk of rejecting the null-hypothesis due to multiple-testing (type I error), which is a problem when analyzing each variable at a time. The MANCOVA also allows for the inclusion of covariates/factors (age, education) assumed to be correlated with the outcome, which may give increased power (209).

Limitations in the MANCOVA and related methods include the problems with handling missing data and the method has been criticised for generating biased results when dropout rates are large and unevenly distributed between study groups (210). The reason for risk of bias is the assumption that the individuals who are still present in the sample no longer are representative for the population from which they were included and randomized. More modern methods like mixed-effects (regression) models have been suggested as a more plausible method when analysing RCT data measured at multiple time points. Advantages of these models include the use of all available data for each individual and provision of a choice of covariance pattern that may lead to a more efficient estimation of the intervention effect (compensating for the “lost” values) compared to more traditional methods. The results are unaffected by randomly missing data, however still affected by data missed not at random (210) which constitutes a problem since in “real life data“ there will most likely be some missing observations that are dependent on either observed or unobserved data (211). Mixed-effects models include high complexity and must be correctly specified in order to lead to correct conclusions (27).

4.2.3.3 *Attrition and imputation of missing data*

Attrition represents a threat to validity and the only way to be confident of avoiding biased results due to attrition is to have high compliance rates (27). Since this is seldom the case in randomized controlled trials, several techniques have been developed in order to deal with the problem. In the current study, the proportion of participants who did not return the six-month follow-up questionnaire was 34% in the intervention group and 5% in the wait-list control group. The method chosen to handle the missing data (27) may have caused under- or overestimated effects depending on the direction of change in the outcome variables between different time points. The reduced number of participants at the six month follow-up may have led to an underestimation, i.e., a reduced possibility to find “real improvements” (Type II error), if those who did not return follow-up assessments had achieved improvements compared to baseline (or compared to the post-intervention follow-up for those who filled out that questionnaire

before leaving the study). If the opposite was true, i.e., those who did not respond at three- or six-month follow-up had deteriorated in mental health and coping self-efficacy after baseline-measure or post-intervention measure, the changes and trends detected would instead display an overestimate of the intervention effect. Since deterioration due to the program or to the disease from baseline up to the six-month follow-up in the mindfulness group is not assumed, the risk of overestimation seems less likely. For those who returned post-assessment questionnaires but not the six-month follow-up questionnaires, the post-assessment value was used, which is a circumstance that may work in the opposite direction if we assume a “real” diminished positive effect of the program. This group was however very small. Information about the reasons for study termination was not obtained from the participants, and the possibility that those who left the study experienced no effects or even adverse effects can, however, not be ruled out (146). Finally, the study may have been underpowered to detect significant effects at six-month follow-up, assuming some reduction in the intervention effect between three- and six months post-intervention (136).

4.2.3.4 Analyses of the impact of practice

The results from the analysis of those who continued regular practice after program completion, can give an indication of the influence of regular practice, but since those who continued to practice may not be representative for the whole group of included participants, generalizations to the rest of the group cannot be made.

4.2.4 Pilot randomized controlled trial

The advantages of the randomized controlled trial design were mentioned in the section describing Study III. In Study IV, additional advantages of an active control-group without knowledge about which of the programs were most effective (blinding), reduced potential effects of either having to wait for the program, or by “higher expectations” of improvement in the intervention group compared to the control group. The use of a potentially effective control condition, may have decreased the possibility to detect an overall effect when comparing the groups on outcomes. However, expressive writing has shown small effects, and in a study among young adults no overall effect was detected (188).

A factor that contributed to a fairly high dropout-rate was the fact that the baseline questionnaire was filled out in connection to program start, when participants had already been allocated to one of the two study groups. This arrangement had practical reasons, but is not to be recommended in general in randomized controlled trials since it can lead to response bias due to the knowledge (and perhaps disappointment) about which group the participant belongs to. This may be a larger problem if there is a wait-list control-group design, where participants can be disappointed over having to wait for the intervention.

4.2.4.1 Statistical methods

Since there was only baseline- and one follow-up measurement, the MANOVA analysis seemed plausible, in accordance with what was discussed in relation to MANCOVA in relation to Study III above. The choice of imputation method, however, can be discussed and there are other methods that could have been used, e.g., replacing any missing value with the mean of that variable for all other cases, or using multiple imputation for averaging the outcomes across multiple imputed data sets. The method

used may have caused an underestimated effect, if the assumption is that the participants improved during the course.

