

# Dilemmas in palliative chemotherapy when approaching end-of-life

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*I am only one, but still I am one.  
I cannot do everything,  
but still I can do something;  
and because I cannot do everything,  
I will not refuse to do something I can do.*

Helen Keller



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# Abstract

## ***Background***

When cure is no longer possible, medical care should aim for a transition to palliative care regardless of disease. Patients with incurable cancer are often treated with palliative chemotherapy (PCT), starting with the intent to prolong life and increase quality of life. Eventually, in the late stages of the disease, the patient reaches a transition phase when further PCT neither prolongs life nor adds any predominantly positive effects.

## ***Aim of the thesis***

- Study I: To analyse the proportion of patients with incurable cancer who received palliative chemotherapy during the last month of life, and to identify their discriminative characteristics.
- Study II: To develop a questionnaire assessing performance status in palliative chemotherapy, and to test its psychometric properties.
- Study III: To explore challenging situations experienced by registered nurses when administering palliative chemotherapy to patients with incurable cancer.
- Study IV: To investigate whether routine use of the Performance Status in Palliative Chemotherapy (PSPC) questionnaire in PCT would affect the proportion of patients receiving PCT during the last month of life, hospital admissions, notifications of performance status, documented decisions of ceasing PCT in the medical records, and/or place of death. A secondary aim was to gather registered nurses' experiences of PSPC in clinical use.

## ***Methods***

In Studies I and IV, information from the medical records of deceased patients with epithelial cancers was used in descriptive analyses of the proportions of patients receiving PCT in counties in northernmost Sweden. A quantitative design was chosen, using non-parametric statistical methods. In Study II, a brief patient-completed questionnaire assessing performance status was developed and psychometrically tested. In Study III, data from research interviews with registered nurses were analysed qualitatively with a narrative thematic approach.

## ***Results***

Studies I and IV showed that about 25% of patients receiving PCT were treated during the last month of life. This group of patients had more hospital admissions, were less likely to die at home, and had fewer instances of documentation of the decision to cease PCT. The questionnaire developed

in Study II was shown to have acceptable psychometric qualities such as reliability, validity, and sensitivity to detect deterioration in performance status. Study IV showed that the questionnaire gave nurses valuable information about patients' performance status. The results also showed that 97% of nurses and 48% of physicians documented their patients' performance status in the medical records. Study III demonstrated that when nurses administered PCT they considered futile, they could experience dilemmas created by the unforeseeable outcomes of PCT or stemming from insufficient communication between nurses, patients, next-of-kin, and physicians.

### ***Conclusions***

Administration of PCT can create dilemmatic situations for both the patient and medical staff when approaching end-of-life. This is underlined by the finding that some 25% of treated patients received their last round of PCT as late as during the last month of life. The decisions to cease PCT were less likely to be documented for patients who had received PCT within a month before death. Nurses described situations where they felt they were in the middle of the decision-making process regarding whether or not to continue PCT. They found the treatments were given on the authority of someone else; the physician's recommendation or the patient's and/or relatives' request.

The unpredictability of PCT was a continuous theme in the work described in this thesis, emphasizing the necessity of individually assessing every patient before PCT in order to minimize the risk of futile treatments. The attempt to develop a reliable and valid questionnaire for systematic assessment of performance status has increased future possibilities to monitor this parameter in PCT when approaching end-of-life. The questionnaire developed as part of this thesis has provided nurses with increased knowledge of patients' performance status. If routinely used, it may help decrease the proportion of patients receiving PCT during the last month of life, though this remains to be rigorously proven. Further research efforts are needed to progress in the task of optimizing rather than maximizing the use of PCT when approaching end-of-life.

### ***Key words***

Cancer, chemotherapy, decision-making, dilemma, palliative care, performance status, questionnaire, registered nurse



# Original Papers

This thesis is based on the following papers, which will be referred to in the text by their roman numerals, I-IV:

- I. Näppä U., Lindqvist O., Rasmussen B. H. & Axelsson B. (2011) Palliative chemotherapy during the last month of life. *Annals of Oncology*, 11, 2345-2348.
- II. Näppä U., Lindqvist O. & Axelsson, B. (2012) Avoiding harmful palliative chemotherapy treatment in the end of life: Development of a brief patient-completed questionnaire for routine assessment of performance status. *The Journal of Supportive Oncology*, 10, 230-237.
- III. Näppä U., Rasmussen B. H., Axelsson B. & Lindqvist O. Dilemmas administering palliative chemotherapy – a nursing perspective. *Submitted*.
- IV. Näppä U., Lindqvist O., Rasmussen B. H. & Axelsson B. Can a performance status questionnaire decrease palliative chemotherapy treatments in the last month of life? *Submitted*.

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# Abbreviations and explanations

|           |  |
|-----------|--|
| AQEL      | Assessment of Quality of Life at the End of Life   |
| ATC       | Anatomical Therapeutical Chemical classification system  |
| Ca        | Calcium  |
| C-rp      | C-reactive protein   |
| ECOG PSR  | Eastern Cooperative Oncology Group Performance Status Rating                                     |
| ESAS      | Edmonton Symptom Assessment System   |
| IBM SPSS  | International Business Machines Statistical Package for Social Sciences                          |
| ICD-10    | International Statistical Classification of Diseases and Related Health Problems, Tenth Revision |
| IQR       | Interquartile range  |
| LDH       | Lactate Dehydrogenase  |
| LM-group  | Palliative chemotherapy last month of life-group   |
| mAb       | Monoclonal antibody  |
| n         | number   |
| NLM-group | No palliative chemotherapy last month of life-group  |
| NRS       | Numeric Rating Scale   |
| NS        | Not significant  |
| NSCLC     | Non Small Cell Lung Cancer   |
| PASW      | Predictive Analytics Software Portfolio  |
| PCT       | Palliative Chemotherapy  |
| PSPC      | Performance Status in Palliative Chemotherapy  |
| SCLC      | Small Cell Lung Cancer   |
| WMA       | World Medical Association  |
| y         | years  |

# Sammanfattning på svenska

## Dilemman i samband med palliativ cytostatikabehandling när livets slut nalkas

### *Bakgrund*

Cytostatikabehandling som ges vid obotlig cancersjukdom kan minska tumörbörda och besvärande symtom som t. ex smärta. Behandlingen ökar livskvalitet och överlevnadstid i många fall och bör därför erbjudas alla patienter som kan ha nytta av den. Dock är cytostatika potenta läkemedel som kan ge besvärliga biverkningar. Diskussionen i många studier pekar på att den förväntade överlevnaden bör överstiga en månad för att behandlingen ska kunna ha avsedd effekt.

Då cytostatikabehandling vid obotlig cancersjukdom inte kan bota patienten är det alltid en tidsfråga innan nyttan med behandlingen avtar för att till sist helt upphöra. Fortsatt behandling med cytostatika innebär då risk för enbart negativa effekter i form av ökad trötthet, nedsatt immunförsvar och till och med livsförkortning. Möjligheterna att klara av fortsatt cytostatikabehandling bedöms inför varje behandling med blodprover och klinisk bedömning. På sjukhus utan tjänstgörande onkologspecialist träffar patienten sjuksköterskan som ger behandlingen. Ansvarig läkare kontaktas när provsvar eller något i patientens tillstånd avviker från det vanliga.

När sjukdomen framskrider och patientens allmänstillstånd börjar svikta, bör syftet med behandlingen utvärderas och överväganden göras huruvida den ska fortsätta, regimen förändras eller avslutas. Min erfarenhet, ur ett sjuksköterskeperspektiv, av palliativ vård och cytostatikabehandlingar givna till patienter med obotlig cancersjukdom, fick mig att vilja undersöka hur många patienter som behandlas i livets slutskede. Jag ville också ta reda på hur bedömningen av patienten inför behandlingen gick till och om den kunde förbättras, samt hur sjuksköterskan upplevde att ge cytostatikabehandlingar i sent sjukdomsskede.

### *Syften*

- I. Att utforska andelen patienter med obotlig cancer som behandlas med palliativ cytostatika under sista levnadsmånaden samt att finna utmärkande karakteristika för denna grupp patienter.
- II. Att utveckla och psykometriskt testa en kortfattad enkät utformad för bedömning av patientens allmäntillstånd vid palliativ cytostatikabehandling.
- III. Att identifiera situationer som sjuksköterskor kan uppleva som utmanande vid cytostatikabehandling av palliativa patienter med cancer.

- IV. Att undersöka om rutinmässig användning av enkäten utvecklad i studie II påverkat andelen patienter som behandlas med palliativ cytostatika under sista levnadsmånaden, andel sjukhusinläggningar, dokumentation av allmäntillstånd, dokumentation av avslutande av behandling i journal och/eller dödsplats.

### **Metod**

Alla inkluderade patienter i studierna hade cytostatikabehandlats med anledning av obotlig, epitelial cancer (utgående från organens slemhinnecceller) och var 20 år eller äldre. Deltagande sjuksköterskor arbetade på cytostatikabehandlingsmottagningar/avdelningar. Både patienter och sjuksköterskor kom från Jämtland, Västerbotten och/eller Norrbotten. I studie I jämfördes journaldata från avlidna patienter som cytostatikabehandlats under sista levnadsmånaden med dem som avslutat behandlingarna tidigare. I studie II erbjöds patienter att delta i utvecklingen av en enkät som tagits fram för att mäta allmäntillståndet före cytostatikabehandling. I studie III intervjuades sjuksköterskor som arbetar med att ge cytostatika och deras berättelser analyserades med narrativ metod. I studie IV jämfördes journaldata för avlidna patienter som använt enkäten från studie II med matchade kontroller och i tillämpliga frågor data från studie I.

### **Resultat**

Studie I visade att 23 % av alla patienter som cytostatikabehandlats någon gång under sista året före sin död även fick cytostatikabehandling under sista levnadsmånaden. Studien visade också en samvariation mellan behandling sista levnadsmånaden och fler sjukhusvistelser inom en månad efter sista behandling, färre dokumenterade beslut att avsluta behandlingen samt att färre patienter från denna grupp avled i hemmet.

I Studie II konstaterades att den utformade enkäten uppvisade tecken på såväl reliabilitet, validitet som förmåga att detektera när patientens allmäntillstånd försämrades.

Studie III visade att palliativa cytostatika kan upplevas som potenta och oförutsägbara läkemedel, som kan skapa dilemman för de sjuksköterskor som genomför behandlingarna när de ges till patienter som är försvagade av sin cancersjukdom. Sjuksköterskorna upplevde att de ibland stod mitt emellan läkare, patienter och närstående inför behandlingsbeslut.

Studie IV visade ingen statistiskt säkerställd effekt av rutinmässig monitorering av allmäntillståndet med det i studie II framtagna formuläret. Varken behandling under sista månaden i livet, sjukhusvistelser, dokumenterade beslut att avsluta behandling eller dödsplats påverkades. Däremot rapporterade sjuksköterskorna att formuläret gav dem värdefull information om patientens allmäntillstånd inför behandling.

### ***Klinisk nytta för framtiden***

Fynden i studien kan vara till nytta för alla inblandade i cytostatikabehandlingen; patienten, närstående, sjuksköterskan och läkaren. Särskilt i beslutsprocessen om cytostatikabehandlingen ska fortsättas eller avbrytas. Metoder för att bättre bedöma prognostiska faktorer inför cytostatikabehandling behöver utvecklas ytterligare. I en framtida studie skulle formuläret kunna vidareutvecklas för datoriserad användning så resultaten förs in i patientjournalen, där både sjuksköterska och läkare enklare skulle ha tillgång till dem innan behandlingsbeslut.

### ***Slutsatser***

Behandling med palliativ cytostatika nära livets slutskede kan skapa situationer som upplevs som dilemman, både för patienten och för vårdpersonalen. I studierna behandlades 23-25 % av patienterna med cytostatika under sista levnadsmånaden. Dessa patienter vårdades oftare på sjukhus och färre av dem dog i hemmet. Sjuksköterskorna beskrev att de i vissa fall upplevde sig vara "mitt i mellan" i beslutsprocessen om cytostatikabehandling skulle ges eller inte.

Cytostatikabehandlingens oförutsägbarhet visade sig vara ett genomgående tema i avhandlingen. Oförutsägbarheten leder till att individanpassning för varje enskild patient är av största vikt. Försöket till formulärutveckling skulle kunna öka möjligheten att mer objektivt använda allmäntillstånd som en parameter inför behandlingsbeslut när patienten nalkas livets slut. Formuläret visade sig ge sjuksköterskorna värdefull information om patienternas upplevda allmäntillstånd även om denna studie inte visade statistiskt säkerställda skillnader mellan de som använde formuläret och kontrollgruppens patienter. För att ytterligare optimera beslutsfattandet vid palliativ cytostatikabehandling när livets slutskede nalkas krävs fortsatt forskning.

### ***Nyckelord***

Allmäntillstånd, beslutsprocess, cancer, cytostatika, dilemma, enkät, palliativ vård, sjuksköterska

# Suomenkielinen kooste

## Elämän loppuvaiheessa annettuun palliatiiviseen sytostaattihoitoon liittyviä ongelmia

### *Tausta*

Parantumattoman syöpäsairauden yhteydessä annettu sytostaattihoito voi vähentää kasvainkuormaa ja haittaavia oireita kuten esim. kipua. Monissa tapauksissa hoito parantaa potilaiden elämänlaatua ja antaa lisää elinaikaa. Siksi hoitoa on tarjottava kaikille potilaille, jotka voivat hyötyä siitä. Sytostaatit ovat kuitenkin potentteja lääkkeitä, joilla voi olla voimakkaat vaikutukset ja haittavaikutukset. Tutkimukset viittaavat siihen, että jäljellä olevan odotetun eliniän tulee olla yli kuukausi, jotta hoidolla olisi toivottu teho.

Koska parantumattoman syöpäsairauden yhteydessä annettu sytostaattihoito ei voi parantaa potilasta, on aina ajan kysymys, milloin hoidon teho alkaa vähetä loppuakseen viimein kokonaan. Silloin jatkettu sytostaattihoito merkitsee potilaalle vain negatiivisten vaikutusten riskiä lisääntyneen väsymyksen, heikentyneen vastustuskyvyn ja jopa eliniän lyhentymän muodossa. Potilaan mahdollisuus selvittää jatketusta sytostaattihoidosta arvioidaan ennen hoidon aloittamista verikokeiden ja kliinisen arvion perusteella. Jos sairaalassa ei ole päivystävää onkologian erikoislääkärinä, potilas tapaa sairaanhoitajan. Vastaavaan lääkäriin otetaan yhteyttä silloin, kun koevastauksissa tai potilaan tilassa on jotain tavallisuudesta poikkeavaa.

Kun sairaus etenee ja yleistila alkaa heiketä, potilaan elämänlaatu usein heikkenee ja elin aika lyhenee. Tällöin on syytä arvioida hoidon tarkoitusta ja pohtia, jatketaanko vai muutetaanko hoitoa, vai lopetetaanko se kokonaan.

Kokemukseni sairaanhoitajana parantumattomien syöpäpotilaiden palliatiivisesta hoidosta ja sytostaattihoidosta herätti minussa halun tutkia, kuinka moni potilas saa hoitoa elämän loppuvaiheessa. Halusin myös tutkia, miten potilaat arvioidaan ennen hoitoa, onko arvioinnissa parantamisen varaa ja miten sairaanhoitajat kokevat elämän loppuvaiheessa annettavat sytostaattihoidot.

### *Tavoitteet*

- I. Tutkia, kuinka suuri osa parantumattomasta syöpästä sairastavista potilaista saa palliatiivista sytostaattihoitoa viimeisen elinkuukautensa aikana sekä löytää tämän potilasryhmän erottavat tekijät.
- II. Kehittää ja testata psykometrisesti lyhyt lomake, jolla mitataan potilaan yleistila palliatiivisen sytostaattihoidon yhteydessä.

- III. Tunnistaa tilanteita, jotka sairaanhoitajat voivat kokea ongelmallisina syöpäpotilaille annettavan palliatiivisen sytostaattihoidon yhteydessä.
- IV. Tutkia, onko tutkimuksessa II laaditun lomakkeen rutiininomainen käyttö vaikuttanut viimeisen elinkuukautensa aikana sytostaattihoidon saavien potilaiden osuuteen, sairaalahoidojaksojen osuuteen, yleistilan dokumentointiin, päättyneen lääkityksen dokumentointiin potilaskertomuksessa ja/tai kuolinpaikkaan.

