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## Taxane-induced pain

*Experiences of women with breast cancer and  
nurses providing their care*

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### **Abstract**

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Breast cancer patients receiving taxane chemotherapy run a substantial risk of develop taxane-induced pain, but little is known about women's experiences of such pain. The aim of this thesis was to explore women's acute and longstanding experiences of taxane-induced pain, to evaluate the pain intensity and distribution using different assessment methods, and to study nurses' perceptions of taxane-induced pain in people with breast cancer.

The women experienced pain during chemotherapy with 37–48% incidence of acute taxane-induced pain. The subjective burden of taxane-induced pain described by the women covered narratives from manageable pain to very difficult and disabling pain with a major impact on their lifeworld (Study I).

Longstanding pain in the lifeworld of women with previous breast cancer, was explored through a retrospective reflection after 12 months. The descriptions of pain revealed a time perspective; as pain perceived at that specific time, currently ongoing pain, and pain expectations for the future. This resulted in the women sensing themselves of being somewhere between health and illness gazing into an uncertain future (Study II).

A quantitative longitudinal assessment of taxane-induced pain using; the body image, the VAS, and the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-QLQ-C30) showed the women's estimated pain; its intensity, distribution and occurrence - as it appeared during the actual taxane treatment and up to a year afterward. The baseline measurement on the VAS revealed low initial pain, VAS <10, which changed at treatment Cycle 1. The body image revealed intense and widespread pain, and pain after 12 months, as did the EORTC QLQ -C30 (Study III).

The nurses' estimations of taxane-induced pain varied to large extent in both prevalence and intensity. Large parts of the body were expected to be involved in the pain. Nurses lacked local and/or national guidelines reflecting a low level of generalized use of prophylaxis against taxane pain (Study IV).

In conclusion, taxane-induced pain is a common debilitating symptom during taxane chemotherapy for women with breast cancer. Pain impacts women's life during as well as long time after the completion of taxane treatment. Taxane pain can be accurately or successfully estimated using various pain assessment tools. Furthermore, guidelines for dealing with taxane-induced pain are needed.

*Keywords:* taxane-induced pain, lifeworld research, pain assessment, caring

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*To Hannes, Anton and Vidar*  
"You are my dreams of a fairer  
world".



“The phenomena of pain belong to that borderland between the body and soul about which it is so delightful to speculate from the comfort of an armchair but which offers such formidable obstacles to scientific inquiry.”  
Kellgren JH., Lond MB. Deep pain Sensibility, p 642, The Lancet, 1949.

## Prologue: Grasping pain in the lifeworld

When I was a child, other people’s stories had my full attention. I could stay under the dinner table’s tablecloth at my grandmother and grandfather’s house for hours, getting acquainted with the world of adults, hearing about everything under the sun, including the state of things in the world. Everything that was said was not meant for my little ears, but they were sensitive antennae that captured every shift, every excitement, in a voice raised in a statement.

As a young auxiliary nurse on the geriatric ward, my experiences of pain were expanded. There, I met a patient with advanced multiple sclerosis and pressure ulcers so deep they exposed parts of her pelvis. She never complained when we cleaned the necrosis from her wounds, but for me it was painful. Later, I started working at an ear-nose-and-throat clinic. Anyone who has ever taken a culture from the nasopharynx knows how sensitive the mucosa in the nose is, and sometimes in my work as a nurse on that ward I felt like I’d been transported to the land of the barbarians, seeing how much pain of all kinds the patients had. Soon, my care work increased for especially two groups of patients: children and cancer patients. In caring for children, the challenge was getting them involved and cooperating in sometimes painful procedures, for example pre-medication before an operation (at the time this was still done through intramuscular injection). After the operation, it was ensuring that they did not experience breakthrough pain. The other group, cancer patients, often had severe pain and a great deal of life experience – so many revolving life histories. Several times, it happened that I as a nurse was told a story about pain and anxiety by the patient and asked the doctor for help: *Please go in and see how Patient x is doing*. However, the doctor would emerge from the patient’s room and claim that Patient x was doing well.

From that moment, I slowly began to understand the power that comes from telling one’s own story.



# List of Papers

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

- I. Hellerstedt-Börjesson S., Nordin K., Fjällskog M-L., Knutsson Holmström I., Arving C. (2015) Women with Breast Cancer: Experience of Chemotherapy-Induced Pain: Triangulation of Methods. *Cancer Nursing* 38(1):31-39.
- II. Hellerstedt-Börjesson S., Nordin K., Fjällskog M-L., Knutsson Holmström I., Arving C. (2016) Women Treated for Breast Cancer Experiences of Chemotherapy Induced Pain: a past, present and future perspective. *Cancer Nursing* 39(6):464-472.
- III. Hellerstedt-Börjesson S, Nordin K, Fjällskog M-L, Rissanen R, Peterson M and Arving C. (2018). Colored body images reveal the perceived intensity and distribution of pain in women with breast cancer treated with adjuvant taxanes: A prospective multi-method study of pain experiences. *Scandinavian Journal of Pain; ahead of print*
- IV. Hellerstedt-Börjesson S., Nordin K., Fjällskog M-L., Peterson M and Arving C. (2018) Nurses' experiences of taxane-induced pain in people with breast cancer *Manuscript*

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# Abbreviations

BAS	Breast Cancer and Stress study
CNS	Central Nervous System
DFS	Disease-Free Survival
EORTC	
QLQ-C30	European Organization for Research and Treatment of Cancer Quality of Life Questionnaire
HER2	Human Epidermal Growth Factor Receptor-2
IASP	International Association for the Study of Pain
NCRP	National Cancer Rehabilitation Program
SD	Standard Deviation
TRPA1	Transient Receptor Potential Ankyrin Subtype 1 Protein
PAG	Periaqueductal Grey
TNM	Tumor, Node, and Metastasis staging system
WHO	World Health Organization
VAS	Visual Analogue Scale



# Introduction

Cancer of the breast is by far the most common malignancy in women. Breast cancer is a disease with increasing incidence and mortality worldwide, although the trend in the United States and Europe points towards increased survival rates (1-3). A woman in the Western world diagnosed with early-stage breast cancer has a similar chance of survival as a woman without breast cancer (4). The relative 10-year survival of those with breast cancer in Sweden has increased from roughly 50% in the early 60s to more than 80% today (5). Even though it is debated whether breast cancer screening plays a direct role in better survival rates (6), early detection through screening mammograms and advances in treatment are seen as the major contributors to better survival (4). In 2017, 8,531 patients were diagnosed with invasive breast cancer in Sweden, of whom around 40% received adjuvant chemotherapy (7). Taxane-containing chemotherapy regimens are used in the treatment of breast cancer at various stages of the disease, and are among the most important means for improving disease-free survival and overall survival in early stage invasive breast cancer (8). Taxane-containing chemotherapy treatment results in a 13% relative reduction and 1.4-2.8% absolute reduction in breast cancer mortality. However, taxanes administered in moderate to high doses may cause various side effects, one of which is severe pain that interrupts the lifeworld of women receiving chemotherapy for breast cancer (9-11). In the Breast Cancer and Stress (BAS) study (12), a multicenter study investigating the effects of a stress management intervention, women in the intervention who had received taxane-chemotherapy often mentioned severe pain. This aroused our curiosity and prompted additional questions regarding the pain. After the amendment to the study was approved, by the ethical committee in Uppsala, we began including patients who had participated in Study I-III into this thesis. In this thesis, women's experiences of taxane-induced pain during chemotherapy were investigated, as well as nurses' perceptions of people with breast cancer experiencing taxane-induced pain.

# Breast cancer

## Diagnostic procedure

Breast cancer is detected when a woman discovers a lump in the breast or axilla herself, or through screening mammography, approximately half each. The diagnosis is confirmed through microscopic evaluation of a core needle biopsy or fine needle aspiration confirming the presence of malignant cells. A core needle biopsy is preferred as it allows for the subdivision of the cancer into subtypes based on histology (ductal or lobular), detection of the presence of prognostic/predictive receptors such as estrogen, progesterone and human epidermal growth factor receptor-2 (HER2) receptors, and evaluation of the proliferation rate. Breast cancer is mainly divided into three major subtypes: 1) endocrine-dependent (estrogen and/or progesterone receptor positive) 2) HER2 driven (HER2 positive); and 3) triple negative (lacking estrogen, progesterone and HER2 receptors). The largest group – endocrine-dependent – can be further subdivided into two groups depending on hormone receptor content and proliferation rate (luminal A and luminal B). After the breast cancer diagnosis has been confirmed, the breast lump is surgically removed and the local lymph nodes assessed to allow for tumor staging, according to tumor, node, and metastasis staging system (TNM) and further treatment decisions (5).

## Treatment of breast cancer

The primary treatment for breast cancer is surgery: either breast-conserving, whereby a part of the breast is removed, or mastectomy, whereby the entire breast is removed. Adjuvant chemotherapy is administered to patients with disease showing a less favorable prognosis, whereby systemic treatment may potentially improve the outcome, such as patients with large tumors (>2 cm) and/or metastases in the lymph nodes, as well as those with tumors that lack hormone receptors, overexpress HER2, or are highly proliferative. Adjuvant (or neoadjuvant) oncology treatment is a supplementary to surgery and can comprise of chemotherapy, antibodies, endocrine therapy, and radiotherapy; given before (neoadjuvant) or after surgery (adjuvant) (5). Patients with advanced spread to axillary lymph nodes, or otherwise high-risk patients, may receive higher doses of chemotherapy to increase their potential benefit from the treatment (13). Chemotherapy treatment is currently primarily provided in outpatient care settings, which is both cost-effective and efficient. However, in oncology outpatient care there is a risk of missing the identification of patient needs, including triaging for pain due to limited time with the caring staff (14, 15).

## Adjuvant taxane chemotherapy and pain

Sequential chemotherapy was introduced as the dosing regimen of choice in adjuvant chemotherapy in the 2000s. Sequential chemotherapy consists of backbones of anthracycline, such as epirubicin or doxorubicin, and taxanes, such as docetaxel or paclitaxel (9, 16). Taxanes are microtubule-stabilizing drugs that lead to altered mitosis and cell death. Docetaxel is a more water-soluble semi-synthetic analog of the taxane paclitaxel. Docetaxel is produced from the needles of the European yew tree (*Taxus baccata*) (17). However, this life-saving drug may induce severe pain; either peripheral neuropathy, described in the literature as “taxane-induced peripheral neuropathy” or “chemotherapy-induced peripheral neuropathy” (18) or as muscle and joint pain, described in the literature as the “taxane acute pain syndrome” (19), or as the “myalgia and arthralgia syndrome” (20). The clinical picture of taxane-induced peripheral neuropathy and chemotherapy-induced peripheral neuropathy is dominated by sensory signs and symptoms experienced as paresthesia and numbness in the hands and feet. Progressive neuropathy is accompanied by the paresthesia’s becoming painful and disabling, suggesting an impact on small unmyelinated nerve fibers (21). Typical pain characteristics of taxane acute pain syndrome and myalgia and arthralgia syndrome include myalgia and arthralgia, with the taxane acute pain syndrome the pain is occurring about 24–48 hours after taxane-based chemotherapy and lasting for 5–7 days (22). Furthermore, the occurrence of taxane-induced acute pain syndrome can predispose for subsequent chemotherapy-induced peripheral neuropathy (21). The incidence of taxane-induced muscle, joint and neuropathic pain is far from consistent in the literature (18, 19, 23). Saibil et al. reports the highest incidence of taxane-induced pain at 87% (22). There are likely several explanations for this variability in incidence: e.g., the dose and type of the regimen administered, study population and co-administrated supportive care treatments such as the use of growth colony-stimulating factors, which may themselves cause myalgia (24). Other factors explaining the differences in pain incidence include how the pain is estimated (the assessment tools used) and when in the chemotherapy cycle, how often (the timing) and by whom (the assessor) this is done (3, 24). Of importance are also limitations in the ability to prevent the onset of pain or reduce the pain (24, 25). Additionally, patients undergoing chemotherapy commonly deal with numerous side effects to the medication (21), of which pain is one. Adverse effects of chemotherapy may be underestimated, as patients may fear that reporting unfavorable symptoms could result in dose adjustments that may in turn result in less favorable treatment outcomes (26). Symptoms or side effects such as pain may seem affordable in light of the treatment effects, but in both the short and long term, the patient’s quality of life might be impaired due to untreated or poorly treated pain, affecting their daily life (26). Ultimately, it is the patient who suffers from pain during treatment as well as from any residual treatment-induced

pain. This pain might affect their everyday social life and overall well-being during treatment as well as their future life.