4.2.4.2 *Qualitative method*

Like in quantitative research, there are threats to validity also in qualitative research. Validity concerns a number of aspects from data collection to analysis (198). One threat to the validity was the way the interviewees were recruited. Potential interviewees were contacted after study completion, and if not reachable/available, replaced by next person who had completed the program. This may have led to recruitment of non-representative sample with different opinions as compared to those not interviewed. In practice, however, it is hard to avoid biased results due to overrepresentation of persons who have time and are willing to be interviewed in any study, since study participants are allowed to leave the study at any time and cannot be “forced” to participate in any investigation. Eight participants were finally interviewed, which may seem like a small group, however, since no new data seemed to appear after six to seven interviews the interview process was discontinued. The use of a semi-structured interview-guide with quite a few questions may have contributed to short interviews, e.g., 15 minutes on average, and a quick interview process. Perhaps face-to-face interviews would have generated a larger and richer material, however the reasons for similar reporting from the participants may also reflect the fact that they shared similar characteristics, e.g., being young, being students, having more or less the same education level and living in Stockholm. A possible risk of biased results was assumed to be connected to the fact that it was the program coordinator who carried out the interviews. Any tendency to give socially desirable answers may have been more prominent in this situation compared to if an external person had carried out the interviews. The risk of bias was, however, assumed to be connected to an interview question about support from the study coordinator, and not so much regarding technical issues or own experiences from the training.

4.3 Discussion of results

4.3.1 Patterns of sickness absence and disability pension

Study I showed that sickness absence-levels increased substantially in the first year after diagnosis, primarily due to breast cancer diagnosis, but approached the levels of breast cancer-free women in the fifth year. There was no increase in sickness absence due to mental diagnoses during follow-up, which is notable considering the fact that anxiety and depression are quite common among women with breast cancer, although especially prominent around the time of diagnosis (80, 82, 83). One explanation could be that the health problems related to impaired work capacity and subsequent sickness absence or disability pension to a large extent are related to physical symptoms from treatment side-effects. Surgical wound with subsequent pain after the operation, as well as nausea and fatigue, are symptoms connected to the cancer treatment, and prominent in the first 6-12 months after diagnosis (64, 67-70). Persistent physical problems in terms of a swollen arm due to removal of lymph nodes may also impair work capacity during longer periods, as can persistent fatigue (212).

Another possibility is that mental health concerns in women with breast cancer are not recognized (82). There is also a possibility that the mental health concerns are not affecting the work capacity to a level that legitimizes sickness absence. The impaired work capacity may further depend on a combination of physical and mental symptoms,

where a mental diagnosis may be regarded as a secondary diagnosis and therefore not visible in the current study (213). Further research could investigate more closely the kind of physical or mental problems that may contribute to reduced work capacity.

The study showed that pre-diagnosis sickness absence was associated with sickness absence and disability pension post-diagnosis, which is in line with previous studies (95, 105). Women with a pre-history of sickness absence have, or have had, other diagnoses impairing their work capacity and the breast cancer may, or may not, contribute to further reduction of work capacity. Whether these women continued sickness absence post-diagnosis with the same diagnosis, or with a breast cancer diagnosis, was not investigated in this study, but could be investigated in future studies (213). Advanced cancer was further associated with sickness absence and disability pension post-diagnosis (90, 91, 112), which may be due to the treatment-side effects (95, 105). Being born outside of Sweden and having an education below university level were also associated with a higher risk of sickness absence and disability pension, the latter (education level) in line with previous research (101, 103, 105). Possible explanations to this may be physically demanding work tasks or lack of possibilities to adjust the work tasks or the work environment, or both these factors. Work-related factors, such as blue-collar or manual work, work with high demands and a non-supportive supervisor have been shown to be negatively related to return to work (90, 91, 115). Immigrants may have difficulties in getting more qualified jobs, as compared to natives with comparable education level, which might explain the higher risk of sickness absence and disability pension in this group, even after adjustment for education. Being an immigrant, or descendant from an immigrant, was in a Danish study shown to increase the risk for depressive symptoms 3-4 months post breast cancer diagnosis (84). A Swedish population-based register study (214) further showed that immigrants, and particularly refugees, have poorer mental health than native Swedes, supporting the view that mental health concerns might be more prevalent among women with breast cancer born outside of Sweden than among natives. In any case, it is not clear to what extent mental health concerns contribute to the elevated risk of sickness absence/disability pension among immigrated women. More knowledge is warranted on mechanisms behind the higher sickness absence and disability pension risks among immigrants with breast cancer in general and from specific countries and regions in particular.