### ***Menetelmä***

Kaikki tutkimuksen potilaat olivat saaneet sytostaattihoidon parantamattomaan, elinten limakalvosoluista lähtöisin olevaan epiteelisyöpään. Potilaat olivat 20 vuotta täyttäneitä ja asuivat Jämsän, Västernorrlandin tai Norrbottenin alueella. Tutkimukseen osallistuneet sairaanhoitajat työskentelivät saman alueen sytostaattivastaanotoilla tai -osastoilla. Tutkimuksessa I verrattiin tilastollisia menetelmiä käyttäen kuolleiden, viimeisen elinkuukautensa aikana sytostaattihoidon saaneiden potilaiden potilaskertomustietoja niihin potilaisiin, joiden hoito oli lopetettu ennen viimeistä elinkuukautta. Tutkimuksessa II potilaille tarjottiin mahdollisuus osallistua sellaisen lomakkeen kehittämiseen, joka on laadittu mittaamaan potilaiden yleistilaa ennen sytostaattihoidon aloitusta. Tutkimuksessa III haastateltiin sairaanhoitajia, ja heidän kertomuksensa analysoitiin narratiivisia menetelmiä käyttäen. Tutkimuksessa IV verrattiin kuolleiden, tutkimuksen II lomaketta käyttäneiden potilaiden potilaskertomustietoja sopivaan vertailuryhmään ja soveltuvissa osin tutkimuksen I tietoihin.

### ***Tulokset***

Tutkimus I osoitti, että 23 % kaikista potilaista, jotka olivat saaneet sytostaattihoidon viimeisen elinvuotensa aikana, saivat sitä myös viimeisenä elinkuukautenaan. Tutkimus osoitti myös, että viimeisen elinkuukauden aikana annetulla sytostaattihoidolla oli yhteisvaihtelua seuraavien tekijöiden kanssa: useat sairaalahoidot kuukauden sisällä viimeisestä sytostaattihoidosta, vähemmän hoidon lopettamispäätöksiä ja harvemmat ryhmään kuuluvista potilaista kuolivat kotona.

Tutkimuksessa II todettiin, että laadittu lomake osoitti merkkejä sekä reliabiliteetista, validiteetista että kyvystä havaita erot sellaisten potilaiden välillä, joiden yleistila heikkeni tutkimuksen aikana.

Tutkimus III osoitti, että palliatiiviset sytostaatit voidaan kokea potentteina ja ennalta arvaamattomina lääkteinä. Ne voivat kuitenkin olla ongelmallisia hoitaville sairaanhoitajille silloin, kun sytostaattihoidon annetaan potilaille, jotka ovat syöpäsairautensa heikentämiä. Sairanhoitajat kokivat, että he joskus hoitopäätöksiä tehtäessä joutuivat lääkäreiden,

potilaiden ja läheisten ”väliin” olematta kuitenkaan itse osallisia kommunikaatiosta.

Tutkimus IV ei osoittanut, että tutkimuksessa II laaditun lomakkeen avulla suoritettulla rutiininomaisella yleistilan monitoroinnilla olisi mitään tilastollisesti osoitettavaa tehoa. Sillä ei ollut vaikutusta viimeisen elin-kuukauden aikana annettuun hoitoon, sairaalahoidojaksoihin, dokumentoituihin hoidon lopettamispäätöksiin tai potilaan kuolinpaikkaan. Sairaanhoitajat ilmoittivat kuitenkin, että lomake antoi heille arvokasta tietoa potilaan yleiskunnosta ennen hoitoa.

### ***Klininen hyöty tulevaisuudessa***

Tutkimuksen tuloksista voivat hyötyä kaikki sytostaattihoitoon osalliset, potilas, läheiset, sairaanhoitaja ja lääkäri; päätösprosessissa, joka koskee hoidon jatkamista tai lopettamista.

On kehitettävä entistä parempia menetelmiä yleistilan arvioimiseksi ennen sytostaattihoitoa aloittamista. Tulevassa tutkimuksessa voitaisiin tutkimuksen lomakkeesta kehittää sähköinen lomake, jolla tulokset kirjataan potilaskertomukseen, josta sekä sairaanhoitajat että lääkärit saavat tiedot ennen hoitopäätösten tekemistä.

### ***Johtopäätökset***

Elämän loppuvaiheessa annettu palliatiivinen sytostaattihoito voi aiheuttaa tilanteita, jotka voidaan kokea ongelmallisina sekä potilaan että hoitohenkilökunnan kannalta. Tutkimuksissa 23–25 % potilaista sai sytostaattihoitoa viimeisen elinkuukautensa aikana. Näitä potilaita hoidettiin useammin sairaalassa ja harvemmat heistä saivat kuolla kotonaan. Omien kuvaustensa mukaan sairaanhoitajat kokivat tietyissä tapauksissa joutuneensa ”väliin” sytostaattihoitoa jatkamista tai lopettamista koskevassa päätösprosessissa.

Sytostaattihoitoa ennalta arvaamattomuus osoittautui tutkielman läpikäyväksi teemaksi. Tämä ennalta arvaamattomuus merkitsee sitä, että on erittäin tärkeä räätälöidä hoito jokaiselle potilaalle yksilöllisesti. Tutkielman puitteissa laadittu lomake voisi antaa lisämahdollisuuksia käyttää entistä objektiivisemmin yleistilaa parametrina, kun tehdään hoitopäätöksiä potilaan elämän loppuvaiheessa. Osoittautui, että lomake antaa sairaanhoitajille tärkeää tietoa potilaiden kokemasta yleistilasta vaikka tämä tutkimus ei osoittanutkaan tilastollisesti vahvistettavia eroja lomaketta käyttäneiden ja vertailuryhmän potilaiden välillä. Vaaditaan lisätutkimusta, jotta voitaisiin optimoida päätökset, jotka koskevat palliatiivista sytostaattihoitoa elämän loppuvaiheen lähestyessä.

***Hakusanoja*** Kyselylomake, ongelma, palliatiivinen hoito, päätöksenteko, sairaanhoitaja, sytostaattihoito, syöpä, yleistila.



# Introduction

The starting point for my participation in this research project was my work as a nurse in oncology and palliative care. In this work, I often met patients with incurable cancer receiving palliative chemotherapy treatment (PCT). When the patients were in good physical condition, the treatments resulted in few problems and could go on for several months. However, sooner or later all patients receiving PCT gradually deteriorated and began to experience more side effects, becoming too weak and/or not responding to the treatment.

At this point, treatment seemed to be no longer beneficial, and perhaps even harmful. I have seen patients spend the weeks between PCTs in bed, hardly able to eat. However, many of the patients I have met wanted their treatments to go on despite gradual deterioration, as they saw the PCT as a lifeline. The decision of whether to continue or stop PCT is difficult for all parties involved: patients, next-of-kin, nurses, and physicians. PCT may lead to outcomes that were unpredictable, unexpected, or not previously discussed with patients and their next-of-kin; some of these outcomes will be discussed in this thesis. The deciding physician and nurse may encounter difficulties when the beneficial effects of continued PCT are virtually non-existent yet the suggestion of ceasing PCT may be interpreted as removing the patient's last hope of cure. My experience as a nurse is that when administering PCT to deteriorated patients we sometimes feel unsure about whether the indication is right. Sometimes a round of treatment may produce grave side-effects, but another time the patient may recover, and gain both better performance status and prolonged survival from a change of regimen.

Optimizing the use of palliative chemotherapy – treating those patients who will benefit from treatment and excluding those who will only suffer from side-effects – requires a conscious and careful decision-making process. From this perspective, it becomes especially important for nurses and physicians to be able to detect deteriorating patients for whom further PCT will most likely be futile or even harmful. To abstain from making an active decision to pause or cease PCT in a situation of poor performance status may put both the quality and length of life at risk in an ethically problematic way.

These thoughts and experiences served as triggers for my interest to get involved in this research project.

# Background

The treatment of incurable cancer is a dilemma in contemporary society. “Dilemma” is a Greek-derived word which describes an undesirable situation involving a choice between options that are – or seem – equally unfavourable. The need to choose creates a state of uncertainty or perplexity.<sup>1</sup>

Several ethical and moral dilemmas exist in the medical world. Even when a patient with incurable cancer deteriorates, medical professionals might want to provide treatment to fight the disease, despite being well aware that eventually this will always be futile and maybe even harmful. In this position, the logical consequence would be to cease oncological treatment in order to avoid harming the patient. However, ceasing disease-directed treatment does not feel acceptable either, as it could be regarded as giving up.

Answers to dilemmas are contextual and conditional; they depend on the individuality of the situation and can be redefined according to changes in that situation. Dilemmas can change, and no answer is final.<sup>2</sup> To patients and next-of-kin, PCT at least initially symbolizes a hope of improvement and sometimes even cure. As such it is an uncertain and subjective possibility for the patient.<sup>3</sup> Unfortunately, for many patients with cancer, the hope of cure is unrealistic. In Sweden about 22-23000 persons die of cancer every year, which is some 25% of the total number of deaths (90-92000).<sup>4</sup> Cancer cannot be fully controlled, and its incurability and unpredictability make it one of the most feared diseases in our society.

## Palliative care

When cure is no longer possible, medical care should aim for a transition to palliation. Palliative care is provided to patients suffering from diseases that are not only malignant but always incurable. According to the World Health Organization (WHO), providing palliative care to these patients is

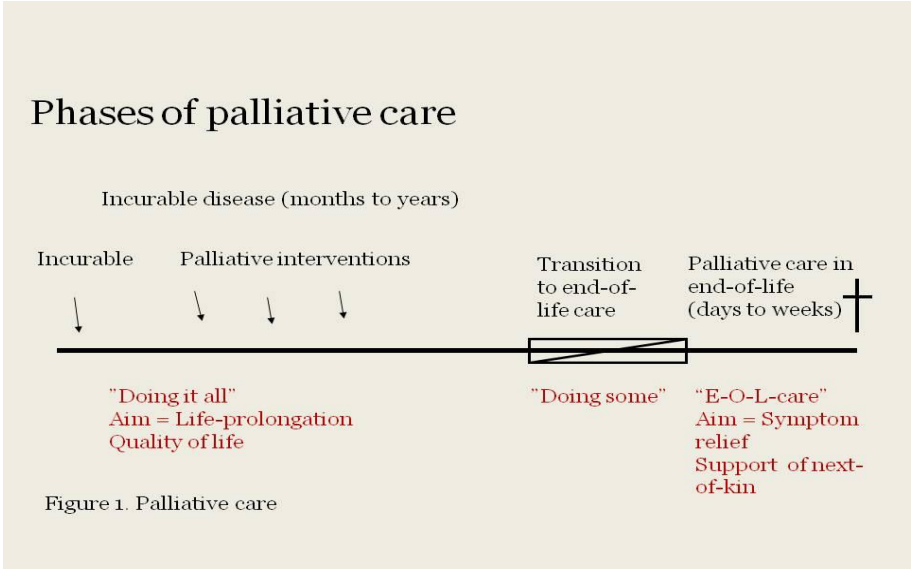
*[. . .] an approach that improves the quality of life of patients and their families, facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual.<sup>5</sup>*

A palliative care philosophy such as this will provide total care, which in the early phases also includes cytotoxic agents, as well as pain and symptom management and proactive engagement of patient and next-of-kin in care planning.

Unfortunately, researchers have frequently confused palliative care with end-of-life care. Most of the scientific literature does not embrace active cancer treatments such as PCT within palliative care.<sup>6,7</sup> However, a new perspective is now emerging where early palliative care includes the optimal usage of PCT and its timely cessation.<sup>8,9</sup> Palliative care should focus on relieving suffering in all of its dimensions, throughout the trajectory of a patient's incurable illness.<sup>10</sup> WHO suggests that palliative care:

*[. . .] is applicable early in the course of illness, in conjunction with other therapies that are intended to prolong life, such as chemotherapy or radiation therapy, and includes those investigations needed to better understand and manage distressing clinical complications.<sup>5</sup>*

Bruera and Hui suggest that, even with on-going PCT a palliative care team including the patient, the patient's family, nurses, and the patient's physician should be formed as soon as possible. This team approach could provide patients with better physical and emotional symptom control, and might encourage them to make decisions about their own care with less distress.<sup>11</sup> Concurrent integration of palliative care with anti-cancer treatments can improve quality of life and decrease the incidence of depressed mood.<sup>12</sup> Combining PCT with early palliative care can also prolong survival.<sup>8</sup>



Palliative care should be a process starting with the intent to prolong life and increase quality of life. Eventually, the patient comes to a breakpoint or zone

of transition where the aim of prolonging life is no longer realistic, and the focus switches to actions aimed at optimizing symptom relief and supporting the patient's next-of kin; in other words, palliative end-of-life care<sup>13</sup> (Figure 1). The realities of these phases of palliative care need to be communicated to the patient at an early stage. The importance of early disclosure about incurability and discussions about end-of-life care has been stressed in broad consensus among health care professionals.<sup>14</sup> Patients who are only given good news about their disease tend to inflate the information and have a less realistic understanding of what is going to happen to them.<sup>14</sup>

Terminology is a significant problem in the field of palliative care and end-of-life care. Care provided to patients with progressive and incurable illness has been referred to as "terminal care", "palliative care", "supportive care", "hospice care" and "end-of-life care". This variation in terminology may reflect an evolving clinical discipline and/or a rather loose and unformulated approach to the problem area. "Palliative care" and "end-of-life" care are used most commonly, with almost similar frequency, though recently the latter term has been the favoured one.<sup>15</sup> This thesis uses both terms: "end-of-life care" meaning palliative care when life prolongation by further treatment of the cancer disease itself is no longer realistic. Accordingly "palliative care" covers a substantially longer period of time and includes "end-of-life care" when death is imminent.<sup>15</sup>

One obstacle in providing end-of-life care is the difficulty of identifying when it begins; the period is usually defined in retrospect after the patient has died. It has been suggested that the term "end-of-life" should apply to at most the last year of life. Usually in cancer the last three months of life are marked by declining objective markers of health, reduced function, and increased symptoms.<sup>15</sup> Instead of an exact definition, the time frame can be viewed as death being inevitable within a foreseeable time, meaning the time left in life is short; maybe hours, days, weeks, or months.<sup>16</sup>

A systematic review including different prognostic factors revealed that the course of most cancers eventuates in a fairly universal clinical picture: decreasing performance status, weight loss, metastases to the brain, spine, or liver, and laboratory abnormalities indicative of inflammation and extensive disease. Most prognostic factors are continuous, independent risk factors for mortality. Decreased performance status in combination with one or more of these factors may predict end-of-life.<sup>17</sup>

Prediction of end-of-life has been attempted in patients suffering from incurable cancer. Frigeri et al. recorded clinical and laboratory parameters such as Eastern Cooperative Oncology Group performance status rating (ECOG PSR), presence of ascites, white blood cells, haemoglobin, platelets, total bilirubin, albumin, LDH, C-rp, and Ca 19.9. Unfortunately, none of the

laboratory tests were able to predict individual survival with sufficient accuracy.<sup>18</sup> Another way to predict survival is using clinical indicators. The care team can ask questions such as: Was this patient's condition expected to deteriorate in this way? Is further life-prolonging treatment appropriate? Have potentially reversible causes of deterioration been excluded?<sup>13</sup> Attempts to use algorithms for death prediction in end-of-life cancer have not been met with general acceptance because of inefficiency, difficult implementation, and finally because in palliative care the patient is viewed holistically and such scoring systems are seen as an undue generalization.<sup>19</sup>

Palliative care should be a proactive rather than reactive approach, to ensure that treatments or referrals are initiated early and appropriately. The physician in charge should enquire at an appropriate time about any advance decisions the patient might wish to make. All health care professionals dealing with incurable persons should have a clear understanding of how to discuss, facilitate, and provide access to these choices.<sup>20</sup> End-of-life care should also imply a changed goal of care, as the striving to prolong life is replaced with symptom relief and support of next-of-kin (Figure 1). The latter could include emphasizing support of end-of-life planning within the family.<sup>13,14</sup> OPCARE9 is a European collaboration which aims to optimize research and clinical care for cancer patients in the last days of life. The nine OPCARE9 countries (Argentina, Italy, Germany, the Netherlands, New Zealand, Slovenia, Sweden, Switzerland, and the United Kingdom) have published quality indicators for good care during a patient's final days. One of these suggested indicators is that fewer than 10% of patients who died from cancer should have received PCT in the last 14 days of life.<sup>21</sup> Hence, providing good palliative care when the patient has apparently reached end-of-life includes timely cessation of PCT.

## **Palliative care in rural settings**

Palliative care needs arise irrespective of where people are living. The Swedish National Guidelines of Palliative Care recommend that palliative care should be provided to all inhabitants of Sweden, regardless of where they are living or cared for.<sup>16</sup> The studies in this thesis were performed in the three northernmost counties in Sweden. The area is a mix of urban areas in the east, close to the Gulf of Bothnia, and sparsely populated rural areas close to the mountains in the west. Home visits from a palliative home care unit to a single patient may require a round trip of up to 500 km, and a one-way journey for a patient to the university hospital could be up to 600 km.