## Development of taxane-induced pain

The pathobiology behind taxane-induced pain is complex and only partly known. In chemotherapy-induced peripheral neuropathy and taxane-induced peripheral neuropathy by taxanes cause functional impairment in neurons mainly through oxidative stress, inflammation, apoptosis, and electrophysiological disturbances (27). Oxidative stress, generated by reactive oxygen species is associated with toxicity to, for example nerves in the peripheral system. Reactive oxygen species can damage neurons through demyelination, mitochondrial dysfunction, microtubular damage, and apoptosis. Reactive oxygen species affects the incidence of chemotherapy-induced peripheral neuropathy and subsequent pain through neuronal degeneration or small fiber neuropathy (27, 28). In mice, docetaxel upregulates the transient receptor potential ankyrin subtype 1 protein (TRPA1), which is believed to be responsible for mechanical allodynia (29), and it is suggested that the upregulation of TRPA1 may cause allodynia in humans. The pathobiology behind taxane acute pain syndrome and myalgia and arthralgia syndrome is unknown, but the pain mechanism suggests sensitization of nociceptors of the central nervous system (3). However, nociceptive mechanisms and the sensitization of the peripheral nervous system cannot be ruled out. The acute pain syndrome arising from paclitaxel is suspected to be a form of nerve pathology has been suggested as a form of neuropathy whereby patients with severe muscles and joint pain also seem to have substantial chemotherapy-induced peripheral neuropathy (30). Today, identified risk factors for developing chemotherapy-induced peripheral neuropathy and taxane-induced peripheral neuropathy with subsequent pain are prior or ongoing neuropathy, obesity, and genetic variations (28). Painful tissue injuries caused by substances other than taxanes may occur during the treatment, through a peripheral and central sensitization due to upregulated bidirectional signaling between, the neuron, glia and immune cells. Reactive oxygen species and reactive nitrogen species play key roles in the development of pain (31).

## Pain: an internal experience shared externally

### Pain definitions

Pain, initially seen as protective mechanism attracting our attention about a bodily threat, (32, 33) demands a response: physically by withdrawal and intellectually by identification of the source and reasons for the pain (32). A commonly used definition by The International Association for the Study of



Pain (34) is "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage," p 69. A broader definition of pain has been developed by Biro (2011) (35) who advocates a phenomenological approach to pain: "Pain is an all-consuming internal experience that threatens to destroy everything except itself and can only be described metaphorically," p109.

## The pain experience

The bottom-up phenomenon of pain (36), can be seen as a biopsychosocial process that begins with activity in a neuron. Pain can be described mainly in terms of 1) nociceptive pain, where nociceptors exist in varying degrees in all somatic tissues. 2) Or/and as neuropathic pain, initiated or caused by a primary lesion or dysfunction in the nervous system, which can arise without the stimulation of peripheral sensory endings in the nervous system (37). When nociceptors are stimulated, the pain sensation begins as a fast, well-localized A-delta activity followed by a more diffuse unmyelinated C-nerve fiber activity. The physiological nerve impulse is described below (38).

Pain results from the activation of a distributed group of structures in the brain, in which nociception is the process by which the nociceptors respond to pressure, heat, cold, and certain chemical stimuli. The nociceptors are a bidirectional signaling machine, consisting of free nerve endings associated with mainly myelinated A-delta and unmyelinated C-nerve fibers. When the nociceptors are stimulated, the pain sensation begins as a physiological nerve impulse from the activated tissue to the spinal cord and onward to the central nervous system (CNS). The cell bodies of the nociceptors, located in the dorsal-root ganglia (for the body), innervate their target organs and the spinal cord. All the nociceptive pathways *from the spinal cord* synapse in the thalamus on their way from cerebrum. The thalamus sorts information to the somatosensory cortex, where the sensory-discrimination aspects of pain such as its location, intensity, and duration are handled. The thalamus also interlinks with the limbic system, which participates in the affective-emotional aspect of pain, and the pre-frontal cortex, which is considered the *bee* an important area as it deals with the cognitive-evaluating dimensions of pain. Activation of these areas may intensify the perception of pain (39).

The pain impulse is then transmitted from the spinal cord *to the brain stem and thalamus* via two main *descending* inhibitory pathways: the spinothalamic pathway and the spinoparabrachial pathway. A major site for descending inhibitory pathways to the dorsal horn is the brain stem nucleus periaqueductal grey (PAG). In the PAG, nociceptive input is received from the dorsal horn and reciprocally connected to the hypothalamus, frontal cortex, and amygdala.

These regions in the brain are important for the control of emotions, particularly anxiety and fear, which might explain how emotions may modulate perceptions of pain (39).

A complementary view of pain is a “*top-down*” (36) view of pain a process shaped by experiences in the lifeworld as personality, expectations, and context and meaning (36). This is a population-based multilayer pain curriculum balancing a biomedical and cellular perspective of pain (40). The importance of this balance is described by Carr (2005) as it offers “... .. *an extended dialogue with disciplines in which a knowledge of narrative offers means for better understanding of the basic subjectivity of pain....*” p3, In Narrative, Pain And Suffering (41).

## Grasping pain in the lifeworld

The lifeworld is the world of the perceived lived experiences of humans (42). To perceive is a basic function through which people keep up to date on relevant aspects of their environment and their own relations to these aspects. The word perception has its etymological origin from the Latin word “*perceptio*” which encompasses occupation, perception, insight and perceives meaning (43). Humans are bodily in the world, and it is solely through their body in the world that they can perceive experience. These experiences provide the background from which all perceptions, actions and emotions are taken and assumed (44). A lived experience of pain can be phenomenological approached in terms of metaphors as argued by Biro, “*Pain is an all-consuming internal experience ... .. and can only be described metaphorically,*” p109 (35). To grasp pain in the lifeworld of people means to listen to and share the internal perceived experiences of pain as they are expressed in narratives. Where a primal fact of being a living human being is the capacity to experience pain, to be alive means to have a relationship with pain (45). The neurophysiological phenomenon of pain, as described above, begins as a *nociceptive activity* and is thereafter interpreted in CNS as a *sensory experience*, a pain (46). As a *sensory experience*, pain has a unique quality: it hurts (47). This feeling of pain is generally perceived in one’s own flesh, in contrast to the sensory experience of smell, for example, whereby one can enjoy or dislike the experience without thinking about it as an olfactory sensation (47). The bodily experienced sensation of a pain, evoking feelings: as a *sensation* presented somewhere in the body, as *emotions* about being in the lifeworld, and as *moods* that determine the way the world seems to us (48). Our mood and other feelings make us suffer. Moods induced by pain have the power to invade a person’s lifeworld and thereby arrest the past and future (48). Here, physical pain and imagination are closely linked despite their diametrically different starting points, with pain by its nature lacking object (objectlessness), contrary to the imagination, which is entirely its object (45). Imagination about pain can make

us suffer, and the suffering can be far more painful than the initial pain itself (49). Since imagination and memory can work together in one's consciousness, there is a risk that the pain will not be over even when it is over (49). When we face pain or want to understand it, we need to turn to all the sources that describe *the phenomenon*, not merely those from a medical scientific perspective. Among other things, pain involves medicine (46), nursing (50), psychosociology (51), ethics (52), philosophy (47), history (53), essays (54) and art (55). Most of all, pain is a personal experience – *a sense* – whereby healthcare professionals who want to make a difference need to listen intently to the story of the individual's perceived pain (56). They must be present, curious, and empathetic.

## The language of pain

In the present thesis, pain as a phenomenon has been captured in different ways. With a “top-down” perspective of pain, efforts and attention have been dedicated to communicating about the experience. Exploring experiences of pain through language is one of the most sensitive components in making them shareable. However, pain in itself has inherent properties that complicate communication about it. In part, the person who is in pain may have difficulty relating and describing what is happening in their body (57). While perceived pain can also be difficult to describe afterward, one of the most important facts regarding pain is that its existence can be neither confirmed nor denied (45, 58). However, language, as the most common way of sharing a pain experience, has limitations when it comes to pain (57, 58). This has to do with the awareness of the “inner state” of things, whereby consciousness follows naturally on what is experienced in the world. For example, the feeling of sorrow is one that targets someone or something. This also applies to other emotional, perceptual, and somatic states that have or take their object: we are pleased, happy, or in love with a person or phenomenon. When it comes to pain, something happens, unlike any other state of consciousness; pain has no referenced content (45). Thus, attempts to invent linguistic structures to define pain in words, by forcing it to become an object that we then try to assess, is a project fraught with consequences (45). The vocabulary of pain is narrow and limited, and contains only a small number of adjectives for describing the pain. Descriptions of pain often cover what it feels *as if* or *is like* (45). The expression of pain contains both the objectified felt characteristics of the pain and the visible referents for these characteristics. Instead of using the narrow, limited adjectives for pain, descriptions are often made using an external agent, a metaphor (45). This agent can make the pain visible by lifting the pain experience out of the body. Here, the metaphor enables us to make the attributes of pain visible and communicable. For example: “*It was as though it was burning inside my body*”. Through the metaphor, an experience of pain can be under-

stood with reference to something else (59). The metaphor creates perspectives of pain and generates meaning, and makes the pain visible and to some extent shareable (59).

The metaphor has strength, a built-in “fuzziness” that enables new metaphors as well as new interpretations to arise (59). A metaphor’s usability may be limited if it pinions the patient into a constricted interpretation of pain. However, the fact that pain experiences are described and communicated using interpretations might qualify the metaphor as the only reasonable way to communicate about pain. Elaine Scarry (1985) argues that the ontological gap between pain as it is experienced and the pain that is observed by health professionals calls into question the very existence of pain (45). This means that for those who have pain nothing is more real, while to the observer it is invisible. Therefore, communication about pain is fragile. An important skill involved with this communication is the ability to make pain visible; to have the courage and desire to truly “see”, and not turn away from what takes shape (60). Crucial is also, what the listener choose to do with the story, which can make differences for the person in pain (61). Another important skill is to listening, to have an open ear and mind in efforts to understand and capture meaning in the communication process (57). A good start is to invite the patient to a "patient-centered communication" an equal communication that takes places in a warm, genuine and empathetic atmosphere. Here, the patient is the center of attention and an equal partner in the nurse’s concern (62). Here the patient's story can take shape, and thereby exercise its full power and ability to relieve pain (56).

## Theoretical framework

### Pain, phenomenology and lifeworld research

Pain is a phenomenon, and in the study of pain, phenomenology offers a broad approach to the subject. The study of essences is the foundation of phenomenology research (44). This could be about the perception of time, bodily presence in world, relations to the world, and other things (44). Phenomenology is also a philosophy putting essence back into existence, offering an account for body, time, space, and relationships. Phenomenology exploration is only reachable through phenomenological methods (44). Phenomenological research explores the lived experiences in the lifeworld, and is a human scientific study of phenomena, as they present themselves to human consciousness (44). The lifeworld is the world of lived experiences, whereby phenomenology explores and asks questions about the nature or meaning of phenomena (30). As humans, our conscious is inseparably connected to the world we experience; in phenomenology, this is called intentionality. Intentionality is only

available retrospectively, as reflection is necessary for a perceived reflected experience (42). As phenomenology requires phenomenological methods one way is to go through pedagogue and researcher Max van Manen (1990) (42). Van Manen has operationalized lived experiences into “the lifeworld perspective,” comprising four human existentials: 1) the *lived body*, which is subjective, including time, space, and past, and present experiences directed toward the future. The lived body covers all the aspects of life simultaneously: physical, psychological, relational, and existential. Every change in the body involves a change in life (63). The body is the point of departure of all dimensions of the world, and also the pregnancy of possibilities (42, 44). 2) *Lived time* is our temporal way of being in the world. Time acquires a history whereby my experiences are represented in the present, and the past and present are orientated to the future. Time incorporates a continuum through which “*The past changes itself because we live toward a future which we already see taking shape, p 104* (van Manen 1990) (42). This future time can contain possibilities such as relief, and is treated as limited time (64). 3) *Lived others*, which are links made to others, create the interpersonal space shared with other people. As Merleau Ponty states, “*We are the network of relationships*” preface xxiii (42, 44). 4) *Lived space* is the landscape that affects and surrounds us, in which the positions of things and ourselves become possible. The lifeworld is the space where I exist and constantly create and re-create alone and together with others (44, 65).

## Rationale

In 2005, taxanes were added to the adjuvant arsenal in the treatment of early-stage invasive breast cancer. At that time, women receiving adjuvant treatment with taxanes also reported pain to their clinical nurses administering this treatment. Participants in the BAS-study (12) being treated with taxanes also described pain. A search in the literature revealed virtually no reports describing pain during taxane chemotherapy; only some contradictory data on the incidence of taxane-induced pain (11). In addition, none of the studies said anything about the burden of pain, as experienced by the patients. This is an important topic, given the rising number of long-term survivors of breast cancer, highlighted by others, for instance Kautio et al. (2011) and Pachman et al. (2011) (66, 67). The discrepancy between a low incidence of taxane-induced pain in clinical studies (68) and the women’s experience of pain during taxane chemotherapy, described by them as very painful, warranted further evaluation. The rationale for this thesis is to describe and explore the subjective burden of taxane-induced pain and longstanding pain in the lifeworld of women diagnosed with breast cancer. To gain a deeper understanding of the pain experiences and to make the pain visible, different methods are used in order to capture the ontological gap between pain as it is experienced by the patients

and as it is observed by health professionals. To highlight the importance of both hearing and listening for pain, the experiences of both the patients the nurses administering the taxanes are explored.

# Aims

The overall aim was to explore women's acute and longstanding experiences of taxane-induced pain, and to evaluate the pain intensity and distribution using different assessment methods. An additional aim was to study nurses' perceived experiences of taxane-induced pain in people with breast cancer.

## Specific aims

### **Study I**

To describe a variety of perceptions, using three different methods, regarding the impact of adjuvant chemotherapy-induced pain on the daily lives of women with newly diagnosed breast cancer.

### **Study II**

To explore the memories of chemotherapy-induced pain and experienced longstanding overall pain in the lifeworld of women with prior adjuvant chemotherapy for breast cancer.