4.3.2 Mindfulness training and health improvements

Study II, III and IV relate to possible ways to promote mental health in women with breast cancer.

4.3.2.1 Does coping influence health related outcomes?

Similar to previous meta-analytic findings, results from Study II showed that more engagement forms of coping are related to better mental and physical health outcomes than more disengagement forms of coping (DC) (45-47). An interesting finding in Study II, however, was the stronger support for strategies to facilitate adaptation to the stressor (SCC), compared to strategies aimed at changing the stressor or related emotions (PCC). An explanation for this may be that a cancer related stressor often is perceived as uncontrollable. Previous research on the health consequences of coping suggest that adapting to a stressor that is perceived as uncontrollable is better than using active attempts to solve the problem (48). Newly diagnosed women and women undergoing treatment seemed to benefit the most from replacing DC coping with SSC coping. This may be related to a perception of even more uncontrollable circumstances

at the time of treatment compared to circumstances experienced after treatment completion.

In the introduction section, a causal chain between a stressor and related emotions was described (127), starting with a stressor stimulus that leads to a primary appraisal, followed by a secondary appraisal in which the individual can attribute meaning to the stressor event. If the individual reconstruct the event as benign, valuable, or beneficial, adopting positive reappraisal, positive emotions are likely to occur. This view was partly supported by the results in Study II, in the sense that the most obvious associations between coping and mental health occurred between SCC strategies, including positive reappraisal, and higher positive affect and lower negative affect. Regardless of the associations between different coping strategies and health, an interesting question in this thesis is whether maladaptive coping behaviors can be changed through different interventions, for example mindfulness training. Support for long-term beneficial effects of an intervention focusing on the improvement of coping skills for better health was gained in a randomized controlled trial among 110 women with breast cancer scheduled for medical treatment. In this group, an intervention of a self-management multimodal comprehensive coping strategy program, focusing on cognitive restructuring and coping skills enhancement, showed beneficial effects on quality of life one year later (215).

4.3.2.2 Can mindfulness training lead to longer-term health improvements?

Increase in mindfulness was seen in the intervention group in Study III at six-month follow-up, but no significant effect on mental health outcomes. One explanation to this may be a reduction in daily training after the eight course weeks. Just over a third of the participants continued to meditate regularly. Previous studies have shown that the amount of formal meditation practice (144), as well as informal practice (143), are related to beneficial effects of mindfulness. Perhaps the training in itself leads to additional beneficial effects apart from increased mindfulness, the way it is measured by FFMQ, either other health promoting factors, or increased “mindfulness” not captured in the FFMQ. The fact that the analysis of the group of participants that continued to practice regularly indicated sustained effects regarding post-traumatic avoidance symptoms calls for research on the potential effects of sustained regular training, but also on other potentially moderating factors, in order to clarify when and for whom mindfulness interventions are efficient.

Another possible explanation of the diminished effects of the mindfulness training program is lack of group- and instructor support after the eight course weeks. An interview study among participants in a mindfulness-based stress management training program shortly after course termination, showed that the influence of group process, the sharing of experiences with persons with similar experiences, and practicing together with other participants were perceived as very positive parts of the course (145). It is likely that the psychological support from the group and the instructor made the training more pleasant. One of the participants mentioned explicitly that it was hard to practice at home without being able to process the experiences together with someone. Despite any discomfort connected to home practice, 60% of the participants meditated regularly (at home) during the course weeks (216), compared to 38% after course completion, indicating that the weekly course sessions were supportive for home practice.

A third circumstance to reflect over when interpreting the results from the current study is factors connected to the disease phase and symptom levels in the individuals enrolled. The included participants did not have to show a certain degree of symptoms of stress in order to be included, which may have influenced the “room” for improvement of psychological states. It is possible that larger effects had been achieved if participants had experienced more symptoms of stress and related outcomes at baseline. Support for such assumption is given in a meta-analysis based on 39 studies including 1140 individuals receiving mindfulness-based therapy for a number of conditions, among those anxiety (217). This study found that mindfulness-based therapy was more effective in reducing symptoms among individuals with an anxiety diagnosis at baseline than in the overall sample. Additionally, most of the participants in study III, had received their cancer diagnosis more than one year before the time point for inclusion and none were receiving adjuvant treatment during the study period. In the light of the results from Study II, and the reasoning about mindfulness’ possible effects on coping, the question arises regarding if effects on health-related outcomes would have been more prominent or more sustained if a larger number of newly diagnosed participants and participants undergoing treatment had been included in the study. The reason for not including individuals undergoing treatment was the assumption that it would constitute a challenge for these persons to travel to and participate in group training, while at the same time having to handle possible side effects from cancer treatment.