This situation exists not only in Northern Sweden, but also in locations such as, Kansas,<sup>22</sup> British Columbia,<sup>23</sup> and rural Australia.<sup>24,25</sup> Sabesan et al. described how oncologists travel to larger rural centres with a frequency

ranging from weekly to three monthly, while in between these visits the patients are managed by local medical officers.<sup>25</sup> In an Australian study from 2009, PCT was given by chemotherapy-trained nurses (61%) as well as other nurses at rural hospitals administering chemotherapy; only 33 of these 157 hospitals (21%) had a resident medical oncology service.<sup>24</sup> Palliative care is presumed to be provided via teamwork involving all professions.<sup>16</sup> In rural areas, the population base is too small for care to be provided in the same way as in urban areas. Oncologists are employed at bigger hospitals and cannot manage to visit smaller units more often than, for example, once a week. Physicians and nurses at smaller units are thus required to work more independently; performing interventions that otherwise might not have been done at all outside the university departments. This is a pragmatic solution as long as it is accompanied by the required competence and skill; the patient can avoid tiring travelling, and the medical care system saves money by providing the patient with treatment closer to home.

## **Palliative chemotherapy**

Chemotherapy as a means to treat cancer has been under development since the 1940's.<sup>26</sup> Palliative chemotherapy is by definition unable to cure the cancer, but is used with the intent to decrease harmful symptoms, tumour burden, and pain while increasing quality of life and/or prolonging life. Hence, PCT should be considered as a treatment option in every case of incurable cancer.<sup>20,27-31</sup> The decision to treat is tailored by the treatment's expected effectiveness and a clinical assessment by the oncologist or physician in charge, and is dependent on the patient's informed consent.<sup>27,32</sup>

PCT is not the best choice for all patients and all cancer diagnoses, as some cancers are more insensitive than others. To illustrate the existing range of sensitivity to PCT, patients with breast cancer or small cell lung cancer (SCLC) may respond positively to treatment even if the patient has an advanced disease. At the other end of the spectrum, most renal and endometrial cancers are more or less resistant to chemotherapy.<sup>27</sup> Adding to the complexity is that within a specific cancer form it is very difficult to predict the therapeutic response in a specific individual. A person who initially responds well to the chosen type of PCT may progress some months later; if changed to another PCT combination another period of response is possible but not certain, and for each new line of treatment the chance of response becomes progressively less.<sup>27</sup>

As chemotherapy affects all cells in the body – both normal and cancer cells – its apoptosis-promoting potential may sometimes cause more harm than good. A minimal level of general strength/performance status has to be present to avoid detrimental effects on general health. The consequences of

giving chemotherapy agents to very weak patients can be serious or even lethal.<sup>27,29,33,34</sup> To help decide whether PCT should be administered or not, routine blood samples are analysed for haemoglobin, leucocytes, and platelets. Values below established limits are interpreted as a sign of bone marrow suppression, a condition that implies a substantially increased risk for complications such as infections, anaemia, and/or bleeding if PCT is not delayed or stopped.<sup>20,27</sup> More aggressive treatments used near death, irrespective of cancer diagnosis, should be avoided as they do not prolong survival.<sup>8,35-38</sup> Furthermore, PCT given close to impending death decreases the likelihood of receiving hospice care<sup>36</sup> and increases the rate of intensive care unit admissions.<sup>37</sup> Patient outcomes are generally not improved if the chemotherapy does not significantly cause reduction in tumour size<sup>27,33,39</sup> or when the side-effects result in a substantial worsening of quality of life<sup>20,40,41</sup> or even threatens a patient's life.<sup>8,41-43</sup>

One study revealed that acceptance of aggressive treatments in a palliative scenario differed between patients, healthy controls, and medical staff. In general, the patients were most likely to accept aggressive PCT, and were also ready to accept the lowest chance of benefits. Medical oncologists, general practitioners, and cancer nurses were in between patients and the healthy controls.<sup>44</sup> Other studies have shown that many patients are inclined to undergo vigorously toxic treatments even if the beneficial effects are small,<sup>45-47</sup> and their expectations about survival often exceed the actual survival time.<sup>48</sup>

Indications for the use of PCT and the number of available drugs are constantly increasing, although it is not clear that survival has increased in elderly and frail persons.<sup>28,41</sup> Survival is not the only outcome worth measuring when evaluating the beneficial effects of PCT. Chemotherapy can also be a good help to reduce symptom burden, increase time to progression, and improve quality of life. Optimal PCT should alleviate symptoms of disease with a minimum of side effects.<sup>20</sup> However, the experience of the physician can be that death is not accepted socially until every heroic treatment has been tried.<sup>49</sup> International studies show that despite doubting the benefits, physicians are inclined to offer further PCT in order to avoid disappointing patients and/or relatives who are pressing for treatment.<sup>49-51</sup> Reasons for over-treatment include the physician's overestimation of the patient's survival prognosis, reticence among physicians to provide information about the reality of the disease, and/or lack of communication between the oncologists and palliative care providers.<sup>46,50,52</sup> Other reasons not to end PCT despite declining performance status can be that the patient is young,<sup>47,53-55</sup> is highly educated, has pressuring relatives,<sup>50</sup> or has not fully accepted the incurability of the disease.<sup>34,56</sup> Conversely Buiting et al. found that second or third line PCT could help patients to cope with the fear of

approaching end-of-life by keeping their focus on living in the present, regardless of perceived side-effects. However, they also argued that efforts should be made to help patients find other ways to cope with the fear of impending death.<sup>51,57</sup>

The proportion of PCT administered in the last month of life is quite substantial, but varies to a large extent between different reports; studies published from 2003 to 2013 report proportions between 9% and 43%.<sup>18,54,58-60</sup> These variations are probably due to different inclusion criteria, different denominators, and maybe also different local treatment traditions.

Use of the last month of life as a time frame in these studies could be an indication that at least one month of post-treatment survival is needed for PCT to have its intended effect, including the possibility of prolonging the patient's life.

## **Informing the patient about PCT**

According to the Swedish Law of Health Care (HSL 1982:763), a prerequisite for any medical care is that all parties involved, including the patient, should be in agreement based on truthful treatment information. Hence, comprehensible information about the situation should be presented to the patient and/or next-of-kin as personal conversations. The conversation should include information about possible medical effects and/or side-effects, and reasonable treatment alternatives. The patient is also offered a possibility of a second opinion. The National Board of Health and Welfare in Sweden (regulation SOSFS 2011:7 on withholding life-sustaining treatments) states that any cognitively intact patient has a full right to cease or abstain from initiating life-sustaining treatments. At this point, the responsible physician is obliged to document the underlying assessments and the content of the planned care in the patient's medical record. This can be applied to PCT, stressing the necessity of providing comprehensive information to patients before and during treatment as well as a continuous preparedness to detect any signs of the patient being hesitant or unwilling to continue PCT. An important part of this information would be to stress that ceasing PCT will not imply abandonment by medical care, but merely a change of focus and perhaps the gradual introduction of palliative care professionals.

It is a pedagogical challenge for the physician and health care team to empathically inform the patient in a realistic way about the achievable effects and limitations of the proposed PCT. This is also stressed in the literature as a prerequisite for patient autonomy and a true understanding of when continued PCT is no longer the best option.<sup>13,20,27,47</sup>



From the start of contemplating PCT, it is important to begin a dialogue with the patient about realistic aims of the suggested PCT. When a patient's health then deteriorates, the patient must again be informed about both advantages and disadvantages of continued treatment.<sup>57,61</sup> Finally, the process of deciding to cease PCT is a delicate matter involving several players including the physician, nurses, the patient, and family members.<sup>20,62</sup>

## **Performance status in palliative chemotherapy**

Several authors, including the task force of the European Association of Palliative Care on prognostic factors in advanced cancer,<sup>63</sup> have argued that performance status should be an important parameter in the decision to give or withhold PCT.<sup>63-65</sup> Providing a correct estimation of performance status is challenging both for the treating physician<sup>61</sup> and for the health care team.<sup>66</sup> When PCT is given in even rounds, performance status frequently worsens during the 1-2 weeks after treatment, and a dip in bone-marrow function is common 7-14 days after treatment. Usually, both blood samples and patient recover during the third week, and performance status is at its best when the next PCT is due.<sup>27,29,33</sup> As mentioned above, blood tests are currently conducted as a routine screening test before PCT, but performance status is not routinely measured.<sup>67</sup> An accurate assessment of the patient's overall performance status at this time is not an easy task for any professional, but is recommended as an integrated part of every treatment decision.<sup>20,27,33</sup>

Whether routine assessment of performance status constitutes a quick look by health care professionals when the patient walks into the room, or is bound to be a result of systematic questioning in a predetermined way, may be a matter of debate for which future research can provide further arguments.

Who is best placed to measure performance status: the patient or the health care team? Generally, the patient knows their own status better than anyone. Nevertheless, Conill et al.'s classic study showed that patients' and physicians' assessments correlated fairly well.<sup>68</sup>

Earlier studies on PCT, as measured with ECOG PSR<sup>69</sup> (Table 1), mostly included patients with a relatively unaffected performance status: 0-1, occasionally patients with ECOG PSR 2 (moderate influence on performance status) were included,<sup>27-29,70</sup> but little evidence exists for PCT in patients with performance status worse than this. There is some evidence of beneficial effects from first-line treatment of rather chemo-sensitive tumours with ECOG PSR  $\geq 3$ .<sup>27-29,64,70-74</sup>

Assessment of performance status has been widely used in cancer therapy to measure the impact of disease on the patient in terms of loss of function,

physiological effects, and psychological effects.<sup>68</sup> Performance status in PCT is mainly associated with survival together with demographics, tumour-associated factors, symptoms and psychological wellbeing. Extensive investigation of performance status has revealed an association with survival duration; if performance status decreases, the duration of survival will be shorter.<sup>18,27,29,33,38,74-76</sup> Scales measuring performance status classify the patient's functional level and thereby predict various outcomes in the trajectory of disease.<sup>75</sup> If the patient's tumour is less sensitive to PCT and more than one treatment line has been given, withholding additional treatments should be considered, as there is little probability of a positive response but an increased risk of side-effects regardless of decreased performance status.<sup>20,41</sup> Many questionnaires measure performance status, physical activity, and quality of life.<sup>77</sup> However, well-established performance status measures such as the Karnofsky Index<sup>26</sup> or the ECOG PSR<sup>69</sup> are completed by a physician or nurse rather than the patient. Moreover, these instruments are designed to measure performance status in patients with cancer in general, not specifically patients undergoing PCT (Table 1).<sup>20</sup>

**Table 1. Staff-completed performance scales: Karnofsky Index and ECOG PSR**

| <b>Karnofsky scale</b> | <b>ECOG PSR score</b> | <b>Definition</b>   |
|------------------------|-----------------------|---|
| 90, 100%               | 0                     | Fully active, able to carry on all pre-disease activities without restriction   |
| 70, 80%                | 1                     | Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature            |
| 50, 60%                | 2                     | Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours |
| 30, 40%                | 3                     | Capable of only limited self-care, confined to bed or chair more than 50% of waking hours                                       |
| 10, 20%                | 4                     | Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair.   |
| 0%                     | 5                     | Dead  |

The WHO performance scale is often referred to as an assessment tool. A literature search revealed no validations of this tool, but it is identical with the ECOG PSR, which has been validated. Hence, the present thesis refers only to this validated scale.

Some instruments are designed to be completed by the patient: such as the European Organisation for Research and Treatment of Cancer - Quality of Life Questionnaires for cancer in general (EORTC QLQ -C30)<sup>78-80</sup> or for palliative patients with cancer (EORTC QLQ-15 PAL),<sup>81</sup> the Assessment of

Quality of Life at the End of Life (AQEL),<sup>82,83</sup> and the Edmonton Symptom Assessment System (ESAS).<sup>84,85</sup> ESAS focuses on the assessment of symptoms rather than performance status, but includes two items covering “tiredness”, and “feeling of wellbeing” (Table 2). Generally, staff and patient ratings in scales do not correspond very well.<sup>73,86</sup> In the literature, patient-completed measures are regarded as most valid.<sup>86,87</sup>

**Table 2. Patient completed scale: the Edmonton Symptom Assessment System (ESAS)**

| Please circle the number that best describes   |                           |                        |                                     |
|--|---------------------------|------------------------|-------------------------------------|
| 1  | No pain                   | 0 1 2 3 4 5 6 7 8 9 10 | Worst possible pain                 |
| 2  | Not tired                 | 0 1 2 3 4 5 6 7 8 9 10 | Worst possible tiredness            |
| 3  | Not nauseated             | 0 1 2 3 4 5 6 7 8 9 10 | Worst possible nausea               |
| 4  | Not depressed             | 0 1 2 3 4 5 6 7 8 9 10 | Worst possible depression           |
| 5  | Not anxious               | 0 1 2 3 4 5 6 7 8 9 10 | Worst possible anxiety              |
| 6  | Not drowsy                | 0 1 2 3 4 5 6 7 8 9 10 | Worst possible drowsiness           |
| 7  | Best appetite             | 0 1 2 3 4 5 6 7 8 9 10 | Worst possible appetite             |
| 8  | Best feeling of wellbeing | 0 1 2 3 4 5 6 7 8 9 10 | Worst possible feeling of wellbeing |
| 9  | No shortness of breath    | 0 1 2 3 4 5 6 7 8 9 10 | Worst possible shortness of breath  |
| 10   | Other problem             | 0 1 2 3 4 5 6 7 8 9 10 |                                     |
| Completed by <input type="checkbox"/> patient <input type="checkbox"/> caregiver <input type="checkbox"/> caregiver assisted |                           |                        |                                     |

All these extensive assessment tools include at least ten questions and are constructed to broadly measure symptoms or quality of life, rather than focusing solely on performance status or patients receiving PCT. Furthermore, Tishelman et al. have shown that standardized questionnaires for patient-reported outcomes often miss important patient experiences, as these tools do not use open-ended questions. If the patient is provided with an opportunity to recollect their own experiences without a predetermined question, they might be able to report discrete symptoms or functional disturbances not easily assessed elsewhere.<sup>80</sup> Therefore an open-ended question may be an important complementary item in a questionnaire attempting to assess performance status.<sup>88</sup>

To summarize, performance status may be an aid in trying to prognosticate remaining survival time. Criteria for a performance status assessment tool suitable for repeated use before PCT are that it should be patient-completed, brief, and in Swedish; it should include an open-ended question; and it should be valid, reliable, and sensitive to change. As no such assessment questionnaire was found, the task of trying to develop one emerged.

## **Palliative chemotherapy treatments from a nurse's perspective**

Studies show that patients could be very motivated to receive treatment, and willing to endure toxicity even if the treatment would only extend their life for a short time.<sup>46,89</sup> Although PCT is tailored by the oncologist on the basis of the expected effectiveness and the patient's condition, wishes, and experience of treatments,<sup>27,32</sup> it is usually administered by nurses.<sup>51,61</sup> Earlier studies have shown that nurses spend much time with patients during these treatments,<sup>34,90</sup> and accordingly get to know them and often build close emotional bonds.<sup>91,92</sup> Thus, nurses are in a unique position to observe the variations occurring over time in a patient's general condition and clinical response to PCT.<sup>34,90,91</sup> However, research shows that nurses describe their role as informal "suggestors" or "requestors" to the physician, with no formal role in decision-making about PCT.<sup>51,90,93</sup>

Administering PCT may be problematic for nurses. If the physician and patient have not discussed the possibility of disease progression, it can be difficult for the nurse to initiate conversations about stopping PCT with patients whose general condition has declined.<sup>51,91,94</sup> Both Buiting et al. and McCullough et al. found that patients present slightly different information about their general condition to their physicians than they do to their nurses. As patients are fully aware that nurses do not have the authority to stop PCT, they are much more likely to talk about fatigue and the possibility of postponing treatments with their nurses than with their physicians.<sup>34,51</sup> Sometimes the nurse has a different opinion of the relevance of continued PCT than the patient, which may create an ethically problematic situation.<sup>95,96</sup> Nurses who have to administer PCT that they deemed futile often experience strong emotional and moral distress, and may even experience the intervention as violent and cruel.<sup>95</sup> They may have difficulty in maintaining a positive approach to PCT when they are ambivalent about administering it.<sup>94</sup> In addition, they often feel morally conflicted and dishonest when they cannot understand or explain the benefits of PCT to a patient in whom no improvement or symptom relief is observed.<sup>96,97</sup>

Another problematic situation arises for nurses when next-of-kin insist on PCT. Next-of-kin could sometimes be the driving force behind PCT, and make decisions for the patient to undergo treatment even when medical staff had informed them that it would be detrimental to the patient's condition.<sup>34,94,98</sup> As the number of different regimens of PCT for patients with incurable cancer increases, so does the likelihood of nurses being confronted with difficult situations when treating vulnerable patients.

To enable future improvements of PCT routines, an essential part of this research project is to investigate the nature of any dilemmas experienced by nurses in the existing culture of care.

## **Rationale for the thesis**

The focus of this thesis is palliative chemotherapy treatment when approaching end-of-life, and potential dilemmas relating to this. To explore this topic further following questions arose: Which is the frequency of PCT during the last month of life in the northern region of Sweden, and could any unfavourable effects on these patients be detected? Could routine assessment of performance status before every round of PCT be a way to identify patients too weak for further treatment, and thus minimize the risks of over-treatment? Could we develop a reasonably brief and comprehensive assessment tool for performance status, suitable for routine use? How do registered nurses administering PCT to weak, incurable patients experience their task?