### **Study III**

To document pain reported by women during and after adjuvant chemotherapy (taxanes/anthracyclines) following breast cancer using three different methods: (1) the visual analogue scale (VAS), (2) a colored body image, and (3) the two pain questions included in the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-QLQ-C30).

### **Study IV**

To study nurses' perceived experience of the occurrence of taxane-induced pain in people being treated for breast cancer, and their experienced and identified organizational support for handling pain in people being treated with taxanes for breast cancer.

# Methods

## The Breast Cancer and Stress (BAS) study

The BAS-study (12) is a multicenter study investigating effects of a stress management intervention. The participants were women recently diagnosed with breast cancer over the age of 18 and scheduled for adjuvant treatment in the form of chemotherapy and/or radiation therapy and/or hormonal therapy. The patients were recruited from three hospitals in central Sweden (Uppsala, Gävle, and Falun). Exclusion criteria included an ongoing psychiatric condition or linguistic deficiencies in Swedish (12). According to the inclusion criteria, 821 patients were asked to participate in the BAS study from May 2009 to August 2011. Of these, 372 declined participation, resulting in a total sample of 449 patients. From September 2010 to August 2011, 57 women from the BAS-study were consecutively asked to participate in a sub-study of chemotherapy-induced pain. These 57 women are the participants in Study (I-III) in present thesis.

## Design

Study I and II are explorative qualitative studies and Study III is a longitudinal study measuring pain with different methods at two time points. Study IV is a cross-sectional observational study. An overview of the included studies is presented in Table 1.



Table 1. Overview of included studies

<b>Study design</b>	<b>Data collection</b>	<b>Study sample</b>	<b>Analyses</b>	<b>Time point</b>
I. Explorative qualitative	Semi-structured interviews, Body Image, VAS	n = 16	Inspired by phenomenography	During chemotherapy
II. Explorative qualitative follow-up	Semi-structured interviews	n = 15	Phenomenology, lifeworld perspective	12 months after inclusion
III. Longitudinal	EORTC QLQ-C30, Body Image, VAS	n = 53	Descriptive statistics	During chemotherapy and 12 months after inclusion
IV. Cross-sectional	Questionnaire	n = 161	Descriptive statistics, logistic regression	November 2017 to May 2018

## Participants and procedures

The mean age of the 57 women participating in the studies (I-III) was 53 years. With the exception of one woman, 56 women estimated a VAS score < 1 prior to starting chemotherapy. A nurse or research assistant performed verbal and written information, before the first assessment. Including information on how to use the VAS 1) How to perform the estimates, 2) the function of the VAS, and then 3) for each cycle of the treatment the timing of measurements. The VAS estimates made were filled out at home and then mailed to the researcher, after each cycle of treatment. The EORTC-QLQ-C30 along with a prepaid return envelope, was mailed to the women (n=57), after inclusion; i.e., at baseline at the beginning of the adjuvant chemotherapy treatment, three months after inclusion (i.e. between Cycles 3 and 4 of their chemotherapy treatment), and finally 12 months after inclusion. A maximum of three reminders were sent out if applicable. For a more detailed description of the participants in study I-III, see Table 5.

In study IV, 240 nurses working in outpatient units in Swede, delivering chemotherapy to cancer patients were invited. After permission from the Medical Director and the Head of the respective clinic, the nurses were sent a personal e-mail invitation with a link to the web survey and an attached infor-

mation letter. The information letter described the background, purpose, ethical aspects as well as procedure for management of data. The nurses were informed that participation in the study was voluntary and that informed consent arose when the questionnaire was submitted. Two reminders were sent to non-responders within a period of 2 months.

## Study I

In Study 1, the inclusion values of pain were estimated on the VAS, where the woman made a cross on a straight line, between the points, no pain - worst possible pain. When the pain assessments thereafter is communicated and interpreted, this was done on a scale ranging from 0-10, as a numeric rating scale. This because a scale of 0-100 does not fill any function in this qualitative context. The VAS and the numeric rating scale have proven to be even estimating pain in a clinic context (69, 70). Inclusion criteria in Study I was pain scores on VAS  $\geq 4$  at one or several courses of sequential chemotherapy in doses of  $\geq 75\text{mg}/\text{m}^2$  of docetaxel/epirubicin. VAS  $\geq 4$  in Study I, is seen as ranging from moderate-severe pain similar to VAS  $> 40$ , as described by Breivik (70). A total of 22, (38%) women fulfilled the inclusion criteria. Pain was measured prior to treatment, before each cycle and at Day 10 between two cycles; repeated for each cycle, no.1-6.

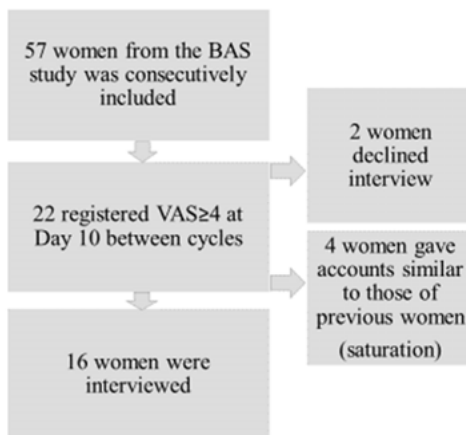


Figure 1. Flow chart

Sixteen of the 22 women participated in an interview; two women declined interview due emergency surgery or experiencing other symptoms related to high-dose chemotherapy. Four of the women gave accounts over the telephone that were similar to those of previously interviewed participants and hence the

data were considered to be saturated; see Figure 1. The 16 women were interviewed approximately three weeks after pain had appeared. The interviews consist of 13 hours of recorded interview material, distributed among the women. The shortest interview lasted 22 minutes and the longest 1.5 hours. At the time of the interview, the women colored the body image (described in the measurement section below); this was done at any time during the chemotherapy cycles. The women in the study reported that prior to treatment they had been socially active in either their careers or their spare time, or both, and all had participated in some form of physical activity. Eight women reported that they had experienced pain previous in their lives because of scoliosis, osteoarthritis, migraine, neck and back problems, muscle inflammation, or neuropathic pain. However, with the exception of 1 woman, all ( $n = 22$ ) estimated a VAS of less than 1 prior to starting their first course of chemotherapy. One interviewed woman was later a subject of the intensive stress intervention in which the interviewer acted as a group leader. At that time, a first interview was conducted. The interviewer was a female nurse with experience of cancer care. At the first interview, the interviewer requested permission to contact the participants again a year later. The interviewer did not take part of the women's care.

## Study II

The participants in Study II were the same women with completed chemotherapy who had participated in Study I. They were phoned, 12 months after inclusion by the interviewer, and asked if they would like to participate in a second interview. The interviews were conducted from September 1, 2011, to August 31, 2012. Meanwhile, one woman had died from her breast cancer, resulting in 15 women being interviewed again. The second interview consists of 11 hours of recorded interview material, distributed among the 15 women. The shortest interview lasted 27 minutes and the longest 61 minutes. The specific time point was chosen because previous research has shown that women are still under stress at this point, even if their lives, from a caring perspective, seem to have returned to normal (71).

## Study III

In Study III all 57 women were included, four did not complete the VAS assessments or EORTC-C30-QLQ questionnaire. This resulted in 53 women being included. Clinical and demographic information was collected from the women's health records and inclusion forms. In Study III, the cut-off value on the VAS was changed to  $>30$ . This cut-off is according to Breivik above mild pain (70). Only the participants with VAS  $>30$ , who had been interviewed in study I ( $n = 16$ ), filled out the colored body image during chemotherapy and twelve months after inclusion ( $n = 15$ ). Meanwhile one woman had died from

her breast cancer. The participants reporting VAS >30 colored the body image approximately 3 weeks after the pain appeared at any time during chemotherapy (Cycles 1-5), and then again at 12 months after inclusion. A maximum of three reminders were sent out if applicable.

## Study IV

Nurses (N=240) working in outpatient units in Sweden, delivering chemotherapy to cancer patients, and n=161 completed a questionnaire about taxane-induced pain in people with breast cancer. Permission were received from the medical director and the head of the respective clinic. The nurses received a personal email invitation with a link to the web survey. In the invitation was an attached information letter describing the background, purpose, ethical aspects as well as procedure for management of data. The participants was informed of the voluntary participation in the study and that informed consent was required when the questionnaire was submitted. Within a period of 2 months, two reminders were sent to non-responders. Answered questionnaire rewarded a cinema ticket.

## Measurements

### *The visual analogue scale (VAS) (Studies I, III)*

The VAS scale comprises a straight line, on which the patient is asked to make a mark reflecting the intensity of the perceived pain. The response levels, from no pain (0) to the worst possible experienced pain (100), are measured in mm. In this study, pain intensity on the VAS is defined according to Breivik as mild pain at 10/100 to 30/100, moderate pain at 40/100 to 60/100, and finally severe pain at 70/100 to 100/100 (70). The VAS is an acknowledged and frequently used instrument for assessing pain (70). The correlation of the VAS and other self-reported measures of pain intensity is high (69, 72). The VAS cut-offs for pain e.g. as mild, moderate or severe pain, varies (70, 73, 74). In present study the cut-offs suggested by Breivik et al. were used (70).

### *Interview guides, Studies I and II*

Two interview guides developed, are presented in Table 2.

Table 2. Interview guides, Studies I and II

#### *Study I*

---

Previous pain problem(s)?

If yes, has the pain gotten worse?

Description of perceived pain, physical dimension; e.g., Can you describe the experience of pain you perceived in your body?

Description of perceived pain, psychosocial dimension (existential dimension); e.g., Can you describe the thoughts you experienced when you were in pain?

Description of the impact of pain; i.e., What did pain prevent you from doing? Physical/psychosocial dimension, e.g., Can you describe a day without chemotherapy-induced pain? Can you describe a day with chemotherapy-induced pain?

Illustration on body image and VAS, level of pain experienced.

#### *Study II*

---

Can you tell me how you feel, and what you think about life right now?

Can you tell me about work and social life today?

Can you describe how your body is right now?

If you have pain, can you describe how the pain turns up in your mind, thoughts and social life?

Do you remember how your body reacted during the treatments? Can you describe these memories?

Can you describe your reactions to the treatment at that time, and how your reactions affected your mind, thoughts and social life?

*The women were invited to speak freely about their experiences and were encouraged to provide specific examples.*

### *The body image, study I and III*

The body image technique was used, see figure 2. In study I was the colors of the body image interpreted qualitatively and in study III to describe the distribution and intensity of perceived pain. The colored body image is a technique where the patient first marks the localization and distribution of pain and thereafter colors its intensity (75). The distribution is reported as percentages

of the total body image area (76) and the pain intensity is reported semi-quantitatively on a four-level scale using the colors of a traffic light, with an additional high-end intensity shown in black. The perceived pain intensity was indicated by green for no pain, yellow for tolerable pain (i.e. daily life was not impaired and the woman could continue going about her daily routines), red for interruptive pain (i.e. daily life and ordinary routines were substantially affected or stopped due to experienced pain) and, additionally, black for unbearable and excruciating pain (33). The colored surface areas can overlap, and in such cases the most dominant color was used in the analysis. The proportion of the total surface area of the body is estimated to be: head and neck 9%, arms 9% each, back and front sides of the upper body 18% each, legs 18% each, and genitals 1%. The colored body image is presented as an average of the percentage of the total body image area of the women's worst experienced pain. The model used for analyzing the colored body image was the Rule of Nines burn area charts (77, 78). However, in this thesis the "colored body image" is used to depict the distribution and intensity of the perceived pain.