4.3.2.3 Does Internet work for mindfulness training programs?

In the light of the results from Study IV and from the study among cancer patients described in the introduction (166), there seems to be a potential for the development and implementation of online mindfulness-based intervention for women with breast cancer.

Several studies of mindfulness-based stress management training programs have shown difficulties in achieving long-term effects (218, 219). A strength with Internet-based programs is that it could be fairly easy to disseminate booster sessions and varying tools for the facilitation of continued training after completion of an initial training program. An important factor to reflect on, whether creating a whole program or single sessions or other tools, is the extent to which support from instructors and other participants is needed. The pilot-study (Study IV) among students was self-instructive and almost totally automated with minimal contact between participants and study-coordinator and resulted in very large attrition rate. A study of an Internet-based mindfulness-based cancer recovery program, which included contact with other participants and common online class sessions with an instructor, had a lower drop-out rate (166).

A US study comparing two Internet-based mindfulness-based programs; one with a message board and one without a message board, found that the completion rate in the program without a message board was only slightly lower (41%) compared to the program that included a message board where participants could make contact with each other (44%) (165), suggesting that contact with other participants does not contribute very much to an increased completion rate in Internet-based programs. But, the importance of contact with other participants may differ between different target groups. Participants in Study III, emphasized the importance of common training and contact with other participants as a very positive component of the program when

interviewed afterwards (145). This type of face-to-face contact is, however, quite different from the contact that can be achieved in an Internet-based program.

Previous research gives support for the importance of support from a therapist (or facilitator) for successful implementation of online (ICBT) programs (172). In the interviews in Study IV, the value of contact with the study coordinator for successful completion of the program was also put forward. Another study, using computer-based mindfulness meditation training, indicated that virtual coach-based training of mindfulness was both feasible and potentially more effective than a self-administered program (220). Future studies could focus on examining how different ways of giving support affect outcomes in different target groups.

4.3.2.4 Applying pilot-study results to women with breast cancer

The possibility to take part in an Internet-based program at home could facilitate mindfulness training among individuals that may find participation in ordinary mindfulness-based programs challenging, e.g., women undergoing breast cancer treatment. A feasibility pilot study (221) with 23 patients receiving chemotherapy who were offered the possibility to listen to MBSR audio recordings during treatment and at home, showed preliminary support for a potential to reduce depressive symptoms (scores change = -6.1 points; 95% CI, -2.9 to -9.4). Participants further reported subjectively that the participation improved their mood and quality of life.

Since caution is warranted when adapting mindfulness training programs into Internet-based programs with minimal support from instructors or therapists, targeted at persons with a serious disease (54), students interested in participating in a program for stress management training were recruited to this first pilot-trial in Study IV. Thus, the results refer to students as a target group and generalizations to women with breast cancer is limited. Our result, however, indicates a need to shorten the time for practicing in order to make the program more feasible. The students' expression of stress in connection to participating in the program, due to a feeling that they "had to" practice a certain amount of time, calls for ways to limit the experiences of stress in relation to mindfulness-based stress management training programs if delivered via the Internet to women with breast cancer.

4.4 Ethics

Three of the studies in the current thesis (I, III, IV) required and got approval by the Regional Ethical Review Board in Stockholm.

5 CONCLUSIONS

Analyses of registry data on sickness absence and disability pension indicate that work capacity among women diagnosed with breast cancer is reduced primarily in the first year after diagnosis and primarily due to breast cancer, not due to mental or other diagnoses. After the first year, the number of women with sickness absence decreased markedly and levels of sickness absence were back to the same levels as before the diagnosis in a few years. However, women with pre-diagnosis sickness absence, advanced cancer stage, lower education, and women born outside of Sweden had higher risk of longer-term sickness absence and disability pension.