It is a difficult balancing act to recognize the apparently seamless transition from stable disease to deterioration to eventual end-of-life care, and to adapt care interventions accordingly. Increasing our knowledge and understanding of PCT could be one step towards further optimization of the palliative care provided to this vulnerable group of people.

## ***Specific aims of the studies***

- Study I: To analyse the proportion of patients with incurable cancer who received palliative chemotherapy during the last month of life, and to identify their discriminative characteristics.
- Study II: To develop a questionnaire assessing performance status in palliative chemotherapy, and to test its psychometric properties.
- Study III: To explore challenging situations experienced by registered nurses when administering palliative chemotherapy to patients with incurable cancer.
- Study IV: To investigate whether routine use of the Performance Status in Palliative Chemotherapy (PSPC) questionnaire in PCT would affect the proportion of patients receiving PCT during the last month of life, hospital admissions, notifications of performance status, documented decisions of ceasing PCT in the medical records, and/or place of death. A secondary aim was to gather registered nurses' experiences of PSPC in clinical use.

# Materials and methods

## Settings and inclusion criteria

This thesis focused on PCT in the three northernmost counties in Sweden: Jämtland, Västerbotten, and Norrbotten, which together cover an area of 203 756 km<sup>2</sup> (almost half of Sweden) and had a total of 636 737 inhabitants in 2013 (3.12 per km<sup>2</sup>).

Table 3 provides the settings and inclusion criteria for the four studies. The area is served by one oncology department, located at the university hospital in the area, and eight local hospitals. Two of the local hospitals received weekly visits from an oncology consultant who saw pre-selected patients to make decisions about their PCT. The other six hospitals had specialist oncology support only by phone or mail resulting in many out-patient visits to the oncology department at the university hospital. Accordingly, specialists in fields other than oncology maintained the everyday medical responsibility for many patients with cancer who received PCT outside the university hospital. These peripheral units were all staffed by registered nurses working more or less full time on administration of PCT. A request was sent to all hospitals in the region for permission to extract data from the medical records. In this thesis, the word “nurses” has been used for all registered nurses and the word “physician” for all medical doctors.

**Table 3. Settings and inclusion criteria**

| Study            | Settings                              | Inclusion criteria   |
|------------------|---------------------------------------|--|
| <b>Study I</b>   | Jämtland, Västerbotten and Norrbotten | Deceased patients who had lived in the region, had had cancer in epithelial tissue, had been treated with PCT at oncology, surgery, gynaecologic, or pulmonary medicine units, and were 20 years or older at time of treatment.  |
| <b>Study II</b>  | Jämtland and Västerbotten             | Patients who lived in the region, had cancer in epithelial tissue, were treated with intravenous PCT at surgery or pulmonary medicine units, were at least 20 years old, were cognitively intact, were able to speak and read Swedish, and had given informed consent to participate in the studies.   |
| <b>Study III</b> | Jämtland, Västerbotten and Norrbotten | Registered nurses who were working in the region at chemotherapy units, had at least two years' experience of administering PCT, and had given informed consent to participate in the study.   |
| <b>Study IV</b>  | Jämtland and Västerbotten             | Patients who had lived in the region, had had cancer in epithelial tissue, had been treated with PCT at oncology, surgery, gynaecologic, or pulmonary medicine units, and were 20 years or older at time of treatment, and had used the PSPC questionnaire developed in Study II or been matched as one of two controls for each patient regarding hospital unit, gender, age ( $\pm 5$ years), year of death ( $\pm 3$ years), and diagnosis. |

At hospitals without a resident oncologist, a physician's confirmation to give a round of PCT was based on the nurses' observation of the patient and normal blood tests for haemoglobin, platelets, and leucocytes. The nurses reported to the responsible physician if there were any changing conditions that could necessitate a new medical assessment whether PCT should be adjusted, paused, or withdrawn. Most patients were seen by a physician only at certain "crossroads" during the treatment, not in conjunction with every round of PCT. Irrespective of who made the decision about the PCT, the patient was continuously followed by a nurse including follow-up calls in between treatments. Accordingly, nurses played an important role in PCT as most of the responsibility of assessing the patients' performance status was transferred to them. Table 4 provides an overview of methods used for data collection, analysis, and design.

**Table 4. Data collection, analysis and design.**

| <b>Study</b>     | <b>Data collection</b>  | <b>Analysis</b>   | <b>Design</b>                             |
|------------------|---|---|---|
| <b>Study I</b>   | Information from medical records                                    | Descriptive and non-parametric statistics                     | Retrospective quantitative study          |
| <b>Study II</b>  | Questionnaires: PSPC, ESAS  | Descriptive and comparative statistics                        | Quantitative                              |
| <b>Study III</b> | Research interviews   | Narrative analysis  | Qualitative                               |
| <b>Study IV</b>  | Information from medical records, questionnaires, and work- journal | Descriptive and non-parametric statistics<br>Content analysis | Quantitative case control and qualitative |

## **Participants**

### ***Study I – Patients receiving PCT***

The data in Study I were retrospectively collected from the computerized medical record system in the three counties. Records were identified by selecting the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10) code for chemotherapy treatment (Z51.1), and a manual search of these was then performed to identify patients who had died from an epithelial cancer disease and who had received PCT during 2007 and/or 2008. The search yielded 374 persons (190 men/184 women, aged 32-87, median 66) who had been treated with PCT and died of epithelial cancer during 2008. Epithelial cancers were chosen in order to allow comparison of results, since most studies found in the literature concern epithelial tumours. The total number of deceased patients who had died from epithelial cancers in 2008 in Jämtland, Västerbotten, and

Norrbotten (N=1200) was identified via data from the Oncology Centre Northern Region.<sup>99</sup>

### ***Study II – Development of the Performance Status in Palliative Chemotherapy questionnaire (PSPC)***

The data in Study II were collected from questionnaires (PSPC and ESAS) completed by patients meeting the inclusion criteria in Table 3. Attending nurses at the chemotherapy units invited eligible patients to the study between 2008 and 2010. The two tests of reliability included a total of 68 patients (33 patients, 14 men/19 women, aged 42-79 years, median 64 years; and 35 patients, 9 men/26 women, aged 37-88, median 64). Sensitivity to change was tested in 106 patients (47 men/59 women, aged 38-90, median 64.5), readability in 5 patients (2 men/3 women, ages unknown), and validity in 47 patients (17 men/30 women, aged 37-80, median 62).

Participants in the studies of readability and reliability were contacted by the author by phone and mail, and participants in the studies of sensitivity to change and validity were invited by the attending nurses at the units. Written and verbal information was provided to all participants by the author or nurses at the units, and signed informed consent was acquired before participation.

### ***Study III – Participating nurses at chemotherapy units***

The data in Study III were collected via research interviews. All head nurses at the chemotherapy units at the eight hospitals administering PCT in the area were contacted by mail and asked to send a participation request for an interview to the nurses working at their units, with the aim of including one or two nurses per unit. The inclusion criteria are given in Table 3. The nurses who agreed to participate (17 women, aged 32-62, median 49) suggested a time and a place for the interview, and all chose to be interviewed at their respective workplaces between May 2011 and October 2011. Written and verbal information was provided, and signed informed consent was acquired before the interview.

### ***Study IV – Patients using the PSPC and matched controls receiving PCT***

The data in Study IV were collected from the Oncology Centre Northern Region,<sup>99</sup> medical records, and questionnaires filled in by patients receiving PCT at chemotherapy units at four hospitals. Patients (n=80) receiving PCT were invited by the nurses on duty at the units to participate in the study between January 2010 and April 2013. The nurses provided written and verbal information to all participants, and signed informed consent was acquired before participation. After the patients had died, each one was



manually matched with two deceased control patients (240 patients, 104 men/136 women, aged 32-91, median 65). All potential control patients were identified by the ICD-10 code for chemotherapy treatment (Z51.1) in the computerized medical record system. The total number of deceased patients who had died from epithelial cancers in 2012 in Jämtland and Västerbotten was 786. Data from informal interviews conducted with nurses at the units were collected in work-journals.

## **Data collection**

### ***Medical records***

Retrospective medical record studies were conducted to find out the proportions of patients treated with PCT during the last year of life and particularly the last month of life. Medical records were searched for patients who had received PCT, defined as chemotherapy with non-curative intent. Cytotoxic drugs were classified according to the Anatomical Therapeutic Chemical (ATC) Classification System. Drugs used could be chemotherapy, protein kinase inhibitors, or monoclonal antibody (mAb) treatments.<sup>100</sup> The term “chemotherapy” is used for all these drugs.

The following data were manually collected according to a predetermined study protocol: gender, residential area, age, diagnosis, median duration of PCT, time from first PCT to death, time from last PCT to death, chemotherapy line and type, number of hospital admissions with or without PCT-related reasons, documented decision to cease treatments, and place of death. Reasons defined as PCT-related were deterioration, infection, nutrition difficulties/nausea, and chemotherapy treatment administered during a hospital admission.

### ***Questionnaires***

Many tools exist for assessment of factors such as quality of life<sup>82,83</sup> performance status,<sup>26,69,84,85</sup> anxiety and depression,<sup>101</sup> and grief.<sup>102</sup> Having located one or more scales of possible interest, the choice remains of whether to use these or to develop a new questionnaire which is more appropriate for a specific area of interest. The focus must be on the area of application. The decision of how to proceed should be guided by a judgement of whether the items of the scale are suitable for research, but should always be supplemented by a critical review of the evidence in support of the instrument.<sup>103</sup> The benefits of choosing an established questionnaire include the possibility of directly comparing the data with other studies using the same tool, and the time- and cost-effectiveness of not spending time in constructing a new tool. Established questionnaires can also give reliable results if they have already been validated.<sup>104</sup> A new assessment tool can be

constructed as a questionnaire which can then be used either for a momentary picture of the patient's status or as a tool to detect changes. However, in doing this, reliability and validity must be taken into account.

#### *The Performance Status in Palliative Chemotherapy questionnaire (PSPC)*

The eight-item PSPC was developed in Study II by the author and the main supervisor, on the basis of the ECOG PSR and clinical experiences from patients treated with PCT. It was intended to be brief enough to enable repeated use (i.e. before every PCT), appropriate to use regardless of phase of incurable disease (i.e. stable or deteriorating), and able to detect change over time. The questionnaire was designed as a patient-completed tool including an open question to allow the patient to share their thoughts in their own words. The first four questions used numeric rating scales (NRS) from 0 to 10. An improved status in the numeric scales corresponded to either a high or a low number, depending on how the question was formulated; this format was chosen to counteract response bias by minimizing the tendency to answer on the same side of the questionnaire.<sup>82,103</sup> The next three questions used Likert scales with five alternatives ("much better – better – neither yes or no – worse – much worse" and "definitely not – doubtful – neither yes or no – probably – absolutely").<sup>103</sup>

The final question was open-ended and asked the patient to describe the most evident effects of their last PCT. The questions concerned the patients' feeling of performance status and wellbeing in relation to receiving PCT. Questionnaires were provided at every PCT to be completed at the chemotherapy unit before PCT was started.

#### *The Edmonton Symptom Assessment System (ESAS)*

The PSPC was validated by comparing it to the Swedish version of the ESAS questionnaire completed on the same occasion as PSPC. ESAS is a ten-item NRS symptom assessment questionnaire. Its focus is wider than just performance status in palliative patients,<sup>84</sup> and it has been validated in many languages including Swedish<sup>105</sup> (Appendix 1). There are minor differences between the questionnaires; the PSPC asks about the patient's condition during the last few days while ESAS asks about the condition right now, and ESAS has all the "positive" answers on the left-hand side of the page.

### **Interviews**

#### *Research interviews*

Study III was based on open-ended research interviews which were conversational in nature,<sup>106-108</sup> the purpose of which was to obtain description of the nurses' experiences of administering PCT. An interview is

an occasion when the interviewee offers a piece of their life, giving the possibility to understand their life-world.<sup>106,109</sup>

The participants were asked to describe their experiences of a situation when administering PCT to a patient they were unsure had the strength to receive treatment. The initial question in the interview guide was: *“Could you tell me about an occasion when you gave palliative chemotherapy to a patient as prescribed even if you, due to the patient’s general condition, felt unsure about whether it was right to give additional treatment?”* Storytelling was encouraged by probing/encouraging questions such as: *“Could you tell a little more about that?”*, *“What happened next?”*, and *“Could you give another example?”* Interviews lasted from 14 to 42 minutes (mean 25 minutes) and were recorded and transcribed verbatim. The transcriptions were validated by sending a copy of each transcription to the relevant participant to let them comment on the content and tenor, and further validation was achieved by comparing the transcriptions with the recordings. The interview excerpts were translated, and pauses, hesitations, and repetitions were removed for clarity.<sup>107</sup> Quotations are presented in the results section with the words used by the participants in italics. Pseudonyms are used for the participating nurses, and the term “physician” is used without reference to medical speciality (e.g. oncologist). After each interview reflective notes, containing additional information, reflections on the interview, and ideas for analysis were written in a work-journal.<sup>108,110</sup>

### *Informal interviews*

As a complement to the patients’ use of PSPC, Study IV included informal interviews<sup>110</sup> with registered nurses working at chemotherapy units. These interviews aimed at eliciting the nurses’ experiences of the patients’ use of the PSPC questionnaire. The interviews were conducted during personal meetings at six times at all participating sites and complemented by phone and mail contacts. Nurses were asked to evaluate the patients’ comments about the questionnaire and whether patients wanted to participate in the study. They were also asked how they found the experience of using the questionnaire to assess performance status. The content of each interview was written down in a work-journal<sup>108</sup> directly after talking to each nurse.<sup>110</sup>

## **Quantitative analyses**

### ***Statistics***

Descriptive statistics were used in Studies I and IV to describe the characteristics of the populations. Versions 17 and 22 of the International Business Machines Statistical Package for Social Sciences (IBM SPSS) were used in the analysis.

Statistical comparisons were performed between the groups in both studies, to reveal any associations and differences. Non-parametric methods were used as the data were nominal and in some parts skewed. Depending on the type of variable, the chi-square test, Fisher's exact test, the Kruskal-Wallis test, or the Mann-Whitney *U*-test was performed. *P*-values  $\leq 0.05$  were considered significant. The material in Study I was divided into two groups: patients who had received PCT during the last month of life (LM group:  $n=87$ ), and patients who had not received PCT during the last month of life (NLM group:  $n=287$ ). The search included all patients in the region who had received PCT according to documentation in their medical records.

The original plan in Study IV was to perform a cluster randomized trial comparing the effects of PSPC use at certain study units with a control group of patients who had not used the PSPC when receiving PCT at other units in the region. The intention was to provide comparisons between the two counties without a resident oncology department, as well as internal comparisons in the county with resident oncologists. To detect a decrease from 23% to 18% in the proportion of patients receiving their last PCT less than 31 days before death, a study group of 160 patients was needed. Power calculations were performed aiming at 80% power and a significance level of  $p < 0.05$  with a two-sided test. An interim analysis was performed when half of the required study population had been recruited: 80 participants who had used the PSPC before PCT (PSPC users) were compared to two matched controls for each (non-users;  $n=160$ ). Matching was done for hospital unit, gender, age ( $\pm 5$  years), year of death ( $\pm 3$  years), and diagnosis. Existing documentation by nurses and physicians from the last two rounds of PCT was searched for ECOG PSR scores, scores from other formal assessment tools, and freely-worded comments on patients' performance status.

The frequencies of patients' comments in the open question in the PSPC questionnaire were counted and categorized in terms of whether they described worsening, neutral, or better appearance. Comments on worsening were sorted into six main groups: gastrointestinal problems, tiredness, pain/neurological sensations, skin/mucosa, general, and miscellaneous. No statistical calculations were performed on these data.

### ***Psychometric testing***

Descriptive statistics were used in Study II to describe the characteristics of the populations, with version 18 of the Predictive Analytics Software Portfolio (PASW) being used for the analysis. Non-parametric statistical methods were chosen. The PSPC questionnaire was tested for readability, reliability, sensitivity to change, and validity in four different tests.

In the test of readability, five patients with ongoing PCT were asked to read through the questionnaire and comment on the text and layout.

Reliability was explored using the test-retest method. Patients completed the PSPC twice: first before arriving at the chemotherapy unit, and again 2–6 hours later at the unit (without seeing their previously completed questionnaire). Questionnaires were completed prior to receiving antiemetic steroids and prior to administration of the PCT, as both of these treatments can affect the patient's sense of wellbeing.<sup>111</sup> Questionnaires were compared using Spearman's rank test and the weighted kappa. Correlation values  $\geq 0.75$  were considered acceptable. According to Cohen's guidelines,<sup>112</sup> correlation values from 0.10 to 0.29 are small, those from 0.30 to 0.49 are medium, and those from 0.50 to 1.0 are large. Weighted kappa coefficients were calculated to quantify the discrepancies between the two occasions for questions 1 to 6. Streiner and Norman<sup>103</sup> have identified several criteria for kappa, all suggesting that values from  $<0$  to 0.40 are "poor" or "poor-slight-fair", values between 0.41 to 0.60 are "moderate", "fair", or "fair to good", and values between 0.61 to 1.00 are "substantial", "excellent", or "almost perfect". In this study, values  $\geq 0.60$  were considered acceptable. Answers to the open-ended questions were counted, and compared to see the extent to which they covered identical topics on both occasions.