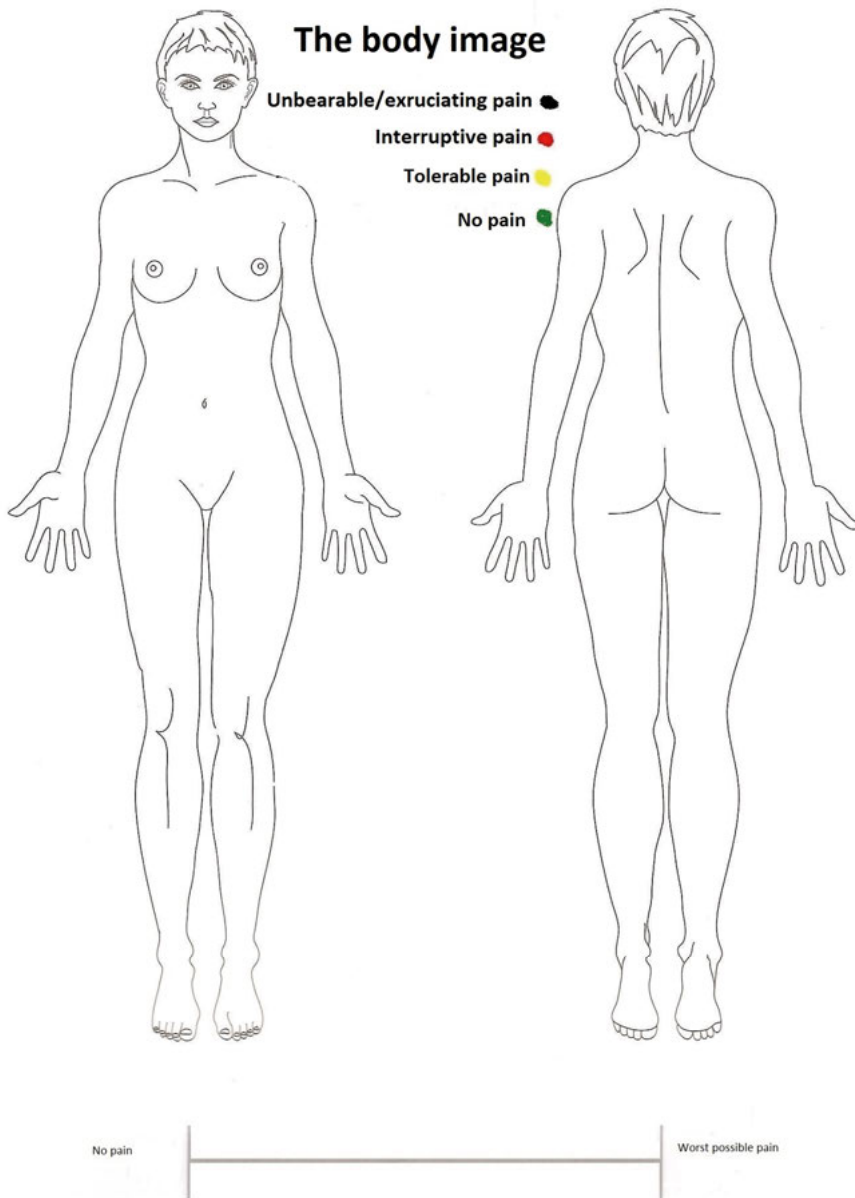


Figure 2. The body image

*The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-QLQ-C30), Study III*

The EORTC-QLQ-C30 version 3.0 is a cancer-specific self-reported multidimensional instrument, translated into and validated in different languages, and applied across a range of cultural settings (79). Of 30 items, assessing function and various symptoms, two questions are assessing pain and are used in this study. The time perspective in the questions concerns the past week and the questions used in this study were, *Have you been in pain?* and *Have your daily activities been affected by pain?* Higher scores on the questionnaire represent higher symptom burden. The response choices range from 1 (not at all) to 4 (very much); these values are converted through a linear transformation of the raw scores and applied to obtain scores of 0–100 (80).

*The questionnaire Study IV*

This study was developed based on views of the women from Studies I and II and the results from Study III. The women described a frequent, very intense pain distributed on large areas of the body (33, 81, 82). Nine nurses at an oncology day care unit contributed by testing a draft of the questionnaire “Nurses’ perceived experiences of taxane-induced pain among breast cancer patients.” With five of the nurses, the questionnaire was discussed through a “think aloud” procedure (83). The other four nurses provided viewpoints and written comments, and the results from the “think aloud” as well as these comments were used to revise the questionnaire. Finally, the questionnaire was discussed at a research seminar with both senior and junior researchers before the final version was established.

Regarding the questions and response levels in the questionnaire, the areas covered are: demographic data; nurses’ perceived experiences of the incidence, intensity and duration of pain; nurses’ perceived experiences of the treatment and prevention of pain; and nurses’ knowledge of and experienced patient satisfaction and supportive features – see Table 3. The main response levels are set with help from the VAS scale, (see Studies I and III). The VAS in the questionnaire constitutes a straight line from 0 to 100 mm (74) on which the respondents were asked to make a mark on the line according to the response level whereby 0 equals “never occurs/not at all/no pain at all” and 100 equals “always occurs/always/worst possible pain.” Other response levels were Likert scales or yes, no, don’t know; see Table 3. The questionnaire consisted of 34 questions and took approximately nine minutes to complete.



Table 3. Summary of the questionnaire

	<i>Number of Questions</i>	<i>Data level</i>
Demographic data	3	Sex, age and workplace
Education	1	Oncology specialist education, other specialist education
Work experience	2	Years
Incidence	1	VAS
Intensity	2	VAS
Distribution, comprising: head and neck, arms and hands, front trunk, back trunk, legs and feet, joints, muscles, and skeleton	1	Five permanent options: don't know, not at all likely, probably to some extent, quite likely, most likely
Percent of the body involved in pain	2	Five permanent options: don't know, 0-27%, 28-54%, 55-72%, 73-100%
Estimated day when the pain starts and the day when the pain declines	2	Numbers
Caring model as contact nurses and person-centered care	1	Three permanent options Yes/No/Don't know
Information and communication	2	VAS
Local guidelines and shared available documents	2	Three permanent options Yes/No/Don't know
National guidelines and shared available documents	2	Three permanent options
Regular ordered premedication during treatment such as for nausea	1	Three permanent options Yes/No/Don't know
Regular ordered premedication against pain to take at home such as for nausea	1	Three permanent options Yes/No/Don't know
Whether the patient receives premedication to take at home	1	VAS
In case of pain, how well does received pain treatment work	1	VAS
I know how to help patients with taxane-induced pain	1	VAS
I have the knowledge I need to be able to help patients with taxane-induced pain	1	VAS
I'm supported by local instructions in managing taxane-induced pain	1	VAS
I'm supported within my team in managing taxane-induced pain	1	VAS
I experience that the patients are pleased with pain control in case of taxane-induced pain	1	VAS
I experience that the patients feel safe with advice in case of taxane-induced pain	1	VAS
Open questions (This is effective, I need this, and Other)	3	

# Data analysis

## Study I

The data analysis, inspired by phenomenography, began with a verbatim transcription of the interviews. Thereafter, the ongoing analysis was discussed with the coauthors and at research seminars. The focus of the analysis was to capture experienced pain perceptions, assessed through triangulation: interview, body image, and VAS, with regard to chemotherapy-induced pain. First, the interviews were analyzed in stepwise manner as described by Larsson (84) and Larsson and Holmström (85). Firstly,

- a) Interviews were read through several times in their entirety to get an overview of the women's opinion of the pain experienced.
- b) Answers to the interview questions were examined by identifying the significant perception of pain as indicated in the text.
- c) Central components of experienced pain were identified by looking for similarities and differences between perceptions at an individual level and then in all interviews.
- d) When the experienced pain perceptions displayed qualitative similarities, they were grouped into a category.
- e) Categories were compared and combined, resulting in the formation of the final three categories of perceived pain.
- f) The categories of pain were analyzed and arranged hierarchically based on the differences and unique descriptions of each category, and the central components were arranged horizontally, see table 4.

Secondly, a visual analysis was performed based on the body image colorings, which explored the distribution and intensity of pain in the body. The analysis was based on how much of the body was colored and which colors were chosen. The body images were then categorized based on the VAS estimates and interviews. Third, the pain assessments on the VAS that explored pain intensity were first ranked with numerical values and were thereafter categorized based on the body image colorings and interviews. The descriptive categories were defined as (1) manageable pain, (2) pain beyond imagination, and (3) crippling pain. These descriptive categories were formed from the women's perceived perception of pain as captured in the interviews, their coloring of the body image and their VAS estimations as described previously.

## Study II

The interviews were recorded digitally and transcribed verbatim. The results were analyzed through guided reflection as described by van Manen (42, 86). The interviewer made a first tentative analysis. After this, a part of the interview material was jointly analysed by two of the members in the research group. Thereafter, the same part was analysed by the other two members in the same research group, this to obtain congruence. Continuing, the interviews were read several times and categorized into 4 fundamental existentials lived: body, time, space, and other (42). Each existential was divided into past, present, and future perspectives. To achieve a main structure in the material, the themes in each perspective for all interviews were compared and combined. The essential qualities of the theme aspects were identified and presented in a phenomenological description of chemotherapy-induced pain, as experienced in the women's lifeworld.

Pre-understanding, ie, beliefs, assumptions and knowledge, has been actively taken into account throughout the entire research process in study I and II.

## Study III

The data on background characteristics and disease characteristics were analyzed using descriptive statistics such as means, standard deviations (SD) and frequencies. Mean and SD values are presented for the VAS and the EORTC-QLQC30's two pain questions' estimates. The colored body image charts were analyzed according to the following procedure: estimated pain distribution using the Rule of Nines burn area charts as the as the percentages of the total body image area colored (76). Pain distribution and intensity were analyzed based on the colors used (77). For example, areas colored red on the left arm were summed and then divided by the number of participants. Thereby, the average area with pain intensity colored red on the arm was calculated.

## Study IV

Data on background characteristics as age education and work experiences were analyzed using descriptive statistics such as means, SD and frequencies. Mean and SD were presented for the VAS-assessed questions. Bodily pain areas, pain distribution and pain onset and decline were presented as percentages so were the six questions of systematic approach to counteract taxane-induced. Associations between nurse characteristics (nurse age, -work experience in oncology care, -specialist education in oncology) and their perceived predicted prevalence and intensity of taxane-induced pain was investigated by a bivariate logistic regression. The cut off for the dependent variable "occurrence of pain" were set to a mean value  $\geq 49$ , the cut off for "occurred pain

intensity” were set to a mean value  $\geq 60$ . The selected cut-off value is supported by the literature, “occurrence of pain” (19) and so are the cut off for “occurred pain intensity” (20). The findings are reported as odds ratio with 95% confidence intervals (CI) with  $p < 0.05$  for statistical significance, the collinearity was examined and the outcome of each variable was checked.

## Ethical considerations

The BAS project was reviewed by the ‘the Ethical Committee of Uppsala’ and was approved March 25, 2009, Dnr. ma 2008/382; and the sections containing Studies I-III, through an amendment, that was approved in May 2010. All approved women were given oral and written information on the studies prior to participation. The women were informed that they could withdraw from study participation at any time without giving a reason, and that participation was voluntary. Study IV was approved by the Ethical Committee of Uppsala (Dnr. 2017/340). All participating nurses were given written information on the study prior to their participation. They were informed that they could withdraw from study participation at any time without giving a reason, and that participation was voluntary. The risks and burdens concerning the approached participants (Studies I-IV) were estimated in relation to the importance of the studies’ outcomes, according to World Medical Association, Declaration of Helsinki (87) and for Studies I-III also according to the Patient Act (75).

In Studies I-II, permission to record the interviews was obtained before each interview. In the interviews, one of the ethical questions concerns the balance of power that may arise between interviewer and interviewee through movements between closeness and distance during the interview. The interviewer might push the interviewee to share experiences beyond what the interviewee actually intends to communicate (88). Another question is whether the second interview could bring up past memories of chemotherapy-induced pain, thereby increasing the woman’s vulnerability. However, during the interviews the women quickly recognized and began to talk about their past and present experiences of pain. They seemed to confirm their memories, as if they and the interviewer shared common experiences. The women were positive to a second interview. They were also urged to contact the interviewer again if any questions arose afterward that they wanted to share or clarify. During the interview, the interviewer tried to show all appropriate respect for the interviewee as a person and according to the situation. The interviews were also carried out in a non-judgmental and empathetic manner. They were also conducted with sensitivity to the different women’s inequality and vulnerability (89).

# Results

## Study I

Three qualitatively different variations of the women's perception of chemotherapy-induced pain were found and categorized. This based on participants interviews, their colored body images and the VAS estimates, see Table 4. Firstly, in *Category A*, reflected the women who describe a tolerable pain were that they could manage the pain. The pain is congruent with received information and previous pain experiences. Their body image colored is predominantly covered with, green, yellow and some red. The assessed pain on the VAS range from 5-8.5. The pain continues from 3-7 days. Thought the pain caused anger, irritation, frustration, and stress the pain has only small to moderate impact on daily life.

We extended the period with corticosteroids and stepped

it down during several days. I also took Tramadol,

anti-inflammatory painkillers, and paracetamol; it all

worked well. (Woman 6), p35, Cancer Nursing, Vol. 33, No 1, 2015

Secondly, in *Category B*, was a more complex and debilitating pain were the women's ability to manage pain is faltering. The pain is beyond received information and previous pain experiences. The body images colored with, some green, yellow-red and black. The assessed pain on the VAS range from 6-10. The pain continues from 2-10 days. Thought the pain caused dark thoughts, fear, anger, irritability, uncertainty, and helplessness the pain has moderate to strong impact on daily life. Making the women withdraw and they are in need of some help with daily life for some days.

The painkillers did not help at first, but then I realized if

I took the weaker painkiller in between the stronger

ones, then it got better, but until I understood that.”

(Woman 10), p36, Cancer Nursing, Vol. 33, No 1, 2015

Thirdly, in *Category C*, highly complex and challenging pain were the pain is difficult to manage. The pain is far beyond information and previous pain experiences. The women questioned whether they would survive; the body images colored predominantly or partly with yellow-red and black. The assessed pain on the VAS range from 9-10. The pain continues from 0-17 days. The pain cause feelings like fear, desperation, uncertainty, helplessness, and feelings of being seriously ill. The women become isolated and reclusive some days they were unable to manage daily life of their one.

Then I received morphine pills. I started taking them on

Monday evening, but they only took away the 10th

grade on a VAS scale. (Woman 11), p36, *Cancer Nursing*, Vol. 33, No 1, 2015

However, there were also body images that were predominantly colored green but with the legs colored black; this pain was described as unbearable. Despite the severe pain and insufficient pain relief, some women in the two last categories kept struggling at home without contacting the health care services. Intensity and duration in all three categories was described as most intense 3-7 days after treatment. The worst pain developed mainly after the first course. For some women, pain remained after each course of therapy. A reduction in the chemotherapy dosage for the subsequent course occurred for women in Categories A and C. The pain primarily related to the sequence with docetaxel, however, some women develop and experienced worsening pain during the epirubicin-sequence. When the pain did subside, some of the women in *Category A* reported positive reactions to the pain experience. The pain signaled that the treatment had worked.