The review of the extensive literature on coping with breast cancer showed that some ways of coping with a diagnosis are related to more positive and less negative health outcomes. In particular, women reporting adaptive ways of coping reported better mental health and those reporting disengagement forms of coping had poorer mental and physical health. Supportive rehabilitation interventions for women after breast cancer diagnosis should encourage adaptive and discourage disengagement ways of coping. Encouraging adaptive strategies might be particularly beneficial among newly diagnosed women and among those under current treatment.

Despite increase in self-reported mindfulness at six-month follow-up after a mindfulness-based stress management training program for individuals with a cancer diagnosis (76% with breast cancer), no statistically significant improvement in mental health was found. Regular meditation practice after program completion might promote long-term mental health improvements, but more knowledge is needed on the underlying mechanisms and moderating factors for achieving long-term benefits of mindfulness training.

The Internet could be a promising way to disseminate programs and tools facilitating mindfulness training in different phases of the disease trajectory, but if retention and compliance to a full program is important, additional modification of the type of mindfulness-based stress management training program assessed in Study IV is needed. A shorter program period, as well as less demanding exercises, seemed to facilitate program completion. Making a personal contact with participants and providing more regular reminders, either personal or automated, could also be a way to facilitate the daily training among participants. Finally, screening of health concerns and motivation to participate in an Internet-based mindfulness-based stress management training program among potential participants could be tested as ways to improve the completion rate.

6 FUTURE RESEARCH

6.1 Sickness absence and disability pension after breast cancer

Based on results from Study I, with population data for all women with a first breast cancer diagnosis in 2005, studies on sickness absence and disability pension among female immigrants are warranted. Analyses of country- or region specific data on sickness absence and disability pension among women born outside of Sweden and diagnosed with breast cancer are called for in order to develop the understanding of the elevated risk of sickness absence and disability pension in this group.

6.2 To gain and sustain beneficial effects of mindfulness training

Mindfulness-based training is one of many interventions directed to women with breast cancer, aimed to improve health and support regaining of ordinary life, functions and roles. Obviously, there are still many questions to be answered regarding how to sustain beneficial effects over time, i.e., Which are the specific components in the programs leading to positive effects? How much practice is needed? Who may benefit and when? Is it possible to achieve benefits through Internet-based programs? How should such programs be designed in order to promote health and not lead to adverse effects?

6.2.1 Central components

Future research should continue to focus on understanding which elements of the mindfulness training influence health outcomes. By differentiating between formal (taking time to meditate for an extended period of time) and informal (bringing mindfulness to an activity) practices when measuring meditation practice, a clearer picture regarding which type of practice should be encouraged can be obtained.

6.2.2 Amount of practice needed

Since we do not yet know the optimal length of mindfulness-based programs to maximize outcomes, or the shortest intervention that can still derive benefits, it is warranted to further investigate the relationship between amount of training and health outcomes. This could be studied by tracking daily practice with detailed diaries or by logging amount of training in suitable mobile applications in future studies.

6.2.3 Target groups that may benefit

This thesis highlights the possibility that women undergoing treatment may benefit from mindfulness training. Preliminary support for a mindfulness-based intervention to reduce depressive symptoms in cancer-patients undergoing treatment in a small non-randomized study (221) calls for more well-designed studies among these women. In order to explore additional target groups that may benefit from mindfulness-training, or perhaps other types of interventions promoting the same coping strategies or other beneficial coping strategies, future studies on coping could focus on testing additional moderating factors in the breast cancer group. Future research could also focus on the effects of mindfulness training on the outcome “remaining in paid work”, or “return to work” among those sickness absent, since many of the women with breast cancer are of working age and work has been shown to be an important factor for health (10).

6.2.4 Benefits from using the Internet

The promising results from studies of Internet-based programs carried out in different patient groups suggest that mindfulness-based stress management programs for women with breast cancer adapted for the Internet could be used as an efficient tool for rehabilitation. The role of therapist support and/or support from other participants for beneficial effects of mindfulness training could be studied by comparing effects of self-administrated programs (without support/with little support) with ordinary mindfulness classes. Future studies could also examine the potential of additional Internet-based intervention tools to encourage prolonged post-intervention meditation after program completion, both for class-based and Internet-based programs. Considering the reasoning on coping outlined above, and the promising preliminary support for a mindfulness-based intervention in cancer-patients undergoing treatment (221), future studies of mindfulness-based Internet-based interventions could focus on women with breast cancer undergoing treatment in larger well-designed studies.

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