Sensitivity to change was tested longitudinally. The PSPC was completed by the patients before each PCT from inclusion until treatment ceased or the study ended. Patients were dichotomized into two groups: a deterioration group (PCT stopped because of death, progressive disease, or low performance status) and a stable disease group (PCT ongoing at the end of the study). The responses from the first and the last PSPC were compared using Wilcoxon's signed-rank test. Response rates for the open-ended question were compared using the chi-square test. *P*-values  $\leq 0.05$  were considered significant.

Convergent validity was tested by comparing the results of the PSPC with results from a Swedish translation of the ESAS,<sup>105</sup> that was completed at the same occasion. The ESAS questionnaire contains ten symptom items, two of which also appear in the PSPC ("tiredness" and "feeling of wellbeing"). To measure discriminant validity, the ESAS item "anxiety" was compared with the PSPC item "tiredness" and the ESAS item "appetite" was compared with the PSPC item "wellbeing", as these were the items which were considered to differ most from each other. Responses were analysed using Spearman's rank correlation. Correlation values  $\geq 0.50$  were deemed acceptable in the test for convergent validity, and values  $\leq 0.25$  were deemed sufficient to express discriminant validity.

## **Qualitative analysis**

### ***Narrative analysis***

Narrative inquiry gathers events and happenings as its data and uses narrative analytical procedures to synthesize or configure elements into explanatory stories.<sup>113</sup>

Study III was inspired by the narrative research tradition,<sup>107</sup> and Labov's approach of identifying structural commonalities across interviews, including the six elements of an abstract, an orientation, a complicating action, an evaluation, a resolution, and a coda in which the action is brought back to the present.<sup>114</sup> All researchers individually read each interview to identify the stories and to gain a first impression of the challenging situations nurses faced in administering PCT. The interviews were then discussed amongst the researchers to identify content areas, and the method of constant comparison was applied to the texts in these areas to elicit the meanings of different situations. A relationship between giving/not giving PCT and the nurses' perceptions of the treatment as right or wrong before and after the decision was elaborated in joint discussions. The author's work-journal was used in the discussions to support the analysis. The identified stories were again reviewed and compared in the light of meanings of the different situations, and various storylines were generated.

### ***Content analysis***

In Study IV, a manifest qualitative content analysis was used.<sup>115</sup> The author's notes in the work-journal were re-read and categorized in relation to the nurses' experiences of the patients' use of the PSPC.

## **Ethics**

The study was performed in accordance with the World Medical Association's Declaration of Helsinki (WMA 2013)<sup>116</sup> and approved by the Regional Ethics Committee at Umeå University (ref: 08-173M, 2011-189-32M, and 2013-93-32M). Permission to conduct research in medical records and to perform interviews during working hours was given by the directors and managers of the different departments.

Written and verbal information was sent to participants in Studies II-IV, and signed informed consent was acquired before inclusion. Participants were told that participation was voluntary, that confidentiality was guaranteed, and that they could drop out of the study without specifying a reason. The results are presented at group level with no possibility to identify any individual in Studies II-IV, and the quotations in Studies III and IV have been anonymised.

Ethical issues are of crucial importance when studying persons in vulnerable situations, such as patients suffering from incurable cancer. Throughout this work, I tried to be aware of signs of negative impact among the participating patients, as well as indications of a need for further professional counselling among the nurses. However, no such signs were detected.

## Results

### Study I

This study identified the number of patients with cancer in a year cohort who received PCT during the last month of life. Sorting the data into frequency tables revealed that 374 (31%) of 1200 deceased patients with epithelial cancers were treated with PCT during the last year of life.

#### *Discriminative characteristics for PCT last month of life*

Proportionately more patients younger than 75 years were treated in comparison to their older counterparts: 294 of 576 patients <75 y (51%) versus 80 of 624 patients ≥75 y (13%). Of the 374 patients included in the study, 87 (23%) received PCT during the last month of life (LM group) and the remaining 287 did not (NLM group). The LM group did not differ significantly from the NLM group in terms of residential area, gender, age, diagnosis, number of chemotherapy lines, or choice of chemotherapy drug. Time of cessation of PCT in the LM group was evenly distributed from 1 to 30 days before death (median = 14.5 days before death). In comparison to the NLM group, patients in the LM group had significantly shorter duration of PCT (median 85 vs. 138 days) and a significantly shorter time from first PCT to death (111 vs. 288 days). The proportion of patients admitted to hospital within 30 days after last PCT was significantly higher in the LM group, both with (52% vs. 29%) and without (79% vs. 50%) chemotherapy-related reasons for admittance. The chemotherapy-related reasons for admittance were deterioration, infection, nausea/nutrition difficulties, or being due for another round of PCT; the numbers reporting each of these reasons did not differ between the groups. A significantly larger proportion of patients in the LM group died in hospital, hospice, or nursing home rather than at home (76% vs. 62% in the NLM group), and a documented decision to cease PCT was significantly less frequent (21% vs. 70% in the NLM group) (Table 5).

**Table 5. Socio-demographic data and discriminative characteristics**

| Characteristics (n, % unless otherwise specified)  | LM-group<br>n=87 |    | NLM-group<br>n=287 |    | p-value             |
|--|------------------|----|--------------------|----|---------------------|
|  | n                | %  | n                  | %  |                     |
| <b>County of residence</b>   |                  |    |                    |    | NS <sup>a</sup>     |
| Västerbotten (257 728 inhabitants)   | 37               | 42 | 108                | 38 |                     |
| Norrbottn (249 811 inhabitants)  | 36               | 42 | 107                | 37 |                     |
| Jämtland (126 851 inhabitants)   | 14               | 16 | 72                 | 25 |                     |
| <b>Gender</b>  |                  |    |                    |    | NS <sup>a</sup>     |
| Male   | 49               | 56 | 141                | 49 |                     |
| Female   | 38               | 44 | 146                | 51 |                     |
| <b>Age</b>   |                  |    |                    |    | NS <sup>a</sup>     |
| Range (years)  | 33-86            |    | 32-87              |    |                     |
| Median (years)   | 65               |    | 66                 |    |                     |
| < 65 years   | 39               | 45 | 156                | 42 |                     |
| 65-74 years  | 34               | 39 | 152                | 40 |                     |
| ≥ 75 years   | 14               | 16 | 66                 | 18 |                     |
| <b>Diagnosis</b>   |                  |    |                    |    | NS <sup>a</sup>     |
| Cancer in upper gastrointestinal tract   | 29               | 33 | 75                 | 26 |                     |
| Lung cancer  | 19               | 22 | 60                 | 21 |                     |
| Colorectal cancer  | 13               | 15 | 55                 | 19 |                     |
| Other cancer   | 9                | 10 | 12                 | 5  |                     |
| Gynaecological cancer  | 7                | 8  | 21                 | 7  |                     |
| Breast cancer  | 5                | 6  | 41                 | 14 |                     |
| Urological cancer  | 5                | 6  | 23                 | 8  |                     |
| <b>Median duration of PCT (days)</b>   | 85               |    | 138                |    | <0.001 <sup>b</sup> |
| <b>Median time from 1<sup>st</sup> PCT to death (days)</b>   | 111              |    | 288                |    | <0.001 <sup>b</sup> |
| <b>Median time between last PCT and death (days)</b>   | 15               |    | 84                 |    | <0.001 <sup>b</sup> |
| <b>Chemotherapy line</b>   |                  |    |                    |    | NS <sup>a</sup>     |
| First line   | 41               | 47 | 153                | 53 |                     |
| Second line  | 22               | 25 | 65                 | 23 |                     |
| Third line or more   | 24               | 28 | 69                 | 24 |                     |
| <b>Patients admitted to hospital within 30 days after last PCT</b>                                   | 69               | 79 | 145                | 50 | <0.001 <sup>a</sup> |
| <b>Patients admitted to hospital within 30 days after last PCT with chemotherapy-related reasons</b> | 45               | 52 | 83                 | 29 | <0.001 <sup>a</sup> |
| <b>Documented decision to cease PCT</b>  | 18               | 21 | 202                | 70 | <0.001 <sup>a</sup> |
| Median time from last PCT to decision (days)   | 14.5             |    | 28                 |    |                     |
| Median time from decision to death (days)  | 7.5              |    | 45                 |    |                     |
| <b>Place of death</b>  |                  |    |                    |    | 0.011 <sup>a</sup>  |
| Hospital   | 59               | 68 | 139                | 48 |                     |
| Hospice  | 6                | 7  | 24                 | 8  |                     |
| Nursing home   | 1                | 1  | 15                 | 6  |                     |
| Home   | 21               | 24 | 109                | 38 |                     |
| <sup>a</sup> Chi-square test   |                  |    |                    |    |                     |
| <sup>b</sup> Mann-Whitney U-test   |                  |    |                    |    |                     |



Reasons for cessation in the LM group were progress of disease, deterioration, and patient's wish; and reasons in the NLM group were progress of disease, deterioration, no further rounds planned, patient's wish, or side-effects. Eight persons received only one PCT and died within a month of this first treatment. Only two of the eight patients had a disease regarded as highly sensitive to chemotherapy such as SCLC.

## **Study II**

The PSPC was initially developed with eight questions, but the tests of readability, reliability, sensitivity to change, and validity decreased this number to five. Chronological alterations of the questionnaire are shown in Table 6.

### ***Readability***

There were several reasons for changing and removing some questions. In the pilot test of readability, the main comment was about the word "palliative" in the heading. This word evoked uneasy feelings, as some patients could not fully identify themselves as being in a palliative phase of their disease. Accordingly the word "palliative" was omitted from the heading in the next version. Nothing else was changed.

### ***Reliability***

Thirty-three patients were asked to complete the questionnaire twice, and the resulting correlation values exceeded the required level of 0.75 in all items except questions 5 and 6. Some patients commented verbally that those questions and question 7 were difficult to interpret. These three questions were revised, and data were collected from 35 new participants. The correlation values increased, but still did not exceed 0.75 for questions 5 and 6. Weighted kappa coefficients exceeded 0.60 except in questions 2 and 5 (Table 7). This process resulted in the removal of questions 5 and 6.

**Table 6. PSPC items and development of the questionnaire.**

| No        | Question   | Pi-<br>lot      | Test<br>re-<br>test<br>1 | Test<br>re-<br>test<br>2 | Long<br>test | Va-<br>lid |
|-----------|--|-----------------|--------------------------|--------------------------|--------------|------------|
| <b>H</b>  | Performance status before chemotherapy   | HC <sup>1</sup> | HR                       | →                        | →            | →          |
| <b>1.</b> | How many hours have you been resting between 9 am – 7 pm during the last few days?<br>None 0–1–2–3–4–5–6–7–8–9–10 hours or more                                  | QR              | →                        | →                        | →            | →          |
| <b>2.</b> | How tired have you been during the last few days?<br>Worst possible tiredness 0–1–2–3–4–5–6–7–8–9–10 Not tired   | QR              | →                        | →                        | →            | →          |
| <b>3.</b> | How has your sense of wellbeing been during the last few days?<br>No wellbeing 0–1–2–3–4–5–6–7–8–9–10 Best wellbeing   | QR              | →                        | →                        | →            | →          |
| <b>4.</b> | How many days after the last chemotherapy were you exceptionally tired?<br>No days 0–1–2–3–4–5–6–7–8–9–10 days or more   | QR              | →                        | →                        | QW           | QW         |
| <b>5.</b> | Compared to the last chemotherapy (the one some weeks ago), has your physical capability changed?<br>I feel much better 0–1–2–3–4–5–6–7–8–9–10 I feel much worse | QR              | QC <sup>2</sup>          | QW                       |              |            |
| <b>6.</b> | What effect on your wellbeing do you experience from the ongoing chemotherapy?<br>It is much better 0–1–2–3–4–5–6–7–8–9–10 It is much worse                      | QR              | QC <sup>3</sup>          | QW                       |              |            |
| <b>7.</b> | Do you think you can manage to receive today's chemotherapy?<br>Definitely not – doubtful – neither yes or no – probably – absolutely                            | QR              | QC <sup>4</sup>          | QR                       |              |            |
| <b>8.</b> | What have been the most evident effects of your last chemotherapy?   | QR              | →                        | →                        | →            | →          |

H=heading HC=heading changed HR=heading remains QR=question remains QC=question changed QW=question withdrawn

<sup>1</sup> Original wording: Performance status in palliative chemotherapy

<sup>2</sup> Original wording: Comparing to your physical capability some weeks ago to today, has it changed? Is it: Much better – a little better – unchanged – a little worse – much worse

<sup>3</sup> Original wording: What effect on your well-being do you experience from the ongoing chemotherapy? Is it: Much better – a little better – unchanged – a little worse – much worse

<sup>4</sup> Original wording: Do you think you can manage to receive the forth coming chemotherapy? Definitely not – doubtful – neither yes or no – probably – absolutely

**Table 7. Test-retest of PSPC before and after item corrections**

| <b>PSPC question</b>                  | <b>Spearman's correlation<sup>a</sup><br/>1<sup>st</sup> version</b> | <b>Spearman's correlation<sup>a</sup><br/>2<sup>nd</sup> version</b> | <b>Weighted kappa<sup>b</sup><br/>2<sup>nd</sup> version</b> |
|---------------------------------------|--|--|--|
|                                       | n=33   | n=35   | n=35   |
| PSPC 1. Resting between 9 am – 7 pm   | 0.925  | 0.927  | 0.89   |
| PSPC 2. Tiredness                     | 0.953  | 0.811  | 0.58   |
| PSPC 3. Sense of well-being           | 0.896  | 0.860  | 0.66   |
| PSPC 4. Tired after last PCT          | 0.946  | 0.921  | 0.90   |
| PSPC 5. Change of physical capability | 0.501  | 0.748  | 0.59   |
| PSPC 6. Effect of PCT on well-being   | 0.658  | 0.720  | 0.62   |
| PSPC 7. Manage to receive today's PCT | 0.933  | 0.853  |  |

<sup>a</sup> Correlation values of 0.10-0.29 = small, 0.30-0.49 = medium, 0.50-1.0 = large.  
<sup>b</sup> Correlation values of 0-0.40 = poor, 0.41-0.60 = fair, 0.61-1.0 = excellent.

### ***Sensitivity to change***

A total of 106 patients were included in the test of sensitivity to change. Of these, 33 were in a clinically stable phase of their disease during the study, and 73 deteriorated during the study (45 died, 26 ceased PCT because of deterioration/and or tumour progression, and two decided on their own to cease treatments due to negative effects of PCT). In the group of deteriorated patients, Wilcoxon's signed rank test showed that three questions – question 1 (resting time), question 2 (tiredness), and question 3 (well-being) – revealed significant worsening, while questions 4 and 7 showed no significant differences. In the group of patients with stable disease, no significant differences were found in any questions during the study period (Table 8). The open-ended question was answered by 85 participants (81%) in the first questionnaire and 82 participants (77%) in the second questionnaire. More than one item could be mentioned by each person. The chi-square test showed no significant differences in response rate between the stable and deteriorated groups (first questionnaire  $p=0.079$ ; second questionnaire  $p=0.105$ ).

**Table 8. Sensitivity to change in PSPC.**

| <b>PSPC question</b>                   | <b>p-value of deteriorating group<sup>a</sup> (n=73)</b> | <b>p-value of stable disease group<sup>a</sup> (n=33)</b> |
|--|--|---|
| PSPC 1. Resting between 9 am – 7 pm    | 0.014  | 0.871   |
| PSPC 2. Tiredness                      | 0.001  | 0.608   |
| PSPC 3. Sense of well-being            | <0.001   | 0.819   |
| PSPC 4. Tired after last PCT           | 0.165  | 0.417   |
| PSPC 7. Manage to receive today's PCT  | 0.705  | 0.166   |
| <sup>a</sup> Wilcoxon signed-rank test |  |   |

Each question's ability to assess deterioration was measured as a statistically significant change in the median value in a worsening direction (Table 9). In the deterioration group, the median value changed by one step in the worsening direction in questions 1, 2, and 3. In the stable group, the numbers did not change. In question 3 (wellbeing), initial ratings in the deterioration group were worse than those in the stable group, but initial ratings did not otherwise differ between the groups. There was no change in the median value in question 4 (tiredness after treatment) in either group. In question 7 (managing to receive today's treatment), more patients in the deterioration group than in the stable group were doubtful about treatments, though the difference was not significant. These findings resulted in the removal of question 4 from the PSPC. Question 7, "Do you think you can manage to receive today's chemotherapy treatment?" was retained to act as a red flag; if a patient responded "definitely not" or "doubtful", the planned administration of PCT was to be thoroughly reconsidered.