Table 4. Categories and central components of the pain experience\*

<b>Pain in:</b>	<b>Category A Manageable</b>	<b>Category B Beyond imagination</b>	<b>Category C Crippling</b>
<i>Manageability</i>	Good	Faltering	Nonexistent
<i>Information and experiences</i>	The pain is congruent with received information and previous pain	The pain is beyond received information and previous pain experiences	The pain is far beyond received information and previous pain experiences
<i>Emotions</i>	Anger, irritation, frustration, and stress	Dark thoughts, fear, anger, irritability, uncertainty, and helplessness	Fear, desperation, uncertainty and helplessness, feelings of being ‘‘seriously ill’’
<i>Social life and self-care</i>	Small to moderate impact, manages daily life	Moderate to strong impact, withdrawal, needs some help with daily life	Isolated and reclusive. Some days, unable to manage daily life on their own
<i>Pain quality</i>	Dull, nagging, pulling, a stiffness	Bunching, pressing, squeezing	Pushing, burning, bunching, pressing, squeezing
<i>Duration, days after treatment</i>	3-7	2-10	0-17
<i>Pain distribution</i>	Joints and larger muscles	Joints, back, legs, stomach, head, and large muscles	The whole body, or parts such as joints, back, legs, stomach, the skeleton, and large muscles
<i>Worst experienced pain intensity, VAS</i>	5-8.5	6-10	9-10
<i>Confidence in the future</i>	Unchanged	Affected	Faltering, partly broken

\* Categories based on interviews, colored body images, and VAS estimates

## Study II

Twelve months after chemotherapy treatment, the women described their past, present and future experiences of chemotherapy-induced pain. The pain experiences were perceived in the women’s *bodies*, affected their *time perception*, influenced their *relationships*, and made them more aware of *being in the world*.

*Past*, during chemotherapy, the bodily experience of pain was often described in metaphors, leading to dramatic changes in the lifeworld. Time was perceived as periodic, and the women became entirely dependent on others at the same time as the pain made them withdrawn, increasingly isolated, and alone.

Existential pain was described as a feeling of being completely vulnerable and alone with thoughts of annihilation.

*Present*, signals of bodily pain often incorporate the same parts of the body as during chemotherapy. The pain intensity was lower, but made the women perceive time in a more conscious way, with an experience of a higher present “here and now”. Expectations of returning to an unperceived normality complicated and affected their social life, in both private and formal relationships. The women described a painful existence in-between health and illness.

*Future*, the women expressed beliefs that some bodily pain would remain and continue to remind them of time and their insecure future. They were not fully aware of whom to turn to if they needed to talk about their pain experiences. A painful and increased vulnerability arose, contributing to an awareness of their own fragile existence as well as that of other significant people in their lives. Finally, they experienced a fragile trust in being and a growing acceptance that this fragility is among life’s premises:

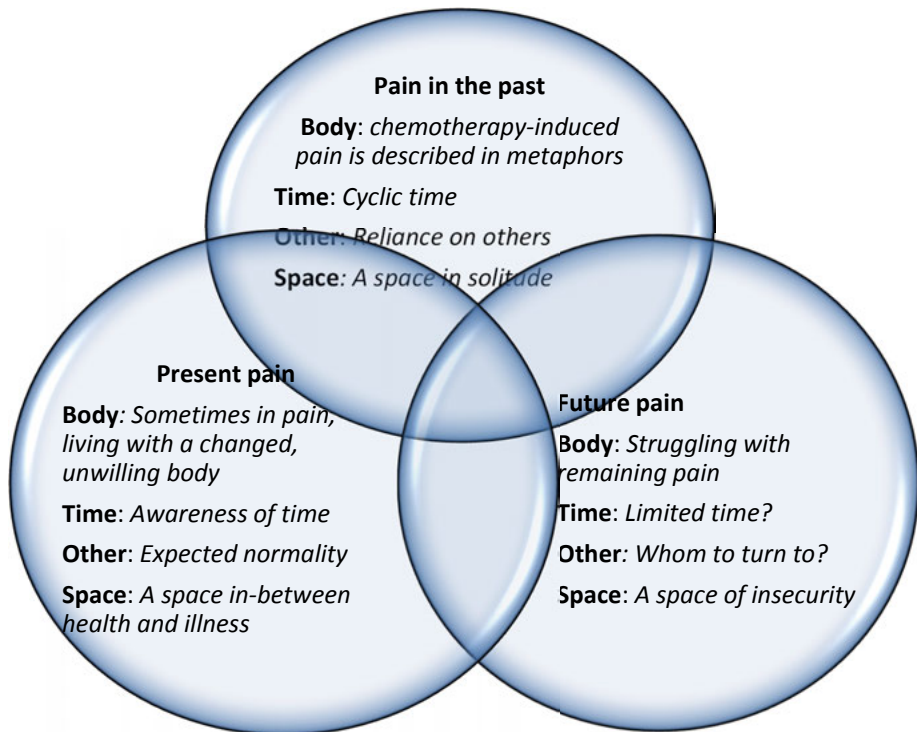


Figure 3. The four existentials and pain from past present and, future perspectives



## Study III

For the demographics of the participants in Study III, see Table 5. A widespread, intense pain was detected using a multi-method approach. The colored body image showed pain being perceived on 51% of the body surface area during treatment. At that time was the pain intensity of the body image areas colored red (interruptive pain) the most common, covering 25% of the total body surface area, followed by the body image areas colored yellow (acceptable pain) covering 20%, and finally, the body image areas colored black (excruciating pain), which covered 6%. Body areas involved in pain was most commonly the lower back, knees, thighs and footpads. Twelve-months after inclusion the colored pain distribution of the total body area was 18%. At this time point the pain intensity, colored yellow (acceptable pain) was the most common with 13% of the total body area colored. For the pain intensity colored red (interruptive pain), was the total colored area 4.5%. Traces of black (excruciating pain) 0.2%, were noted on the upper front of the trunk, while the largest part of the body image area, 82%, was colored green and was thus painless. Body areas involved in pain was most commonly the trunk, the legs and feet, arms and hands and the head. In general, the pain on the VAS started and peaked in intensity after the first cycle of taxane. After Cycle 3, most women reported an increase in pain on the VAS. Some women continued to report some pain even during the epirubicin cycles. The VAS scores dropped after the last chemotherapy cycle, but not to the baseline level. At baseline, three months and 12 months after inclusion, the women who estimated VAS >30 reported higher levels of pain on the pain questions of the EORTC-QLQ-C30.

Table 5. Participant characteristics

<b>Demographics</b>	<b>VAS &gt; 30 (n=25)</b>	<b>VAS ≤ 30 (n=28)*</b>
Age, median, range	57 (37-76)	49 (29-73)
Mean VAS at baseline (SD)	1.16 (2.14)	0.357 (0.55)
Annual household income (EUR), mean	359,000	477,000
Working	17	14
Retired	7	4
On sick leave	15	26
<b>Residential area</b>		
Dalarna	5	8
Gävleborg	14	6
Uppsala	6	14
<b>Type of surgery</b>		
Breast-conserving surgery	11	12
Mastectomy	14	14
<b>Hormone receptor status</b>		
ER+/PR+	14	13
ER+/PR-	6	2
ER-/PR+	-	1
ER-/PR-	4	10
Her2 amplified	7	7
Triple negative	3	6
Not evaluable	1	2
<b>Tumor grade</b>		
I	2	2
II	13	9
III	9	13
Not evaluable	1	2
<b>Sequential taxanes/epirubicin</b>	25	28
Radiation	15 (missing 0)**	17 (missing 3)**
Endocrine therapy	20 (missing 3)**	18 (missing 4)**

Abbreviations: ER estrogen receptor; PR progesterone receptor. \*no personal BAS data ejected (n=2).

\*\*Data missing

## Study IV

The results of this study, based on the answers from 161 respondent nurses, showed a contradictory picture regarding nurses' perceived prevalence and intensity of taxane-induced pain among patients. Overall, the confidence intervals in the present study were wide. There was some consensus regarding when the pain began, but not regarding when it subsided. Large parts of the body were expected to be involved in the pain, such as muscles, joints, legs,

feet, and mainly the back of the trunk; see Table 6. The nurses described poor access to local and/or national guidelines for how to manage taxane-induced pain. Allowing patients access to pre-emptive painkillers during chemotherapy or at home was described as not common, and neither was this supported in guidelines. In a logistic regression analysis, the nurses' specialist education in oncology, age, and work experience were shown to not significantly affect the outcome variables: the experienced occurrence of taxane-induced pain and pain intensity, see table 7.

Table 6. Expected body parts and body area (%) to be involved in taxane-induced pain

Fre- quency & %	Head and neck	Arms and hands	Front trunk	Back trunk	Legs and feet	Joints	Muscles	Skeleton	Body area in pain	Worst pain	Least pain
Don't know	30 19%	6 4%	18 11%	10 6%	6 4%	8 5%	8 5%	12 7%	Don't know	8 5%	7 4%
Not at all likely	77 48%	11 7%	35 22%	15 9%	4 3%	4 3%	4 3%	12 7%	0-27%	20 12%	111 69%
Likely to some extent	22 14%	58 36%	54 33%	43 27%	21 13%	20 12%	20 12%	33 20%	28-54%	34 21%	13 8%
Quite likely	2 1%	45 28%	21 13%	45 28%	50 31%	51 32%	51 32%	39 24%	55-72%	56 35%	2 1%
Very likely	0	19 12%	2 1%	24 15%	66 41%	65 40%	65 40%	44 27%	73- 100%	16 10%	1 0.6%

Table 7. Logistic regression models of nurses estimated occurrence of pain and pain intensity  
 Crude OR (95 % CI) Adjusted OR (95 % CI)

Estimated perceived occurrence of pain		50-100	Adjusted OR (95 % CI)
	0-49 Number of Respondents (%)	Number of Respondents (%)	
<b>Age</b>			
<35	11 (29.7)	26 (70.3)	1.15 (0.43-3.05)
35-55	27 (32.9)	55 (67.1)	1
>55	8 (22.2)	28 (77.8)	1.17 (0.39-3.58)
Test			P=0.937
<b>Years in oncology nursing</b>			
0-4	10 (25.6)	29 (74.4)	1
5-10	15 (39.5)	23 (60.5)	0.53 (0.20-1.40)
11-18	13 (39.4)	20 (60.6)	0.53 (1.20-1.45)
>18	5 (14.3)	30 (85.7)	2.07 (0.63-6.79)
Test			P=0.047
<b>Specialist education oncology</b>			
No	29 (30.9)	65 (69.1)	1
Yes	17 (27.9)	44 (72.1)	1.16 (0.57-2.35)
Test			P=0.691
Estimated perceived pain intensity		>60	Adjusted OR (95 % CI)
	<60 Number of Respondents (%)	Number of Respondents (%)	
<b>Age</b>			
<35	19 (51.4)	18 (48.6)	0.95 (0.44-2.06)
35-55	41 (50.0)	41 (50.0)	1
>55	12 (35.3)	22 (64.7)	1.8 (0.80-4.19)
Test			P=0.289
<b>Years in oncology nursing</b>			
0-4	20 (51.3)	19 (48.7)	1
5-10	19 (51.4)	18 (48.6)	0.99 (0.41-2.45)
11-18	19 (57.6)	14 (42.4)	0.78 (0.31-1.97)
>18	11 (31.4)	24 (68.6)	2.30 (0.89-5.94)
Test			P=0.138
<b>Specialist education oncology</b>			
No	47 (50.5)	46 (49.5)	1
Yes	25 (41.7)	35 (58.3)	1.43 (0.74-2.75)
Test			P=0.282

\* Italic represents statistically significant association at 5% level

# Discussion

## Summary of findings

This thesis highlights taxane-induced pain in people with breast cancer. This is the most common malignancy in women, with around 40% of 8,531 patients in 2017 receiving adjuvant chemotherapy. The benefits of taxane-containing chemotherapy include better survival rates, but it also has various side effects, one of which is severe pain that interrupts the lifeworld of women. The pathobiology behind taxane-induced pain is complex and only partly known. Pain can be seen as a biopsychosocial process that begins with an activity in a neuron (*the bottom-up phenomenon of pain*) or as a *top-down* phenomenon of pain, which opens up for an extended dialogue of pain. To investigate taxane-induced pain in this thesis, different methods are used: interviews, the VAS, a body image, and the EORTC QLQ-C30. Each of the methods contributes to the puzzle of the experience of taxane-induced pain. The contribution of the interviews and the colored body images provides a deep understanding of the pain the women experienced and described. With their experiences as narratives reflected in a body image giving a picture of a widespread and very intense pain. The body image and the use of the colors of a stoplight to describe the pain distribution and intensity developed for this purpose allow for the reflection of different individual experiences of pain. The body image was analyzed, in Studies I and III, in two different ways: firstly, through a qualitative analysis, in which distribution and intensity was highlighted based on the woman's story; and secondly, through a quantitative analysis in which the pain distribution and intensity were calculated. Both ways are useful, and the determining factor for how the analysis is done is whether the results should reflect individuals' experiences or mean values in a study population. Assessing pain with the VAS is a common method. What was exciting in this study was to discover that high pain estimates on the VAS could be completely manageable under the right conditions (Study I). That is, the pain was perceived as expected when there were reasonable explanations for why it hurt, and help – both painkillers and strategies – was available for the pain. If these conditions are not met, even lower pain estimates on the VAS may be a difficult to handle problem for patients with pain. Another important finding when using different methods (interviews vs. the VAS) to detect pain is that the timing of the pain assessments is crucial to the outcome. This is reflected today by a widely disseminated opinion in the research literature regarding how

common, and intense, taxane-induced pain is (19, 22, 90, 91). Even among nurses at oncological day care units, the perceived experiences are far from congruent concerning patients' taxane-induced pain with regard to incidence and pain intensity. The study also unambiguously shows that there are no guidelines for nurses to enable a uniform work to deal with taxane-induced pain.

### Experienced pain documented using different methods (Studies I, II, III)

To capture their experienced pain, 53 women with breast cancer assessed the possible development of taxane-induced pain using three methods: the VAS, a colored body image, and the two pain items of the EORTC QLQ-C30 (Study III). This multi-method approach revealed different pain characteristics and a surprisingly widespread and intense pain. Forty-seven percent (n=25) of the women scored pain >30 on the VAS on one or more occasions after chemotherapy. After Cycle 1, the VAS increased the most for the women with VAS >30 (n=25). Many of the women were in pain after Cycle 3 (the last docetaxel treatment); thereafter, there was a decline in pain as reported on the VAS. However, the women with VAS >30 seem to have had some pain during the epirubicin sequences as well (Study III). Pain during the epirubicin sequence was also found by Saibil et al. (22). This is an interesting finding that needs to be further explored in light of the risk of chronic pain development (92). In the baseline estimates on the EORTC QLQ-C30, the group of women (n=25) who reported VAS >30 tended to report higher pain. Opposing this finding, though, is the fact that on the VAS measurements, before the first cycle of chemotherapy, the whole group (n=53) recorded low levels of pain (Study III). On the body image, however, the colored pain intensity shows a widely distributed intense pain. One can discuss whether the average pain intensity on the VAS after Cycle 1 for the women with VAS >30 (n=25), average VAS=42, is congruent with these findings (Study III). The VAS is a scale between two points on a straight line, and might be hard to understand even if it has been explained (70). Here a numeric rating scale (NRS) might have been better, with the pain intensity measured somewhere from 0 to 10. Measuring pain intensity (Studies I, III) might be seen as a simple measurement, however this assessment also measures the full impact of the patient's overall life situation. Thus, in Studies I-III the women had a potentially life-threatening diagnosis, which might be reflected in the pain intensity assessment. With a breast cancer diagnosis and a tough treatment, a great many things in life can become painful (Studies I and II). This is also highlighted by others, for instance Little et al.(2004) (50) and Johannsen et al.(2018) (51). Therefore, every pain estimate should be made with communication about the results; no one should be left alone with the thoughts that can grow in their loneliness from imagining why

the pain is present (Studies I and II). Were the inherent properties that complicate communication about pain should be in mind of the listener (the health care personnel) (45). This by for example, expanding the narrow, limited adjectives for pain by inviting the use of metaphors (59). The pain assessment methods contribute their own unique information. However, only the interviews and body images reveal the clinical picture of a highly complex, high-incidence pain as described in later research literature (18, 20, 21, 92) (Studies I, II, III).

This proves the benefits and the importance of using multiple parallel methods of measuring taxane-induced pain. A thorough mapping of the pain enables an informed dialogue around it, which in turn forms the foundation/basis for tailoring good pain relief.

## Grasping pain in the lifeworld

### The language of pain and perceived time (I and II)

The pain experience in the lifeworld as described by the women in (Studies I and II) included descriptions of severe acute muscle, joint, and skeletal pain. They defined the pain experienced in their bodies as, for example, “flu-like pain or menstrual cramps”, as being like “having surgery without anesthesia”, or as feeling like being “pulled and ripped apart.” The pain was described along a spectrum from being mild with the situation under control, to a very severe pain, making everything else impossible, a paralyzing pain that awoke feelings of being totally out of control. According to Leader, when pain becomes severe, we as humans are nothing but pain (47), we suffer. Suffering, at its essence, is a feeling or a mood (48) and, when we are suffering, the world is completely different from the days when we are not suffering (48). We are bodily in the world (43) when our body is in pain; our very “I” is suffering, and this “I” is present in the world at the heart of everything (44). When we are in pain, something happens to our language; the pain makes it disappear into a black hole (93). The person in pain becomes bereft of language (45). As argued by Scarry (1985), the pain itself has no referential content (45), as pain is not of or for anything; thereby, pain resists objectification. In order to objectify the pain we feel, the metaphor comes to our aid and makes the characteristics of the pain visible and thereby sharable (45). The metaphor offers a solution that helps us understand one “thing” in terms of another (59). One strength of the metaphor, as argued by Loftus (2011), is that metaphors and narratives not are all-inclusive; the crevices in the narrative can open up for new ways of thinking, and at the same time help us gather thoughts about what we need to pay attention to (59). In Studies I and II, the women with more severe taxane-induced pain used a more complex metaphoric language of pain



to describe their pain experience. They tended to use traditionally female metaphors, including “menstrual cramps”, “dryer”, “fabric calender”, “needles”, and “the second stage of labor pains”:

It felt like I'd been thrown into a dryer and I was being tossed back and forth, back and forth; it pulled and ripped me apart. (Woman 3), p 35, *Cancer Nursing*, Vol. 33, No 1, 2015.

Otherwise, the metaphorical language of pain is mainly a male-created language, conceptualized by men with metaphors drawn from a world of machines, tools, and war (48, 59).

In pain management, the power of language becomes the intellectual tool we have for deepening our shared experiences of pain (59). This highlights how utterly important it is not only to assess pain, but also to communicate and share experiences of it; especially in contexts in which pain could be interpreted as a sign of a fatal disease. The experience of pain is one of a multi-layered phenomenon. The understanding of the experience of pain, and the ability to deal with the pain, will never become greater than our understanding and ability. Pain must first be recognized if it is to be assessed and treated. The recognition of pain begins with the story of the person in pain.

By communicating, we can avoid misconceptions, which can complicate pain treatment in cancer care. Common misconceptions include a lack of pain assessments and pain management, patients' reluctance to state their pain, and health professionals' inadequate knowledge of pain and pain management (94). There can also be misconceptions among patients, relatives and health professionals about the use of painkillers, especially if they contain morphine (95). No matter what the barriers are, there is no shortcut to good pain control; it always starts and ends with good communication. It is the encounter between health professionals and the person in pain that gives meaning to the assessment and treatment of pain (59).

Thoughts frequently expressed by phenomenological philosophers such as Heidegger and Merleau-Ponty concern how pain and illness affect the human perception of time (44, 96). In Study II, the women described this disruption of experienced time and the sense of alienation that followed. It also disrupted how they understood the sensation of pain in the past in light of the present, and at the same time had an eye on the future. This was described by one woman (Study II) as a feeling of “being in a hurry” as her “time was running out.”

When we are in pain time is disrupted, its also disrupt our connections to others. We become entirely alone (47). Bodily in our one universe (45). Gergel

(2010) writes something similar to what is described by the women in Study II, that our time perception is about our relationship to the world, and is always aimed at the future while taking shape with its starting point in our present and past (97):

I couldn't even imagine that it was like this to have such a disease (silence). A disease you don't know anything about, a disease that has the power to live its own life in your body. At last I've found acceptance. I can't step out of myself. I can just fold my hands and hope for the best (Woman 1), p 469, *Cancer Nursing*, Vol. 39, No 6, 2016.

### Memories of pain in the lifeworld of the women (Study I and II)

The moment our pain starts, our access to the pain-free condition we had the second before is lost. We cannot remember how this pain-free condition felt (47). When the women revived their memories of the taxane-induced pain they had experienced about a year previously, two things happened. Some of the women enhanced their memories, while others diminished them. Those who had previously described more severe pain used a complex metaphorical language to a higher degree. Their stories of the pain experience were almost identical to their descriptions of taxane-induced pain the previous year (33). The metaphor had become part of their lifeworld. The women experiencing less severe taxane-induced pain were vaguer in their descriptions, as if their memory of the pain was blurry. Their memories of the taxane-induced pain gave access to the pain in different ways. On the one hand, their memories made them more aware of their own presence in the world, whereby memories had the capacity to affect their everyday life with a more conscious awareness of time and being. On the other hand, the women described a distant future threat, raising a tangible painful awareness of what it means to be mortal (33, 50). This is not unique to this context of taxane-induced pain, but is rather a general experience shared by cancer patients in their trajectory of cancer (50, 98).

### Am I healthy or not (Study II)

When the treatment ended, the women described feeling unprepared for the emotions that arose. They longed for a disease-free life and no more tiring treatments, but discovered that they had become utterly lonely. When there were signs of pain, this triggered thoughts of something “undefined” in the body, causing worries. The worries awoke feelings of increased vulnerability, dark thoughts, and pronounced loneliness, something that is described in other studies as well (98, 99). Life is gradually moving toward some sort of normality, but it is not like before. Being regarded as “healthy” and on one’s way out of the health care system can arouse new painful experiences.

## Nursing and pain (Study IV)

In Study IV, the nurses' reported ability to assist patients in dealing with taxane-induced pain showed a wide confidence interval and standard deviation. This means that there is no coherent view among the nurses. Some of them are of the opinion that they can help their patients avoid taxane-induced pain, while others have a diametrically opposed view. In a previous study, nurses expressed concern that they did not have enough knowledge of pain to best help their patients with pain management (100). A lack of available clinical supportive guidelines for preventing pain might impede nurses in their pain management for patients for different reasons. Firstly, they might feel hindered in communicating about pain with their patients due to their own lack of knowledge; secondly, they may not know what to do. This is supported by fact that a lack of standardized guidelines in oncology care is identified as one of the most important barriers to providing high-quality cancer care (101). In a study of oncology patients' satisfaction with outpatient care by Kleeberg et al. (2008) (102), three of the patients' major concerns were too little information about possible side effects, insufficient information on how to handle pain at home, and insufficient information on the side effects of pain management (102).

Perhaps the form of care itself, outpatient care, requires a highly conscious attitude among nurses to achieve good pain management. Oncology nurses as a collective need to have good knowledge of pain management; the confidence intervals of perceived knowledge for helping patients in pain demonstrate a widespread perception among the nurses of their knowledge. This outcome can affect pain management. The essence of good care rests on a bedrock of communication. If the communication becomes entirely procedure-focused – that is, all the focus is on the treatment process itself – both nurses and patients might lose other areas of importance in the communication, and no one will hear what the other is saying (103). Nurses may be more preoccupied with the physical state of pain than with the patient's emotional and personal experiences of the phenomenon of pain (103).

Being an oncology specialist nurse did not affect the estimation of prevalence of pain and intensity of pain. Other studies show that taxane-induced pain is common and has high estimated pain intensity and it is easy to reflect that nurses with specialist training would be more up-to-date and responsive to the symptoms. Meanwhile, Beck et al. (2016) (104) argue that specialist education itself is not enough; the workplace/organization must also be organized so that knowledge is effectively applied – otherwise, the knowledge will not be used (104). The latter explanation (104) is most likely valid for the oncology specialist nurses in study IV. Their workplace may not be fully implementing new

ways of working or benefitting from the knowledge which the further educated nurses have acquired. The situation might in time lead to the oncology specialist nurses adapting to the existing routines and ways of thinking at the workplace and using their deeper knowledge less and less. This could be the reason for the lack of differences in the data between undergraduate personnel and further educated oncology nurses.

The Institute of Medicine (IOM) proposes six aims of high-quality health care. It must be safe, effective, timely, efficient, equitable, and patient-centered. Patient-centeredness argued to be an aim entailing respectful and responsive care in which the patient's values guide clinical decisions (105). Timely care, the third aim, is a care that, when translated into pain management, means a care delivered just in time before the pain has full power; thereafter, the pain treatment is evaluated and upgraded regularly until the risk of pain is limited (105). To expound patient involvement in the pain treatment, the nurse must discover and capture the pain in daily care. Here, nurses and their patients, who may be suffering from taxane-induced pain, are in need of clinical guidelines (101). These guidelines should provide support, and information regarding: a) reasons for the pain development; b) the use of pre-emptive painkillers to avoid severe pain; and thereby c) how and when pain is to be measured; d) pain assessment criteria and tools to be used; e) how the pain estimation is to be evaluated; f) painkillers to be used in developed pain (90); g) evaluated effects of the pain management (106); and h) alternative pain-relieving methods, such as physical activity, massage and TNS (107, 108). In addition, they should i) provide support in an extended, more reflective communication on pain, highlighting the importance of pain metaphors for the interpretation and description of pain (57). Lastly, they should j) suggest smooth solutions for close contact between patients at risk of severe symptoms and nurses/physicians on days when the patient is at home (109, 110).