### ***Validity***

To test validity, the ESAS questionnaire was chosen as the standard for comparison with similar items in PSPC. A total of 47 patients answered the ESAS and PSPC questionnaires on the same occasion. The analysis showed convergent validity (correlation exceeding 0.50) in the items concerning tiredness and wellbeing. Question 4 in the PSPC had no correlation to any questions in the PSPC or the ESAS, a finding that supported the decision to withdraw the question (Table 6). There were low correlation values between anxiety in the ESAS and tiredness in the PSPC, and between appetite in the ESAS and wellbeing in the PSPC. These findings were interpreted as signs of discriminant validity (Table 10).

**Table 9. Median value and range for questions in test of sensitivity to change.**

| Question   | Deterioration<br>group 1 <sup>st</sup><br>questionnaire<br>n=73 | Deterioration<br>group 2 <sup>nd</sup><br>questionnaire<br>n=73 | Stable disease<br>group 1 <sup>st</sup><br>questionnaire<br>n=33 | Stable disease<br>group 2 <sup>nd</sup><br>questionnaire<br>n=33 |
|--|---|---|--|--|
| <b>1. How many hours have you been resting between 9 am – 7 pm during the last few days?</b>                       |   |   |  |  |
| Median   | 2   | 3   | 2  | 2  |
| IQR  | 3   | 3   | 2.75   | 3  |
| Range  | 0-10  | 0-10  | 0-9  | 0-10   |
| <b>2. How tired have you been during the last few days? (higher score = worse)</b>                                 |   |   |  |  |
| Median   | 5   | 6   | 5  | 5  |
| IQR  | 3   | 3   | 4  | 4  |
| Range  | 0-9   | 0-10  | 0-9  | 0-10   |
| <b>3. How has your sense of wellbeing been during the last few days? (higher score = worse)</b>                    |   |   |  |  |
| Median   | 4   | 5   | 3  | 3  |
| IQR  | 3   | 2   | 5  | 3  |
| Range  | 0-8   | 0-9   | 0-8  | 0-8  |
| <b>4. How many days after the last chemotherapy treatment were you exceptionally tired? (higher score = worse)</b> |   |   |  |  |
| Median   | 3   | 3   | 3  | 3  |
| IQR  | 5   | 4   | 4  | 5  |
| Range  | 0-10  | 0-10  | 0-10   | 0-10   |
| <b>7. Do you think you can manage to receive today's chemotherapy treatment?</b>                                   |   |   |  |  |
| Definitely not   | 0   | 2   | 0  | 0  |
| Doubtful   | 3   | 1   | 1  | 0  |
| Neither y or n   | 2   | 4   | 0  | 1  |
| Probably   | 19  | 18  | 14   | 9  |
| Absolutely   | 47  | 48  | 18   | 23   |
| Missing  | 2   |   |  |  |

To summarize, the questionnaire was revised four times, according to the patients' comments on the wording of some items and the suboptimal performance of three items.

**Table 10. Correlations between ESAS and PSPC (N=47).**

| PSPC      | ESAS        | Spearman's correlation <sup>a</sup> |
|-----------|-------------|-------------------------------------|
| Tiredness | Tiredness   | 0.588                               |
| Wellbeing | Wellbeing   | 0.615                               |
| Tiredness | Anxiousness | 0.206                               |
| Wellbeing | Appetite    | 0.186                               |

<sup>a</sup> Correlation values of 0.10-0.29=small, 0.30-0.49=medium, and 0.50-1.0=large

This procedure resulted in the present version, with the first four questions using numeric rating scales and the fifth being an open-ended question (Table 11; Swedish version in appendix 2).

**Table 11 The final PSPC questionnaire.**

**Performance status before chemotherapy**

1. How many hours have you been resting between 9 am – 7 pm during the last few days?

None 0–1–2–3–4–5–6–7–8–9–10 hours or more

2. How tired have you been during the last few days?

Worst possible tiredness 0–1–2–3–4–5–6–7–8–9–10 Not tired

3. How has your sense of wellbeing been during the last few days?

No wellbeing 0–1–2–3–4–5–6–7–8–9–10 Best wellbeing

4. How many days after the last chemotherapy were you exceptionally tired?

No days 0–1–2–3–4–5–6–7–8–9–10 days or more

5. What have been the most evident effects of your last chemotherapy?

\_\_\_\_\_

Completed by: ☐ patient ☐ caregiver assisted ☐ caregiver ☐ cannot participate

If blood tests are taken before chemotherapy treatment, send the questionnaire by fax to number \_\_\_\_\_

### Study III

In the interviews the 17 nurses told a total of 28 stories. Some stories were based on recent experiences related to administering PCT, others on experiences dating several years back, and some on stories discussed among colleagues. All stories contained varied expressions related to four content areas in which dilemmatic situations could appear (Table 12).

**Table 12. Content areas in which dilemmatic situations could appear.**

|   |
|---|
| Nurses relationship to the patient.   |
| Patients' general condition and appearance.   |
| Possibility of reflecting together with the patients, relatives, and/or physicians. |
| Judged meaningfulness of the palliative chemotherapy treatment.                     |

Each of the 28 stories included more than one of the content areas presented above.

Eight stories were uncomplicated; either the patients themselves wished to terminate treatment because of its grave side-effects or their own weakness, or, the nurse, the patient, and the physician all agreed to postpone or cease the PCT. The nurses did not experience these specific PCT situations as problematic. In these stories, communication with patients and physicians seemed to be good, consensus was achieved, and the nurses felt that pausing or ceasing PCT was the right thing to do.

However, in the remaining 20 stories, three storylines encompassing six dilemmatic situations were identified (Table 13).

**Table 13. Storylines and dilemmas**

| Storyline  | Dilemma  |
|--|--|
| Storyline I: Felt right – treatment given – wrong to give.   | a) I thought I did good by giving PCT, but it turned out to have dire consequences for the patient.                            |
| Storyline II: Felt unsure – treatment given – wrong to give  | b) If the physician had listened to me, the patient might have survived or been spared from suffering.                         |
|  | c) If the patient and/or relatives had been convinced to discontinue PCT, the patient’s remaining life might have been better. |
|  | d) I thought the patient was misled; PCT was given on the wrong grounds.   |
| Storyline III: Felt unsure – treatment given – right to give | e) If the physician had listened to me, the patient would have died.   |
|  | f) From a medical perspective, we knew it was wrong to give PCT, but from the patient’s perspective it felt right.             |

### ***Storyline I: Felt right – treatment given – wrong to give***

In relation to this storyline, the nurses spoke about treatments that had seemed appropriate and right to give, but after seeing the outcome for the patient, they described the treatment as wrong (dilemma a, Table 13). One nurse said:

*...actually she [the patient] was feeling quite well when she came to us [for PCT]. But she didn’t survive her time... with us. She died from the treatment instead. I mean, she was like [...] all her [blood] counts hit rock bottom, then she got pneumonia over and over again, and then she died. [...] Who knows? She might have lived a better life without the treatments.*

Patients described in this storyline seemed to be in relatively good condition at the beginning of the PCT, but after one or more treatments they developed infections leading to death. The dilemma in this storyline is embedded in the potency of PCT and the difficulty of predicting whether a patient in relatively good condition has the strength to withstand the treatment.

### ***Storyline II: Felt unsure – treatment given – wrong to give***

In the most frequent storyline in the interviews, PCT was given as prescribed even though the nurse was unsure about whether it was right to give additional treatment. In retrospect, the nurse felt that giving the PCT had been the wrong action. Three different dilemmatic situations were identified (b-d in Table 13). For example, one nurse described a situation illustrating dilemma b (“If the physician had listened to me, the patient might have survived or been spared from suffering”):

*And when I saw the patient, my first thought was that this patient is in such terribly bad shape; so haggard [...] his skin was ashen grey, he had difficulty breathing. [...] It just felt wrong to give the PCT. But when the doctor came, who had met the patient before, his assessment was, “Ah, it’s alright.” So the treatment was given anyway. [...] The patient died that evening after the PCT.*

The nurse concluded her story with this reflection:

*It doesn’t feel right to have given the PCT, but, at the same time, in this particular case, I did say what I thought beforehand. And then it’s someone else above you who makes the decision.*

The three dilemmas embedded in this storyline all relate to insufficient communication and/or a lack of shared understanding of the possibilities and purposes of the PCT amongst the nurse, the physician, and the patient and/or relatives. The physician overruled the nurse, the relatives did not listen to the nurse’s questions and doubts about the appropriateness of PCT, and the nurse did not talk to the patients about the meaningfulness of the treatment.

### ***Storyline III: Felt unsure – treatment given – right to give***

Like the previous storyline, this storyline was based on stories of nurses giving PCT to a patient as prescribed despite feeling unsure about its efficacy. In this storyline, however, the nurses retrospectively evaluated giving the PCT as having been the right thing to do. Two distinctly different dilemmas were related to this storyline (e and f in Table 13). In dilemma e the patient recovered unexpectedly after a change of treatment regimen, and



in dilemma f the patient's last wish was fulfilled. One nurse said about dilemma f:

*...once I gave a “psychological” [PCT] treatment. You shouldn’t do that, of course, but there’s an exception to every rule. The PCT was prescribed in a very low dose by the oncologist. It was a dying patient and it was her last wish. She still had an unrealistic hope, I think, and I waited for her relatives to arrive before I sat down and gave the PCT. We knew she would die soon, and she did before the next morning. But we followed her last wish! And it kind of felt good to give it [...] despite knowing it was wrong. That was the only time I have given a “psychological” treatment.*

In both dilemmas the nurses were unsure whether it was right to give PCT, but their doubts were based on different grounds. One reason was grounded on worries about the possible results of trying new treatments on vulnerable patients without being able to foresee a good outcome. In other cases, the outcome was more foreseeable but there was uncertainty related to the clash between what was appropriate from a purely medical standpoint and what would best serve the patient from the life-world perspectives of patients and relatives.

## **Study IV**

In Study IV, users of the PSPC questionnaire were compared to matched controls that had not used the questionnaire. Some data were also compared to data collected for Study I in 2008. Data from the Oncology Centre Northern Region showed that 786 persons died of epithelial cancers in Jämtland and Västerbotten in 2012: 384 men and 402 women, 305 (45%) of whom were aged 75 or over. Of these, 286 (36%) were treated with palliative chemotherapy; 117 of them (38%) were aged 75 or over.

### ***Matching and duration of PCT***

The data from the medical records revealed no statistical differences between the study patients (PSPC users) and controls (non-users) in terms of setting, gender, age, or diagnosis (Table 14).

Most of the PSPC users (n=68) were recruited from one intervention unit without an oncology department.

**Table 14. Matching of patients**

| Characteristics  | PSPC-user |      | Non-user |      | p-value           |
|--|-----------|------|----------|------|-------------------|
|  | n=80      | %    | n=160    | %    |                   |
| <b>Setting</b>   |           |      |          |      | 0.33 <sup>a</sup> |
| Jämtland   | 69        | 86.3 | 130      | 81.2 |                   |
| Västerbotten   | 11        | 13.7 | 30       | 18.8 |                   |
| <b>Gender</b>  |           |      |          |      | 0.64 <sup>a</sup> |
| Male   | 33        | 41.3 | 71       | 44.4 |                   |
| Female   | 47        | 58.7 | 89       | 55.6 |                   |
| <b>Age</b>   |           |      |          |      | 0.33 <sup>a</sup> |
| Range (years) <sup>b</sup>   | 38-91     |      | 32-83    |      |                   |
| Median (years)   | 66        |      | 65       |      |                   |
| < 65 years   | 17        | 21.3 | 22       | 13.8 |                   |
| 65-74 years  | 26        | 32.5 | 59       | 36.9 |                   |
| ≥ 75 years   | 37        | 46.2 | 79       | 49.3 |                   |
| <b>Diagnoses</b>   |           |      |          |      | 1.0 <sup>a</sup>  |
| Colon cancer   | 23        | 28.8 | 45       | 28.1 |                   |
| Breast cancer  | 14        | 17.5 | 27       | 16.9 |                   |
| Cancer of the upper gastrointestinal tract   | 20        | 25.0 | 41       | 25.6 |                   |
| Urological cancer  | 9         | 11.3 | 17       | 10.6 |                   |
| Other cancers <sup>c</sup>   | 4         | 5.0  | 7        | 4.4  |                   |
| Lung cancer  | 3         | 3.7  | 8        | 5.0  |                   |
| Gynaecological cancer  | 7         | 8.7  | 15       | 9.4  |                   |
| <sup>a</sup> Chi-square test   |           |      |          |      |                   |
| <sup>b</sup> to find controls for all patients, >±5 y were accepted in four cases  |           |      |          |      |                   |
| <sup>c</sup> other diagnoses were melanoma, tumour in the abdomen, oropharyngeal cancer, and cancer in the thyroid glands, tongue, or tonsils. |           |      |          |      |                   |

The PSPC users had a longer duration of PCT than the non-users, and were less likely to have received only a single round of PCT or only first-line PCT. In the total group, 61 patients of 240 (25.4%) received PCT in the last month of life; there was no significant difference in proportions between PSPC users and non-users (23.8% vs. 26.9%;  $p = 0.60$ ; Table 15).

**Table 15. Duration of PCT, hospital admissions and place of death.**

| Characteristics   | PSPC user |      | Non-users |      | p-value             |
|---|-----------|------|-----------|------|---------------------|
|   | n=80      | %    | n=160     | %    |                     |
| <b>Deceased within a month of last PCT</b>                        | 19        | 23.8 | 43        | 26.9 | 0.60 <sup>a</sup>   |
| <b>Median duration from 1<sup>st</sup> PCT to last PCT (days)</b> | 314.5     |      | 120       |      | <0.001 <sup>b</sup> |
| <b>Median time from 1<sup>st</sup> PCT to death (days)</b>        | 430       |      | 267.5     |      | <0.001 <sup>b</sup> |
| <b>Median time between last PCT and death (days)</b>              | 58        |      | 65        |      | 0.619 <sup>b</sup>  |
| <b>Only one single treatment</b>                                  | 1         | 1.3  | 21        | 13.1 | 0.003 <sup>a</sup>  |
| <b>Chemotherapy line</b>  |           |      |           |      | <0.001 <sup>a</sup> |
| 1 <sup>st</sup> line  | 20        | 25.0 | 83        | 51.9 |                     |
| 2 <sup>nd</sup> line  | 28        | 35   | 40        | 25.0 |                     |
| 3 <sup>rd</sup> line or more                                      | 32        | 40   | 37        | 23.1 |                     |
| <b>Admissions to hospital within 30 days</b>                      |           |      |           |      | 0.53 <sup>a</sup>   |
| Admission after last PCT for non-PCT related reasons              | 15        | 18.8 | 22        | 13.8 |                     |
| Admission after last PCT for PCT-related <sup>d</sup> reasons     | 31        | 38.8 | 60        | 37.4 |                     |
| No hospital admission   | 34        | 42.4 | 78        | 48.8 |                     |
| <b>Place of death</b>   |           |      |           |      | 0.09 <sup>c</sup>   |
| Institution   | 41        | 51   | 98        | 61   |                     |
| At home   | 39        | 49   | 62        | 39   |                     |

<sup>a</sup> Chi-square test  
<sup>b</sup> Mann-Whitney *U* test  
<sup>c</sup> Fisher's exact test  
<sup>d</sup> PCT-related reasons were infection, anaemia, thrombosis, deterioration, nausea/nutrition difficulties, or planned PCT

### ***Documentation of performance status***

Performance status was documented in free text in the medical records by at least one team member in all cases. One physician wrote: “[the patient] becomes tired if she walks a lot but is not bedbound. OK to give treatment in reduced dose.” A nurse wrote: “Very tired, sleeps most of the time [...] Blood tests shown to Dr X, treatment OK to give.” Performance status measured by any formal assessment tool was rarely documented in either group (approximately 5%), and in no cases by nurses. Performance status was documented by the physician in 114 cases (48%), with no difference between the study and the control groups. There was a trend in the PSPC group ( $p=.051$ ) for a shorter time from last PCT to decision to cease treatments (Table 16).

The 80 study patients completed 316 PSPC questionnaires (median: 2 per patient; range: 1-13). Due to the amount and complexity of information needed by patients starting their very first PCT, nurses frequently chose to postpone the study invitation to a later round. The nurses reported that patients found the PSPC questionnaire easy to complete, but some found it a bit tedious to complete before every single round of PCT when in a stable phase of disease. The nurses advised these patients not to complete the PSPC before every single PCT, but to do it regularly again when deteriorating.