## Methodological considerations

### Studies I and II

Several quality criteria were considered throughout study I and II, following the Consolidated Criteria for Reporting Qualitative research, and Lincoln and Guba's evaluative criteria as presented in the Qualitative research guidelines project (111, 112). To achieve *trustworthiness*, which includes credibility, dependability, confirmability, and transferability, a systematic methodical approach was used. For *credibility*, a strategic sampling was used, where women from three different oncology day care units participated; they represented both rural and urban areas. They were young, middle-aged, and elderly women

with different family constellations and education levels. This provided confidence in the findings. A prolonged engagement was maintained through the model where the same interviewer conducted all the interviews. A peer debriefing was used during the analysis process (Study I and II). *Dependability*, in both studies (Study I and II), was supported by the research process, which can be easily followed and repeated. Additionally, a strengthening factor was that the interview guide and the body image in Study I was previously tested in a pilot-study. This pilot-study was carried out as a focus-group interview with four women with breast cancer who developed taxane-induced pain. During the interview session in the pilot-study, a clinical lecturer participated as an observer. The interview guide and the body image were then revised based on the discussion together with the women in the pilot-study and the clinical lecturer. The results from the pilot-study are not included in Study I or II. *Confirmability* of the data was strengthened through triangulation, whereby rich, robust, comprehensive and well-developed accounts were received by different data collection methods; interviews, a colored body image and VAS estimates. The dissimilarities between the women with experience of chemotherapy-induced pain during breast cancer treatment contributed to a variety of perception of the phenomenon observed. Concerning *transferability*, the women's story was told on the basis of the context in which the women felt at home. This meant that the pain experienced was reflected in their social and culture context, for example, if there were small children to take into account; daily chores expected to be done; or a life in social loneliness. All of this contributed to a rich comprehensive description of taxane-induced pain, which is transferable to other contexts where taxane-induced pain is experienced in the lifeworld of people.

A weakness in Studies I and III is that the pain estimates for inclusion were set to Day 10 between the cycles. During the interviews, it became quite clear that pain was the most prominent from Days 3 through 7 in the cycles. If more frequent VAS estimates had been performed, there would likely have been more women with estimates of  $VAS > 30$  or  $VAS \geq 4$ , and thereby more participants in the "pain group". Another weakness may be that the VAS values in the studies, were used in such frank interpretation, i.e.  $VAS \geq 4$  as used in Study I, is argued to have similar value as VAS from 40 and above, even though similarity in the values is supported by the literature (69, 74). More frequent VAS estimates could have rendered a clearer picture of pain decrease, which was something the women in the studies called for. However, in their current form the studies were easy to participate in and thus attractive. The Studies I and II, include a small sample of Swedish women; thus, the findings cannot be generalized. However, they may be transferable to similar contexts and patient groups.

### Study III

The triangulation of quantitative methods for assessing pain is a strength, whereby the colored body image is a simple yet effective way to record and evaluate not only the distribution but also the intensity of pain both during and after chemotherapy. The pain was followed up longitudinally, assessed at baseline, during chemotherapy, and 12 months after inclusion. Study limitations include the fact that the VAS assessments between cycles were made by the patient at home, and thus the exact time point of completion is not certain. Additionally, the chosen time point (Day 10) for the VAS assessment is not the best time point for evaluating the highest intensity or incidence of taxane-induced pain (19, 113). In this study, we calculated pain distribution and pain intensity using the Rule of Nines burn area charts. This method for calculating the pain distribution on the body image was initially developed to calculate deep burns and their extent [41]. The colored body image turned out to be easy to understand, easy to fill in, and served as a good overall basis for evaluating pain distribution and pain intensity. Anyhow, there may be other, better ways to evaluate and calculate the distribution and intensity of pain. The recording of pain distribution using a body image can be done using, among other things, the established McGill pain questionnaire, although McGill does not use colors [36]. In the EORTC QLQ-C30 questionnaire's two pain questions, there was uncertainty as to whether they were answered by the patients just before the start of chemotherapy or shortly after. The questionnaire was to be completed within seven days of being received, which means that the treatment could already have begun when the baseline assessment was made as there could have been a delay between the informed consent and the participants receiving a standardized questionnaire including the EORTC QLQ-C30 and patient demographics. However, the EORTC QLQ-C30 reflects the previous week. In the individual patient score the EORTC QLQ-C30 questionnaire is known to have large standard deviations, and thus the confidence intervals are wide [42]. Since there was a low number of participants in this study, the results should be interpreted with caution. The findings might benefit from replication in a larger study to confirm the results.

### Study IV

The questionnaire developed based on patients' experience of taxane-induced pain comprises several dimensions of the nurses work, important for mapping perceived experiences of taxane-induced pain. The strengths of this study include the investigation of several dimensions of nurses' perceptions of patients' experienced taxane-induced pain, a difficult but common symptom. Another strength is the high response rate to the questionnaire. Limitations include the fact that the questionnaire, tested and developed in close collaboration with staff working with taxane chemotherapy, had not been previously

used. This means that there are questions regarding its validity and reliability as well as sensitivity. The results provided wide confidence intervals, but other well-validated questionnaires such as the EORTC QLQ-C30 have the same tendency. The internal dropout for the questions in the survey is relatively low, with six to eight participants not responding to individual questions. Issues regarding taxane-induced pain and the nurses' expected effects of pain relief administered to the patients, how the nurses experience whether they can help their patients with their pain, and whether the nurses had sufficient knowledge to handle their patients' pain had a lower response rate. These are all issues that can be difficult to approach. It might also be difficult to help patients with their pain if no regular pain assessments are conducted; thus, it also becomes difficult to determine the effects of the pain relief provided.

## Conclusions

The overall aim of this thesis was to explore women's acute and longstanding experiences of taxane-induced pain, to evaluate the pain intensity and distribution using different assessment methods, and to study nurses' perceived experience of taxane-induced pain in people with breast cancer. These are the conclusions

- *During taxane chemotherapy* women who developed pain, describe the pain challenging. However, even high pain estimates could be experienced as manageable by the women, this if the pain was perceived as expected, if there were reasonable explanations for the pain and available help to treat it. If these conditions were not met, even low pain estimates could be a "difficult to handle problem" for the women with pain. Women with more challenging pain lacked referential pain experiences in their earlier life. Large areas of the body were involved in the pain. Pain experienced during chemotherapy impacted social life, caused isolation and at the same time dependency on others; the pain raised concerns and existential questions.
- The pain experiences of the women at the second interviewee were perceived in a time perspective. *In the past*, during chemotherapy was pain described in metaphors, and time was experienced as cyclical, with dependency on others and at the same time a sense of solitude. *In the present*, the women are still partly in pain and living with a changed, unwilling body, increased awareness of being bodily in the world. The women expected normality but found themselves in a space somewhere in-between health and illness. *Future perspectives*, involved to maintaining struggle with the body, a feeling of limited

time, and insecurity regarding whom to turn to with questions raised in a space of insecurity.

- *Quantitatively longitudinal assessed taxane-induced pain.* Pain assessed with various assessment tools disclosed by; *the body image*, an intense and widespread pain during taxane chemotherapy and pain remaining after 12 months but not as widespread and intense. *The VAS disclosed*; the highest pain intensity measures after Cycle 1, with most participants experiencing pain after Cycle 3. Some pain continued during the epirubicin based cycles. The pain scores dropped after the last (6<sup>th</sup>) cycle, but not to the level of the baseline estimates. On *the EORTC-QLQ-C30* higher levels of pain was found for women estimating VAS >30 at baseline, three months and 12 months after inclusion. No differences were found in baselines estimate when the pain was estimated using the VAS.
- The nurses' perceptions of taxane-induced pain were contradictory regarding pain prevalence and pain intensity. Some consensus was found among their perceptions of when the pain started, but not those of when the pain declined. The nurses' identified large parts of the body as being involved in pain. Poor access to local and/or national guidelines on how to manage taxane-induced pain was described throughout. This reflects the results of a low-level generalized use of premedication against taxane pain. The results from an adjusted binary regression model of relations between on the one hand nurses age, work experience and specialist nurse education (independent variables), and on the other hand estimated incidence of pain and pain intensity (dependent variables) is presented as odds ratio (OR), confidence intervals (CI) and p-values. None of the independent variables was significant related to the estimation of incidence of pain or pain intensity.

## Implications and future directions

According to the results of this thesis, taxane-induced pain in women with breast cancer is a quite common pain experience and phenomenon described by women undergoing taxane chemotherapy. The pain is described as ranging from manageable pain experiences, to those exceeding decent pain levels and these pain levels are experienced today in modern oncological treatment. The subsequent question concerns how to act on this acquired knowledge, in light of the oncology nurses' regarding, the lack of supportive guidelines for preventing and treating taxane-induced pain. My suggestions included beginning



at the very high-quality chain of well-defined and regulated actions starting when people is newly diagnosed with breast cancer:

- Before the treatment starts, the National Cancer Rehabilitation Program (NCRP) (114), available through regional cancer centres, should be in focus at the multidisciplinary conference. Where inter-linked treatment prospects are evaluated and determined, based on a national breast cancer care program (5).
- The NCRP makes suggestions on symptoms that should be assessed and followed out of a cancer rehabilitation perspective. This rehabilitation perspective, should be used as praxis for to making cancer care plans to reduce or avoid pain when taxane treatment is to be initiated.
- To capture the pain, simple tools can be used whereby patients report their symptoms, for example, through a smartphone application with a variant of “the health assessment tool” (115), or the digitalized “My Care Plan” (116). Integrated with the chosen tool should be a system that enables quick feedback.
- In addition to this, a supplementary region-wide system could be offered, a 1177 for oncology patients, with a nurse available by telephone outside office hours and can support patients with severe symptoms or severe anxiety. To support the nurse in more complicated issues there could be an identified oncologist consultant. Contacts could be scheduled and made at special appropriate times.
- To develop a national based guideline on how to manage taxane-induced pain and available information to patients and their relatives about the symptom what to do about it and whom to turn to in case of pain.

## Epilogue: Grasping pain in the lifeworld

Getting to know the women and the stories they shared during the interviews was like having access to an invaluable treasure – being so openly welcomed to participate in a period of their life when this life was so difficult and many truths needed reconciliation. I stepped into their turbulent everyday life and was met with complete openness. My concerns are about whether I have told their stories fairly or well enough, or whether nothing in their care will change. At the very least, my hope is that the treatment of taxane-induced pain will reach the level of that of nausea and vomiting. In the best of worlds, patients’ at risk of developing taxane-induced pain will be able to assess their pain. At the other end of the spectrum is someone who evaluates these estimates, and can offer help and advice – a person who really listens to the patient’s narrative.

# Sammanfattning på svenska

## Utgångspunkter

Bröstcancer är den vanligaste cancersjukdomen hos kvinnor. Sjukdomen ökar i förekomst och dödlighet över hela världen, förutom i USA och Europa där överlevnaden förbättras. En kvinna i västvärlden som idag diagnostiserats med bröstcancer i tidigt stadium, har samma förväntade överlevnad som en kvinna utan bröstcancer. De bidragande orsakerna till detta anses vara tidig upptäckt genom screening mammografi och bättre behandlingar. Hälften av alla bröstcancerfall upptäcks genom att kvinnan själv känner en förändring i bröstet den andra hälften upptäcks via mammografi. För att reda på vilken sorts bröstcancer det kan vara så görs en fin-nålsbiopsi och förekomsten av maligna celler undersöks. Bröstcancer är huvudsakligen indelad i tre huvudtyper: 1) Endokrinberoende (östrogen och/eller progesteronreceptor positiv) 2) HER2-driven (HER2-positiv); och 3) trippel negativ (saknar östrogen-, progesteron- och HER2-receptorer). Den största gruppen är endokrinberoende tumörer. Efter att diagnosen är satt blir det vanligtvis kirurgi, i form av en sektorresektion varvid en del av bröstet avlägsnas eller mastektomi då hela bröstet avlägsnas. Efter eller före operationen, beroende på vilken typ av tumör som upptäckts, kan det vara aktuellt med en tilläggsbehandling så kallad adjuvant behandling. Adjuvant behandlingen är ett supplement till kirurgi och kan omfatta kemoterapi, antikroppar, endokrinterapi och strålbehandling.

I Sverige under 2017 diagnostiserades 8 511 patienter med invasiv bröstcancer av vilka cirka 40% fick tilläggsbehandling med kemoterapi (cellgiftsbehandling). Taxaner är en av de viktigaste kemoterapiregimer som används vid behandling av bröstcancer, och förbättra överlevnaden vid tidig invasiv bröstcancer. Taxaner kan också orsaka olika biverkningar, varav en är svår smärta. Smärtan beskrivs i litteratur som nociceptiv- och/eller neurogen smärta. År 2005 när taxaner introducerades i adjuvant behandling av bröstcancer var taxane-inducerad smärta inte ett särskilt uppmärksammat symptom. Vidare gav den litteraturen som då fanns en skiftande bild av smärtförekomst vid taxan behandling. Dock, många av de kvinnor med bröstcancer som efter 2005 behandlades med taxaner började beskriva smärta efter behandlingen. Vid en stresshanteringsstudie (för att minska stress hos kvinnor diagnostiserade med tidig invasiv bröstcancer) i Dalarna, Gästrikland och Uppland beskrev kvinnor i stresshanteringsstudien som fick taxaner smärta efter behandlingen. Dessa fynd väckte vår uppmärksamhet och efter utökat etiskt tillstånd så började vi efterhand tillfråga kvinnor i stresshanteringsstudien som skulle få taxaner om de kunde tänka sig att skatta eventuell smärta i samband med sin kemoterapibehandling.

Smärta kan ses som 1) en biopsykosocial process som börjar med aktivitet i ett neuron ”*the bottom-up phenomenon*.” Signalen från nervnet fortplantar sig i nervsystemet och tolkas i hjärnan. Två huvudtyper av

smärta är a) nociceptiv smärta, som innebär att när nociceptorer, som finns i varierande grad i alla kroppslig vävnader, stimuleras gör det ont. b) eller/och som neuropatisk smärta, vilken är initierad eller orsakad av en primär skada eller dysfunktion i nervsystemet. Den neurogena smärtan kan uppstå utan stimulering av perifera sensoriska nociceptorer. En komplementär syn på smärta är 2) "*the top-down phenomenon*" där smärtan ses som en process som formas av erfarenheter i livsvärlden (vår existens, varandet): som personlighet, förväntningar, sammanhang och tankar om mening. Detta sätt att se på smärta balanserar ett biomedicinskt perspektiv och öppnar upp för smärtberättelsens betydelse för förståelse av smärtans grundläggande subjektivitet. Smärta kan ses som ett fenomen, en smärtdefinition med fenomenologisk ansats beskrivs av läkaren och smärtforskare David Biro, och lyder: "*Smärta är en allomfattande intern erfarenhet, som hotar att förstöra allt utom sig själv, och som bara kan beskrivas med metaforer.*" Denna avhandling avser att beskriva och utforska den subjektiva bördan av taxan-inducerad smärta och långvarig smärta i livsvärdet hos kvinnor diagnostiserade med bröstcancer. Detta för att A) få en djupare förståelse av smärtupplevelserna och B) för att synliggöra smärtan med olika metoder och försöka beskriva en del av den ontologiska (varandets natur) klyfta som kan finnas mellan smärta upplevd av patienterna och smärta observerad av vårdpersonal.

## Tillvägagångssätt

Syftet med avhandlingen var att utforska kvinnor med bröstcancers upplevda erfarenhet av smärta i samband med taxanbehandling. Hur smärtan inverkade i deras dagliga liv under själva behandlingen och vid ett år efter den första intervjun. Vidare att undersöka hur olika smärtskattnings metoder fångade smärtan. Tillika var syftet att undersöka sjuksköterskors erfarenheter av taxansmärta vid poliklinisk bröstcancerbehandling.

Studie I, är en explorativ kvalitativ, semistrukturerad intervjustudie. Där syftet var att undersöka kvinnors uppfattningar av kemoterapiutlöst smärta under behandlingen med hjälp av olika metoder. Där en del av smärtupplevelsen undersöktes genom kvinnornas berättelser, den andra delen av smärtupplevelsen, intensitet och utbredning, fångades på en kvinnlig kroppsbild, där smärtan färgglades utifrån ett stoppljus det vill säga, grön = ingen smärta, gult = en smärta som gör kvinnan villrådig, ska hon vila eller vara aktiv i dagliga sysslor (köra eller bromsa?), rött = en smärta som stoppar dagliga aktiviteter till sist, svart = en obeskrivlig smärta, som gick utanför tidigare smärterfarenhet i kvinnornas liv. Den tredje delen i smärtskattning är smärtintensitet skattad på en visuell analog skala (VAS). Sexton kvinnor från stresshanteringsstudien deltog i studien.

Studie II, är en explorativ kvalitativ, semistrukturerad intervjustudie. Studien syfte var att utforska minnen av kemoterapiutlöst smärta och all upplevd

långvarig smärta i kvinnans livsvärld efter tidigare kemoterapi behandling mot bröstcancer. Kvinnorna intervjuades 12 månader efter inklusion, 15 kvinnor från Studie I deltog, en kvinna hade under tiden dött av sin bröstcancer.

Studie III, är en kvantitativ deskriptiv longitudinell studie där syftet var att fånga smärta hos kvinnor som först opererats för bröstcancer sen behandlats med taxaner och utvecklade taxane-inducerad smärta. Detta med hjälp av olika metoder, kroppsbild, VAS och två smärtfrågor från det cancerspecifika livskvalitetsinstrumentet: The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire, (EORTC QLQ-C30). Smärtan skattades med kroppsbilden under själva behandlingen och vid 12 månader. Vidare skattades smärtan med VAS-skalan under kemoterapi behandlingen, inför varje kur och på dag 10 mellan kurerna (sammanlagt 6 kurer). Slutligen skattades smärtan med EORTC QLQ-C 30, när kvinnorna gick med = inkluderades i studien, tre månader efter inklusion och 12 månader efter inklusion. Femtiotre kvinnor från stresshanteringsstudien deltog i undersökningen.

Studie IV, är en tvärsnittsstudie där syftet var att med hjälp av en enkät studera sjuksköterskors upplevda erfarenhet av förekomsten av taxan-inducerad smärta hos personer som behandlas för bröstcancer. Vidare hur sjuksköterskorna uppfattade organisatoriskt stöd till hjälp för att hantera smärta i samband med taxaner. Vidare om ålder, arbetslivserfarenhet och specialistutbildning i onkologi påverkade den erfarna förekomsten av taxan-inducerad smärta eller smärtintensitet. Hundrasextioen sjuksköterskor som arbetar på onkologiska dagvårdsavdelningar i Sverige deltog.

## Övergripande resultat

Studie I. Kemoterapiutlöst smärta upplevdes i varierande grad av kvinnorna i studien. Kvinnornas beskrivning av smärtupplevelse sträckte sig från berättelser om influensaliknande symtom, mensliknande smärtor till smärtor värre än utdrivningsskedet under en förlossning. Deras kroppsbilder färglades med en hel del grönt till kroppsbilder där med än tre fjärdelar av kroppsytan var täckt av svart. Den värsta upplevda smärtintensiteten mätt med VAS gav skattningarna från VAS 5-10. Några kvinnor med relativt högt skattad smärta beskrev att förutsättningarna: bra information, smärtlindrande läkemedel och egna strategier gjorde smärtupplevelsen hanterbar. Andra kvinnor hade en rakt motsatt erfarenhet med mycket smärta, dålig information och sent insatta smärtlindrande läkemedel för dessa kvinnor blev smärtan mycket besvärlig. Även lågt skattad smärta kunde upplevas som svår relaterat till ett vagt svar på smärtupplevelsen från vården och kvinnans hela livssituation.

Studie II. Kvinnornas beskrivning av smärta speglas i ett då, nu och sen perspektiv. Minnena av smärtan under själva behandlingen beskrivs tydligast av de kvinnor som tidigare använde metaforer i sin smärtberättelse. Kvinnorna

beskriver att smärtan i kroppen finns på ungefär samma ställen som under behandlingen men inte lika utbredd eller intensiv. Kroppen beskrivs som ovillig och osäker. Kvinnorna beskrev att under behandlingen var de stundtals helt eller delvis beroende av andra samtidigt som de kände sig ensamma. I den ”friska” situation ett år efter behandlingen som de nu befinner sig i, är de osäkra på vem som har ansvar för frågor som dyker upp när kroppens signaler blir svåra att tolka. Framtiden betecknades som osäker, och de befinner sig i ett mellanrum mellan det sjuka och det friska livet.

Studie III. Kvinnornas kartlagda smärta innan behandlingen, det vill säga innan start av kemoterapi, påvisade en lågt skattade smärtintensitet på VAS för alla kvinnor. Efter första behandling sköt smärtintensiteten (VAS) i höjden och nådde sitt högsta värde. Vid behandling tre, fick flest kvinnor ont enligt VAS. Kroppsbilden visade att 51% av kroppsytan var involverad i smärta under behandlingen, i huvudsak rött, gult och en del svart. De kroppsdelar som var mest förlagda var nedre delen av ryggen och nedre delen av benen och fotsulorna. Ett år efter behandlings avslut är 18% av kroppen färglagd som smärta, i huvudsak med gult, lite rött och spår av svart. Smärtfrågorna på EORTC QLQ-C30 visade att gruppen av kvinnor som skattade smärtintensitet högre än 3 på VAS skalan, hade mer smärta på EORTC QLQ-C30 när de gjorde första mätningen än de kvinnor som skattade smärtintensitet lägre än 3 på VAS skalan. Kvinnorna med högre smärtintensitet skattade högre smärta EORTC QLQ-C30 också vid tre och 12 månader

Studie IV. Sjuksköterskornas uppfattningar om taxan-inducerad smärta varierade i stor utsträckning gällande såväl prevalens som intensitet. Sjuksköterskorna beskrev en enhetlig bild av när smärtan förväntades börja, men inte när den förväntades avta. Stora delar av kroppen förväntades vara involverade i smärtan, såsom muskler, leder, ben, fötter och rygg. Sjuksköterskorna beskrev att de vanligtvis saknade lokala och/eller nationella riktlinjer för hur taxan-inducerad smärta ska hanteras. Patienternas tillgång till premedicinering för att förebygga smärtgenombrott hemma beskrivs inte regelbundet, det stöddes inte heller i riktlinjer. Sjuksköterskans ålder, arbetslivserfarenhet och onkologisk specialistutbildning påverkade inte den erfarna förekomsten av taxan-inducerad smärta eller smärtintensitet av taxaner.

## Reflexioner

För att undersöka taxan-inducerad smärta i denna avhandling användes olika metoder: intervjuer (Studie I och II), VAS, en kroppsbild och EORTC QLQ-C30 (Studie I och III) och en enkät till sjuksköterskor (Studie IV). Var och en av metoderna bidrar till att kartlägga erfarenheten av smärta. Bidraget från intervjuerna och de förlagda kroppsbilderna gav en djup förståelse av den smärta som kvinnorna upplevde och beskrev (Studie I och III). Kroppsbilden såsom den användes i studien är en ny teknik som enkelt och tydligt beskrev

smärtutbredning, smärtintensiteten och den återspeglar olika individuella upplevelser av smärta. Kroppsbilden analyseras i avhandlingen på två olika sätt: a) genom kvalitativ analys, där distribution och intensitet framhävs utifrån kvinnans historia (Studie I); b) genom en kvantitativ analys där smärtutbredning och intensiteten beräknades (Studie III). Båda sätten är användbara, och den avgörande faktorn för hur analysen görs är om resultaten ska återspegla individernas erfarenheter eller medelvärden i en studiepopulation. Bedömning av smärta med VAS är en vanlig metod. Spännande i denna studie var att upptäcka att högt skattade smärta på VAS kunde vara helt hanterbara under de ”rätta” förhållanden (Studie I). Kvinnorna var informerade om att de kunde få smärta, den var förväntad, de fick också hjälp med smärtstillande läkemedel och hade egna strategier för att hantera smärtan. När dessa villkor inte uppfylldes kunde även lågt skattad smärta bli ett svårt problem att hantera på hemmafronten. Ett annat viktigt fynd som klargjordes var att tidpunkten när smärtan skattas är avgörande för utfallet (Studie I och II). Detta återspeglas troligen även i litteraturen som ger varierande besked hur vanligt det är med taxane-inducerad smärta och vilken intensitet den har. Även bland sjuksköterskor på onkologiska dagvårdsenheter i landet är erfarenheterna långt ifrån enhälliga gällande taxane-inducerad smärta. Studien visar också entydigt att det inte finns några riktlinjer för sjuksköterskor som möjliggör enhetliga rutiner för att taxan-inducerad smärta ska behandlas på ett likvärdigt sätt för alla patienter som riskera utveckla sådan smärta (Studie IV).

## Slutsatser

Resultaten från denna avhandling visar att det är vanligt förekommande att kvinnor som genomgår taxanbehandling efter bröstcancer kirurgi upplever taxan-inducerad smärta under behandlingen. Vidare att kvinnorna upplever smärta ännu ett år efter avslutad behandling. Smärtan beskrivs som allt från hanterbara till en mycket svår smärta som överstiger vad som kan anses anständigt i modern onkologisk behandling. Den påföljande frågan handlar om vad som behöver göras med denna förvärvade kunskap också i ljuset av att sjuksköterskor på onkologmottagningar i landet har en så varierad bild av problemet. Vidare beskriver sjuksköterskorna bristen på riktlinjer för att förebygga och behandla taxan-inducerad smärta.

## Förslag på åtgärder och vidare forskning

Vid den multidisciplinära bröstcancerkonferensen som föregår behandlingsstart bör det nationella cancerrehabiliteringsprogrammets (NCR) innehåll vara en del av konferensen fokus. I NCRP ges förslag på symptom som bör bedömas och följas ut ur ett rehabiliteringsperspektiv. Detta rehabiliteringsper-

spektiv bör användas som praxis och underlag för en individuell cancervårdplan för att minska eller undvika smärta när taxanbehandling ska initieras. För att fånga smärtan kan enkla verktyg användas, där patienterna rapporterar sina symptom, exempelvis genom en smartphoneapplikation med en variant av "Hälsokattningsinstrumentet" eller en digitaliserade "Min vårdplan". Integrerat med det valda "verktyget" bör finnas ett system som möjliggör snabb återkoppling till patienten. Utöver detta bör ett kompletterande regionövergripande system erbjudas, ett 1177 för onkologipatienter, med en sjuksköterska tillgänglig via telefon utanför kontorstid som kan stödja patienter med svåra symptom eller svår ångest. Till sjuksköterskans hjälp vid mer komplicerade problem kan det finnas en identifierad onkologkonsult. Kontakter med konsulten kan planeras och göras vid speciellt lämpliga tider. Sist men inte minst viktigt, utbildning till vårdpersonal, nationella riktlinjer om hur man hanterar taxansmärta, samt information till patienter och deras anhöriga om symptomen, vad man kan göra om man får ont och vem man kan vända sig till vid problem med smärta.

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