**Table 16. Documentation of assessment of performance status.**

| Characteristics                                    | PSPC users     |      | Non-users         |      | p-value            |
|--|----------------|------|-------------------|------|--------------------|
|  | n=80           | %    | n=160             | %    |                    |
| <b>Documented assessment of performance status</b> | 80             | 100  | 160               | 100  | 1.0 <sup>a</sup>   |
| Using NRS scale                                    | 5              | 6.3  | 7                 | 4.4  | 0.54 <sup>c</sup>  |
| <b>Documentation by</b>                            |                |      |                   |      | 0.86 <sup>a</sup>  |
| Nurse solely                                       | 42             | 52.5 | 84                | 52.5 |                    |
| Physician solely                                   | 3              | 3.8  | 4                 | 2.5  |                    |
| Both nurse and physician                           | 35             | 43.7 | 72                | 45.0 |                    |
| <b>Documented decision to cease PCT</b>            | 59             | 73.8 | 113               | 70.6 | 0.65 <sup>c</sup>  |
| Median time from last PCT to decision (days)       | (n=59)<br>26 d |      | (n=114)<br>28.5 d |      | 0.051 <sup>b</sup> |
| Mean   | 34.8           |      | 66.0              |      |                    |
| <sup>a</sup> Chi-square test                       |                |      |                   |      |                    |
| <sup>b</sup> Mann-Whitney <i>U</i> test            |                |      |                   |      |                    |
| <sup>c</sup> Fisher's exact test                   |                |      |                   |      |                    |

### ***Patients' comments***

In 259 (82%) questionnaires, 76 (95%) patients answered the open question: "What were the most evident effects of your last chemotherapy treatment?". These 259 questionnaires contained a total of 609 different comments on treatment effects: 538 (88%) comments on deterioration (Table 17), 42 (7%) on improvement, and 29 (5%) neutral.

The most common comments concerned gastrointestinal problems (n=153), tiredness (n=140), and pain and/or neurological sensations (n=119 cases). A written comment illustrates: "*Tired, nauseated, and nothing tastes normal.*"

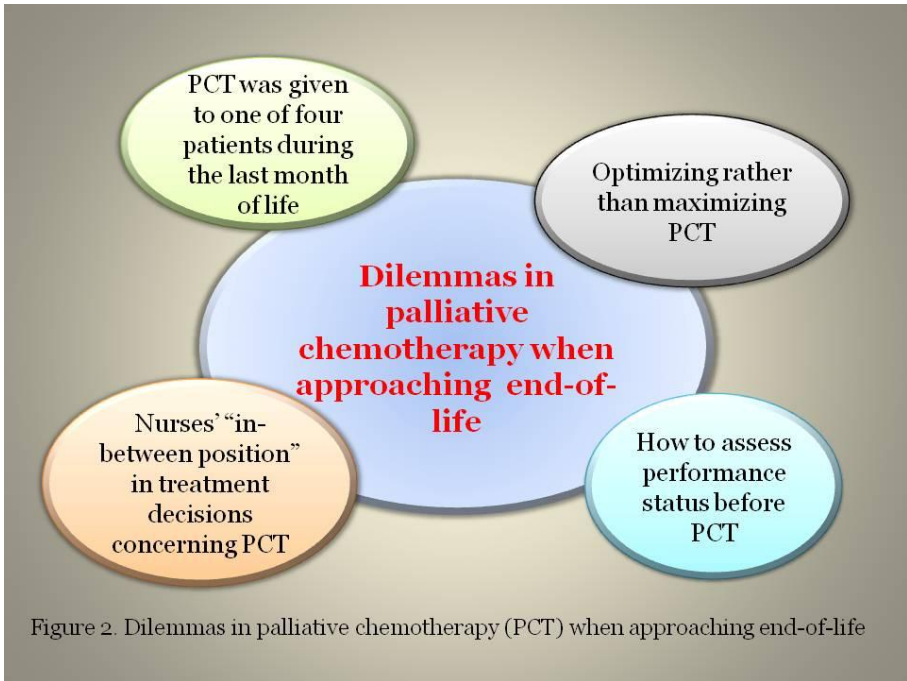
Patients also had comments on improvements and better wellbeing: "*Feeling extremely well, appetite back, working part time. All positive.*" According to the work-journal, the nurses appreciated this additional information as the patients were more honest about their performance status in the PSPC than in the verbal assessment.

**Table 17. Comments on deterioration in PSPC (n=538)**

| <b>Gastrointestinal problems</b>      |     | <b>Skin/mucosa</b>   |    |
|---------------------------------------|-----|----------------------|----|
| Nausea                                | 63  | Irritated mucosa     | 33 |
| Diarrhoea                             | 26  | Rash/itching         | 15 |
| Constipation                          | 23  | Swollenness          | 11 |
| Worse appetite                        | 16  | Wounds               | 10 |
| Change in taste                       | 12  | Bleeding             | 4  |
| Gastritis                             | 9   | <b>General</b>       |    |
| Flatulence                            | 4   | Worse mood/annoyed   | 11 |
| <b>Tiredness</b>                      |     | Sleep-disturbance    | 10 |
| Tiredness                             | 106 | Feeling of influenza | 8  |
| Weakness                              | 20  | Worse well-being     | 2  |
| Extreme tiredness                     | 14  | <b>Miscellaneous</b> |    |
| <b>Pain/neurology</b>                 |     | Difficulty breathing | 9  |
| Worse pain                            | 56  | Hair-loss            | 3  |
| Increased sensitivity; cold, tingling | 46  | Sweating             | 3  |
| Dizziness/balance                     | 12  | Hoarseness           | 3  |
| Worsening vision                      | 5   | Incontinence         | 2  |

## Discussion

The findings from the four studies comprising this thesis provide increased knowledge about PCT administered when approaching end-of-life: the frequency of PCT administration during the last month of life, the potential harm it may cause to patients receiving it, and the type of dilemmas that may arise among the nurses administering it. The unpredictability of PCT effects emerged as a constant theme throughout the work described here. This unpredictability may cause dilemmas not only for patients, but also for nurses and physicians (Figure 2).



### **PCT was given to one of four patients during the last month of life**

Today there is a trend for increased PCT even in a patient's last month of life.<sup>20,54,89,117,118</sup> PCT was given to 31% of epithelial cancer patients in their last year of life in Study I and 36% in Study IV; these are relatively low proportions, as other studies have reported proportions ranging from 39% to 65%.<sup>41,119,120</sup> This could be a sign of a less aggressive treatment culture in end-of-life oncological care in Northern Sweden, but the results in the present thesis are insufficient to prove this hypothesis. Still, Studies I and IV showed that about a quarter of these patients (23% and 25.4%, respectively) received their last PCT during the last month of life, well within the range of

previously presented results covering similar diagnoses in Italy (23% and 33%),<sup>41,121</sup> Korea (31%),<sup>122</sup> and Australia (18%).<sup>123</sup> The studies in this thesis revealed no discriminative characteristics in terms of gender, age, diagnosis, or type of chemotherapy drug between patients who received PCT during the last month of life and those who ceased PCT earlier. Other studies have reported an increased likelihood for PCT to be given to patients with chemo-sensitive tumours,<sup>89</sup> and a decreased probability of PCT being given to women,<sup>30,36,89</sup> and to older patients.<sup>30,36,124</sup>

Approximately half of the patients treated with PCT (LM-group in Study I =47%, and patients who had not used the PSPC in Study IV=51.9%) did only receive first-line PCT, and 20% respectively 13% of these only got the first course of the first line. A majority of patients (six of eight patients) who died close to their very first round of PCT in study I had low or moderately chemo-sensitive cancers. For patients who received PCT in their last month of life, the last PCT was given a median of 14.5 days before death. Are these outcomes illustrative of disease trajectories that suddenly and unexpectedly came to a deadly end? How many of these patients could have been spared further PCT by a more thorough assessment of treatment effects and the patient's performance status? A hypothetical explanation of these results could be the unpredictable progress of disease or detrimental side-effects. Other reasons could be unclear aims of the PCT, inappropriate patient selection criteria, and difficulties in formulating an accurate prognosis. A lower frequency of documented decisions to cease treatment in this group could hint at one or more of these other reasons. PCT during the last month of life creates a dilemma, as PCT is supposed to relieve symptoms but in itself may cause burdensome side-effects.

## **Optimizing rather than maximizing PCT**

The medical intention for any prescribed treatment ought to be to optimize the chance of beneficial effects while at the same time minimizing the risk of detrimental effects on the patient. Studies show that patients who had end-of-life discussions with their physicians received significantly less aggressive PCT near death.<sup>8,40,41,125</sup> Patients enrolled in palliative care in early stages of palliative disease experienced significantly improved quality of life and longer survival time,<sup>8,9,45,125,126</sup> and patients with early cessation of PCT spent more time at home, which is a cost-effective solution involving less need for medical care.<sup>127</sup> Conversely, a lack of end-of-life discussions or no contact with palliative care units could imply more aggressive treatments,<sup>128</sup> which in the final weeks of life could worsen patients' quality of life.<sup>45,125</sup>

A patient with deteriorated performance status may still have a strong wish for continued PCT, due to seeing it as a lifeline.<sup>129</sup> This wish may be strengthened by a relative lack of awareness of how the chances of clinical response decrease and the risks of predominantly negative effects increase as performance status deteriorates.<sup>34,56,94</sup> Palliative care ethics emphasize that any prescribed treatment should be built on respect for the patient's autonomy, but should also be an act in the best interests of the patient.<sup>16,130</sup> Hence decisions about PCT should be made in dialogue and consensus between patients and medical staff. Guidance should be provided by medical staff and the responsibility for medical treatment decisions lies with the responsible physician.<sup>56,130</sup> However, even if the prescription is made by a physician, all registered staff are responsible for their actions which include minimizing the risk of causing harm to the patient. To uphold this ethical principle and to enable an optimal team decision, nurses' and physicians' observations and assessments of the patient's performance status are of greatest importance.<sup>16,34,131,132</sup>

Study I revealed that patients treated by PCT during the last month of life were more likely to die in hospital and had shorter survival from the start of PCT. Keam et al.<sup>35</sup> reported similar results, and Earle et al.<sup>118</sup> found increased proportions of patients visiting hospitals and emergency rooms among patients treated with PCT during the last month of life. Sometimes ceasing PCT might be in the patient's best interests, in order to avoid dire consequences such as an increased risk of hospital admissions near the end-of-life. However, it is still a point of debate whether hospital admissions and dying in hospital are negative consequences. A cross-national study in Western Europe showed that between 51% and 84% of incurable patients approaching end-of-life preferred to stay at home,<sup>133</sup> and another study showed that among patients referred to a palliative care team, the proportions wishing to die in hospital increased from 10% to 30% as death approached.<sup>134</sup>

Studies I and IV showed a substantial increase between 2008 and 2012 in the proportion of patients older than 74 years who received PCT at all (17% in 2008 and 38% in 2012). Earlier research from 2005–2009 confirms that PCT was significantly more frequently administered to younger patients.<sup>28-30,122,123</sup> These results can be interpreted as an improved equality in treatments, with less age discrimination, but may also be due to slightly different inclusion criteria. According to the Swedish National Cause of Death Registry, 12050 of 22094 persons (55%) who died of cancer in Sweden in 2012 were older than 74 years.<sup>135</sup> This implies that the optimal proportion of persons 75 years and older receiving PCT may even be higher, more likely close to the 45% reported from South Korea.<sup>136</sup> PCT given on the right



indications to older persons may still relieve symptoms in late phases of incurable cancer, if performance status is good.<sup>28,74,137-142</sup> Individualization has been shown to be the most important aspect of PCT and other cancer treatments provided to elderly patients.<sup>143</sup>

However, as previously stated, inappropriate use of PCT in palliative care may have detrimental consequences for patients. The major risk for the patient is that of being administered futile, toxic, and potentially life-threatening PCT which results only in worsening quality of life.<sup>40,41</sup> An earlier detection of when patients approach end-of-life could lead to better quality of care and better use of resources.<sup>8,41,43,144</sup> If a patient is not fit to receive PCT, the treatment should not be given. The problem is to decide when this point in the disease trajectory is reached.

### **How to assess performance status before PCT**

Treatment-related decision-making involves a combination of biological and tumour-related factors as well as an informative dialogue with the patient. The balance of these factors provides the overall guideline for appropriate treatment decisions. The most significant factor is argued to be the performance status of the patient.<sup>143</sup>

If staff continuity is suboptimal, or the documentation of earlier performance status assessments is incomplete or absent, the decision process may be considerably more demanding. Even at chemotherapy units with good staff continuity and well functioning communication the routine use of a tool such as PSPC may be a valuable addition.

The PSPC item on “managing to receive today’s treatment” will probably never show significant differences in any sensitivity test, as only 2 of 106 patients in Study II responded “absolutely not” to this question. It has been argued that this attitude, at least for some patients, might be a sign of refusing to accept being too frail to receive more PCT, as it would mean giving up the hope of recovery.<sup>3,46</sup> However, this item is retained in the questionnaire as a red flag; if a patient answers “absolutely not” or “doubtful”, continued PCT should be thoroughly reconsidered.

It has been argued that a low response rate to an open-ended question could mean the patient has deteriorated to such an extent that completing the questionnaire is too difficult.<sup>145</sup> In the PSPC sensitivity test, the number of answers to the open-ended question did not differ significantly over time, nor did it differ between the stable and the deteriorating groups. The nurses felt that the questions provided valuable additional information to help assess the patient’s performance status. Another study showed similar

positive experiences of a computerized pre-PCT assessment tool; nurses and physicians became more aware of patients' symptoms and the patients were more "primed" to discuss their symptoms, but there was no impact on documentation in the medical records.<sup>146</sup> The open question also seemed to be appreciated by the patients, since the answering frequency was high, with 95% of all patients taking the opportunity to write down the most obvious effects of their latest PCT.

Contrary to our hypothesis, Study IV revealed no decisive impact of PSPC use on the decision of whether or not to give PCT. The proportion of incurable patients with cancer who received PCT during the last month of life changed very little between 2008 and 2012 (23% in 2008 and 25% in 2012), so we cannot claim any significant effects of the PSPC questionnaire in the hypothesized direction. The proportions in these studies are lower than reported from another part of Sweden (32%),<sup>54</sup> but this is not necessarily a result of the intervention, as it may rather reflect different treatment traditions. However, the results of Study IV show a tendency among patients who had used the PSPC of shorter time between last given PCT and documented decision to cease treatments ( $p=0.051$ ), and more patients dying at home ( $p=0.09$ ). It is not possible to say whether this is a result of the intervention.

The effectiveness of a tool depends on the outcome that is measured.<sup>147</sup> For example, Groenvold et al., who revised the EORTC-QLQ-C30 into a 15-item questionnaire suitable for palliative patients, suggest that the EORTC-QLQ-C15 is not suitable for use in patients who are still receiving PCT because these patients are expected to survive longer.<sup>81</sup> Still, many patients receive PCT in the last month of life,<sup>41,122-124</sup> which emphasizes the need for a routine assessment tool for performance status when the patient is approaching end-of-life. The psychometric tests of the PSPC questionnaire in Study II showed that it could detect changes in performance status for patients receiving PCT. The median difference was one step in worsening direction longitudinally for the deteriorating group of patients. Despite this numerically small difference, it could at some levels illustrate a difference in ECOG PSR scores.

Patient-reported assessments are preferred,<sup>73,148</sup> and can function as independent indicators for both performance status and survivaltime.<sup>148</sup> Earlier studies have shown that assessment of performance status can be used as a prognostic factor for survival in cancers such as non-small cell lung cancer (NSCLC).<sup>73,76,148</sup> As the results in Study II provide evidence that the PSPC has acceptable psychometric characteristics, this questionnaire may be suitable both to assess baseline performance status when initiating PCT and

to detect deterioration in a later stage of disease. Its brevity will likely promote compliance when it is routinely used before PCT.

Further studies of the effects of routine PSPC use are needed before it can be claimed that the PSPC is an effective assessment tool in aiding decisions about PCT when approaching end-of-life.

### **Nurses' "in-between" position in treatment decisions**

To our knowledge, the literature does not currently contain conceptualizations of some of the unforeseeable outcomes of PCT and the dilemmas experienced by nurses in Study III, namely; d "I thought the patient was misled; PCT was given on wrong grounds"; e "If the physician had listened to me, the patient would have died", and; f "From a medical perspective, we knew it was wrong to give PCT, but from the patient's perspective it felt right". Clinical experience, however, affirms their existence.

Most of the stories turned out to be dilemmatic for the nurses, for example when relatives were pressing for continued PCT administration to a deteriorating patient unable to express their own wishes – a dilemma also found in other studies about similar situations.<sup>49,90</sup> PCT was given despite the nurse's doubts, with a dire outcome for the patient.<sup>51,90,93</sup>

The uncertainty in predicting PCT outcomes for individual patients is presented as a reason not to cease treatments even at end-of-life.<sup>50,51</sup> As shown in recent studies, physicians tend to offer further PCT despite doubting the benefits of treatment, as they do not want to disappoint or take away hope from treatment-prone patients and relatives.<sup>40,50,51,61,149,150</sup> Patients and physicians have mutually reinforcing attitudes of "not giving up",<sup>51</sup> especially if the patients are young, well-educated, parents of young children, or married.<sup>50,54</sup> Many patients do not want to stop PCT because they see it as their only remaining hope. In rare cases, ineffective PCT may be beneficial for the patient.<sup>51</sup> One of the patients described in Study III was given treatment as fulfilment of her last wish. The dilemma described by her nurse appeared to be a clash between the medical world (wrong to give) and the life-world (right to give), even though both the physician and the nurse experienced it as the right thing to do.<sup>51</sup>

If the physician has not initiated a discussion about death and dying with patients in deteriorating condition, nurses may find themselves in dilemmatic situations when having to administer PCT;<sup>51,151</sup> McLennon et al. described this as being "stuck in the middle".<sup>152</sup> When the specific goals of proposed PCT are unclear, nurses feel morally troubled about discussing the

cessation or postponement of treatments with the patients.<sup>51,91,94</sup> In the dilemmas in Study III, the nurses described the treatments as being given on the authority of someone else; the physician's recommendation or the relatives' request. Similar dilemmas for nurses have also been described elsewhere.<sup>51,66</sup> In these dilemmas, the nurse has neither the power nor the knowledge to act according to their own perception of what is right.<sup>66</sup>

In many cases the nurse has worked with the patient for a long time and has a well-founded knowledge about their performance status.<sup>92</sup> Studies from the Netherlands and New Zealand have shown that nurses experienced patients to be more talkative about deterioration with them than with the physicians.<sup>34,51</sup> Still Study III confirmed results from earlier studies that nurses do not always participate in decisions concerning PCT, which illuminates the complexity and gaps in communication between patients, nurses, and physicians around prognosis-related disclosure and treatment goals.<sup>34,51,152-154</sup> It has been argued that these gaps are derived from different disciplinary views, making nurses and physicians work tangentially rather than in tandem.<sup>34</sup> These different responsibilities of nurses and physicians together with the different stories told by patients lead to understandable differences in attitudes to PCT. Nurses are more likely than physicians to question whether further PCT is in the patient's best interests, preferring that patients make the best of their time left in life.<sup>51</sup> Hence an improved communication between nurses and physicians would be beneficial to all parties.

Study III highlights that when this "team effort" does not take place, the result may be a less-than-optimal decision-making process. When the care is provided by multidisciplinary teams, dilemmatic situations can be discussed in joint rounds on selected occasions with the nurse, patient, and physician present; this is a good context in which to discuss and make decisions about further PCT to avoid misunderstandings.<sup>131,155</sup> A lack of dialogue between all involved parties leaves room for ethical dilemmas.<sup>94,96,131,152,156</sup> For nurses, ethical conflicts can be related to care decisions in which they were not involved, but which they have to implement and live with.<sup>157,158</sup> The eight stories in Study III which were not experienced as dilemmatic were characterized by a well-functioning dialogue between all parties. This finding may indicate that at least some of the nurses' experienced dilemmas might be preventable.

## **Methodological considerations and limitations**

The chosen time frame of PCT in the last month of life can be questioned, though it has been used in other studies.<sup>41,59,60,121-124</sup> Asola et al. argued that

two months are needed to benefit from cessation of PCT,<sup>43</sup> while OPCARE<sup>9</sup> suggested the proportion of patients receiving PCT within a fortnight before death as a quality indicator of end-of-life palliative care.<sup>21</sup> Strength of Study I was that it included all patients treated with PCT within a specified geographical area and who died during one year. As the area included both the only university hospital and three whole counties which routinely referred virtually all patients to this university hospital, the risk of substantial selection bias is rather small. A retrospective data collection can always be criticized for suboptimal validity/reliability of data, but the extent of uncertainty depends on the type of data collected. The coding of chemotherapy treatment as such is a well developed routine, and information on hospital admittances and place of death is relatively objective. More uncertain is the validity of a documented decision to cease PCT, which can be missed when searching extensive medical records; in addition a decision may have been made verbally but not documented in writing.

In Study II, the PSPC questions were not generated from interviews with patients, but derived from clinical experience in the research group combined with knowledge of other existing questionnaires touching on the same topic. Another option would have been to collect information about documented assessments of performance status in Study I. This information could have enriched the development of the questionnaire in Study II, and given useful information about the routine use of assessment scales.

The participants in Study III all came from the same geographical and ethnic context, limiting diversity. In addition, a qualitative methodology cannot provide answers regarding the extent to which and how frequently these dilemmas appear in everyday practice. The practice of administering PCT without an attending oncologist exists in other rural areas throughout the world, in locations such as the USA, Canada, and Australia,<sup>22-25</sup> but the hierarchical position of registered nurses in the multidisciplinary team is likely to vary not only between countries but also between different hospitals and departments. However, it is not a matter of whether the findings from these studies can be generalized and applied to other settings, but rather whether an interpretation conveys insights and meanings that enable the readers to understand their own practice in a new and extended way. Further studies are needed to reach a deeper understanding of these dilemmas in everyday life from the perspectives of all parties: the patient, the next-of-kin, the nurse, and the physician.

One limitation of Study IV is that it was an interim analysis performed when only half of the intended study population had been included (80 of 160).

Patient recruitment and data collection was delayed, obstructing the possibility to perform the cluster randomized trial originally planned and decreasing the probability of detecting any significant differences between the groups. Another limitation is that the study and the control groups were not comparable in all aspects. As the control group was selected from the same treatment units as the study group, the risk of contamination is apparent. Another option for creating a control group would have been to select matched control patients from units other than those from which the study patients were drawn.

However, aware of the results from Study I showing a tendency towards a lower proportion of patients receiving PCT in the last month of life in one of the counties, we chose to select controls from the same areas as the study patients in order to minimize the risk of generating false positive differences between the groups.

It is likely that the majority of the study patients had slower disease progression than those in the control group, due to nurses refraining from inviting patients to the study at their first PCT. It is known that nurses working in chemotherapy units may become emotionally close to the patients,<sup>159</sup> and in Study IV this may have increased their tendency for “gatekeeping”; that is, assessing patients as too deteriorated or too frail to participate in a scientific study. This skewed recruitment could also have enabled the team to assess deterioration more accurately in the study group, resulting in an earlier cessation of PCT. However, no signs of this were found in the results.

When data on documentation of performance status by nurses and physicians were collected in Study IV, it was apparent that physicians did not document performance status at all in half of the patients. This finding brings into question how much of the PSPC information was used for decision-making. It is possible that the PSPC was not considered as valuable information, even though the participating physicians had previously expressed their support of the study rationale. Nurses seemed to take on a broader responsibility for assessment of patients’ performance status before PCT; in 93% of the cases where treatments were given, performance status was documented in free text by the nurses. The lower proportion of physicians’ documentation also can be a result of the current routine at units without a resident oncologist.

Routine use of a new assessment tool such as the PSPC in clinical practice is not easily achieved. To succeed requires not only the provision of information to all parties, but also a solid evidence base and some readjustment of priorities.<sup>160</sup> Feifer et al. showed that there is no unifying

theory that can guide an intervention's development. However, there are a number of relevant principles. First, to achieve change in busy clinical settings with their own priorities and barriers, a multidimensional approach must be chosen. As motivation determines behaviour, and is socially influenced, motivation can thus influence a group to participate in a study. Second, it can be assumed that busy nurses and physicians will only be interested in participating if the information appears to be important enough to them. Third, individuals are at different levels of readiness to make practical changes. Successful change is often a stepwise process which addresses the individuals' stage-specific needs.<sup>160</sup> Beside these theoretical prerequisites for moving daily routines in a new direction, there is a need to scrutinize what could have been done differently in this study.

## Clinical implications

The findings in this thesis may be useful for all team members – nurses, physicians, patients, and next-of-kin – when facing the challenge of deciding whether or not to give PCT (Figure 3). Regardless of the method chosen to achieve optimal PCT utilization in end-of-life, it ought to be applied and studied when in routine use. There is also a need for a prevailing culture among the staff of striving for optimal timing of PCT and its timely cessation. One already available step in this direction would be a more generally

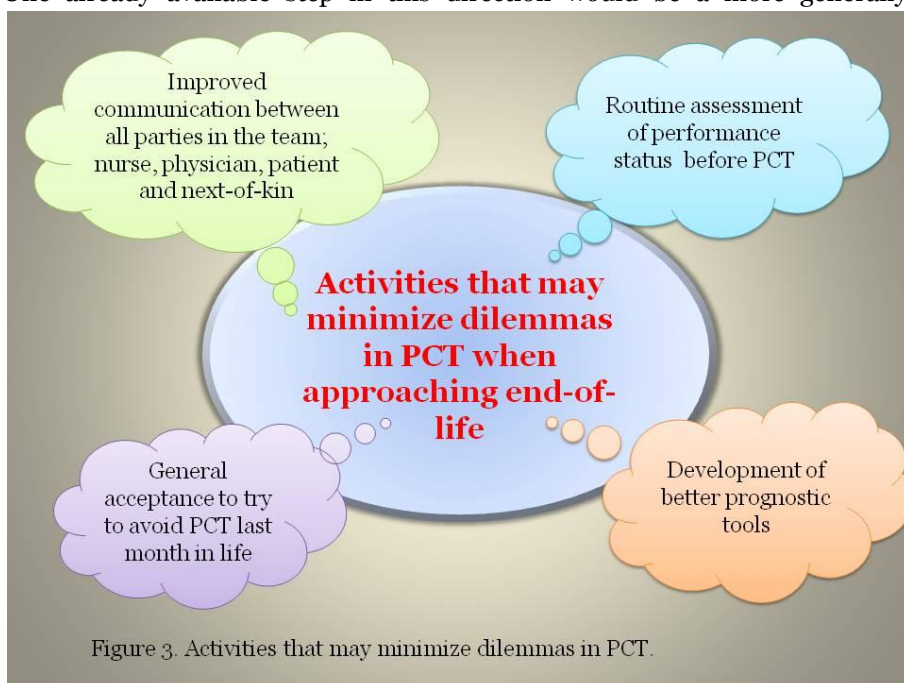


Figure 3. Activities that may minimize dilemmas in PCT.

accepted attitude to thoroughly questioning continued PCT in any patient with an ECOG PSR score >2.

Use of a tool like the PSPC can enable patients to better describe their experience of strength and/or tiredness, thus providing a more accurate and more reliable picture of their actual performance status. A computerized assessment tool completed at home before PCT, with the results transferred to the medical record, could increase the possibility for all members in the care team to share the information and take part in the decision. Computerized assessment of performance status has been shown to be a well-functioning aid in clinical use;<sup>146,161</sup> more than 50% of the patients in one study preferred computerized assessments to a paper and pencil version.<sup>161</sup> However, assessments have no benefit if their results are not used. It is of great importance that assessments of performance status are integrated into the decision-making process.

Future development of any prognostic tool that could help detect when end-of-life is approaching would be of paramount value in avoiding futile PCT. Similarly, better prognostication of individual response to PCT would be very helpful. Dedicated research efforts are needed to increase knowledge in these areas.

## Conclusions

The overall conclusion of this thesis is that administration of PCT can create dilemmatic situations for both patient and medical staff when approaching end-of-life. This is underlined by the findings that some 25% of treated patients received their last round of PCT as late as during the last month of life. This group of patients had more hospital admissions and were less likely to die at home. Nurses described situations where they found themselves in the middle of the decision-making process regarding whether or not continuing PCT.

The unpredictability of PCT was a continuous theme in the work described in this thesis, emphasizing the necessity to individually assess every patient before PCT, thereby striving to minimize the risk of futile treatments. The attempt to develop a reliable and valid questionnaire for systematic assessment of performance status has increased future possibilities to monitor this parameter in PCT when approaching end-of-life. The questionnaire provides nurses with increased knowledge of patients' performance status. If routinely used it may help decrease the proportion of patients receiving PCT during the last month of life, though this remains to be rigorously proven. Further research efforts are needed to progress in the task of optimizing rather than maximizing the use of PCT when approaching end-of-life.



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*Indeed there is no torment quite like hopelessness. But hopelessness  
marks the presence of thwarted hope, not hope's absence.*

H. N. Boris. On Hope: Its nature and psychotherapy,  
*Int. Journal of Psychoanalysis*. 1976;3(2):139-150

# Appendix 1

## ESAS (Edmonton Symptom Assessment Scale)

Namn \_\_\_\_\_

Datum \_\_\_\_\_ Personnummer \_\_\_\_\_

Vi är tacksamma om Du besvarar nedanstående frågor genom att markera en siffra på varje fråga.

Tänk på hur Du har känt det senaste dygnet.

Skalan är som en termometer där siffran 0 alltid motsvarar inga problem  
alls/helt fri från besvär och siffran 10 värsta tänkbara problem.

Svaren behandlas anonymt och påverkar inte den vård Du får.

Din medverkan är frivillig.

- |     |  |                                    |
|-----|--|------------------------------------|
| 1.  | 0 --- 1 --- 2 --- 3 --- 4 --- 5 --- 6 --- 7 --- 8 --- 9 --- 10 |                                    |
|     | Ingen smärta   | Värsta tänkbara smärta             |
| 2.  | 0 --- 1 --- 2 --- 3 --- 4 --- 5 --- 6 --- 7 --- 8 --- 9 --- 10 |                                    |
|     | Ej orkeslös  | Värsta tänkbara orkeslöshet        |
| 3.  | 0 --- 1 --- 2 --- 3 --- 4 --- 5 --- 6 --- 7 --- 8 --- 9 --- 10 |                                    |
|     | Inget illamående   | Värsta tänkbara illamående         |
| 4.  | 0 --- 1 --- 2 --- 3 --- 4 --- 5 --- 6 --- 7 --- 8 --- 9 --- 10 |                                    |
|     | Ingen nedstämdhet  | Värsta tänkbara nedstämdhet        |
| 5.  | 0 --- 1 --- 2 --- 3 --- 4 --- 5 --- 6 --- 7 --- 8 --- 9 --- 10 |                                    |
|     | Ingen oro/ångest   | Värsta tänkbara oro/ångest         |
| 6.  | 0 --- 1 --- 2 --- 3 --- 4 --- 5 --- 6 --- 7 --- 8 --- 9 --- 10 |                                    |
|     | Ingen sömnighet/dåsighet                                       | Värsta tänkbara sömnighet/dåsighet |
| 7.  | 0 --- 1 --- 2 --- 3 --- 4 --- 5 --- 6 --- 7 --- 8 --- 9 --- 10 |                                    |
|     | Bästa möjliga aptit  | Ingen aptit                        |
| 8.  | 0 --- 1 --- 2 --- 3 --- 4 --- 5 --- 6 --- 7 --- 8 --- 9 --- 10 |                                    |
|     | Bästa möjliga välbefinnande                                    | Sämsta tänkbara välbefinnande      |
| 9.  | 0 --- 1 --- 2 --- 3 --- 4 --- 5 --- 6 --- 7 --- 8 --- 9 --- 10 |                                    |
|     | Ingen andnöd   | Värsta tänkbara andnöd             |
| 10. | 0 --- 1 --- 2 --- 3 --- 4 --- 5 --- 6 --- 7 --- 8 --- 9 --- 10 |                                    |
|     | Bästa möjliga livskvalitet                                     | Sämsta tänkbara livskvalitet       |

Ifyllt av;

☐ patienten självständigt

☐ patienten med hjälp av personal

☐ patienten oförmögen att delta

☐ patienten med hjälp av anhörig

☐ patienten vill inte delta

# Appendix 2

## Patientformulär Allmäntillstånd inför cytostatikabehandling

Patientnamn \_\_\_\_\_ Personnr \_\_\_\_\_

Datum \_\_\_\_\_

### 1. Senaste dagarna, hur många av dagens timmar (klockan 09 – 19) har Du vilat?

0 ---- 1 ---- 2 ---- 3 ---- 4 ---- 5 ---- 6 ---- 7 ---- 8 ---- 9 ---- 10

Ingenting

10 timmar eller mer

### 2. Hur mycket har Du orkat de senaste dagarna?

0 ---- 1 ---- 2 ---- 3 ---- 4 ---- 5 ---- 6 ---- 7 ---- 8 ---- 9 ---- 10

Ingenting

lika mycket som friska jämnåriga

### 3. Hur har Ditt välbefinnande varit senaste dagarna?

0 ---- 1 ---- 2 ---- 3 ---- 4 ---- 5 ---- 6 ---- 7 ---- 8 ---- 9 ---- 10

Värsta tänkbara

bästa tänkbara

### 4. Känns det som Du har tillräckligt med krafter för att orka med dagens cytostatikabehandling?

☐ Definitivt inte    ☐ Tveksamt    ☐ Varken ja eller nej    ☐ Troligen    ☐ Säkert

### 5. Vilken/vilka har varit de mest påtagliga effekterna för Dig av föregående cytostatikabehandling?

\_\_\_\_\_

Ifyllt av:

☐ patienten själv

☐ patienten med hjälp av anhörig

☐ patienten med hjälp av personal

☐ kan ej medverka

Om prover inför behandling tas tidigare än behandlingsdagen, fylls enkäten i då och sändes med fax till cytostatikabehandlingsavdelningen, fax nr \_\_\_\_\_