From DEPARTMENT OF CLINICAL NEUROSCIENCE
Karolinska Institutet, Stockholm, Sweden

EXPERIENCES, EXPECTATIONS AND TREATMENT DECISION-MAKING IN MEN WITH METASTATIC PROSTATE CANCER

Sandra Doveson

Karolinska Institutet

Stockholm 2022

Published by Karolinska Institutet.
Printed by Universitetsservice US-AB, 2022

ISBN 978-91-8016-817-5
Cover illustration: Jenny Doveson

Experiences, expectations and treatment decision-making in men with metastatic prostate cancer
THESIS FOR DOCTORAL DEGREE (Ph.D.)

By

Sandra Doveson

The thesis will be defended in public in the Weitner auditorium, Sophiahemmet University, Valhallavägen 91, entrance R, 2nd floor, Stockholm, on Tuesday November 29th of 2022 at 10.00 AM.

Principal Supervisor:
Associate professor Agneta Wennman-Larsen
Karolinska Institutet
Department of Clinical Neuroscience
Division of Insurance Medicine
Sophiahemmet University
Department of Nursing Science

Co-supervisors:
Associate professor Lena Axelsson
Sophiahemmet University
Department of Nursing Science

Professor Per Fransson
Umeå University
Department of Nursing

Opponent:
Professor Karin Blomberg
Örebro University
School of Health Sciences

Examination Board:
Professor Maria Larsson
Karlstad University
Department of Health Sciences

Professor Mia Bergenmar
Karolinska Institutet
Department of Oncology-Pathology
Sophiahemmet University
Department of Nursing Science

Associate professor Magnus Lindskog
Karolinska Institutet
Department of Oncology-Pathology
Uppsala University
Department of Immunology, Genetics and Pathology

To mom and dad.

POPULAR SCIENCE SUMMARY OF THE THESIS

Treatment decision-making and participation in treatment decision-making have been found to be important to patients with cancer, and a lot of research has been conducted about the treatment experiences and experiences of treatment decision-making among men with localised prostate cancer. Their experiences and preferences have been found to be diverse and influenced by a number of factors. Prostate cancer is one of the most common cancers among men worldwide – over 1.4 million men get this diagnosis and over 375.000 men die yearly from prostate cancer. In Sweden, over 11.000 men get a prostate cancer diagnosis each year, making it the most common cancer diagnosis in the male population. Most men who receive the diagnosis have localised prostate cancer, meaning the cancer is confined within the prostatic gland, for which there are several curatively intended treatment options. However, some men are diagnosed with, or develop, metastases, meaning the cancer has spread to other organs or tissues in the body. For metastatic prostate cancer, there is no curative treatment available. Instead, men with metastatic prostate cancer receive hormone treatment, since a few years sometimes combined with other treatments, to stop the disease from progressing further. Nevertheless, men who undergo these hormone treatments will eventually become resistant to them and develop what is called metastatic castration-resistant prostate cancer (mCRPC), which is considered to be the most advanced prostate cancer stage. The treatment landscape for mCRPC has undergone rapid development over the past one and a half decade, and there are now several treatments with the intent to prolong life available for these men. While there is a large body of research on treatment decision-making and treatment experiences among men with localised prostate cancer, research is, however, scarcer among men with more advanced prostate cancer. Given how the treatment options for mCRPC have increased in recent years, it is important to know how men with mCRPC experience making decisions about, and undergoing, life-prolonging treatments.

Against this background, the overall aim of this thesis was to explore experiences, expectations and treatment decision-making in men with metastatic prostate cancer. The participants in the first study were two groups of men who started out with localised prostate cancer and underwent radiotherapy with curative intent, one group developed metastatic prostate cancer (106 men) and one did not develop metastases (214 men) over the course of five years. The men in both groups answered repeated questionnaires containing questions about their quality of life, symptoms and functioning over the five years. Quality of life, symptoms and functioning were then compared between the groups to detect if, and when, differences between them occurred. The remaining studies of this thesis comprised men

with mCRPC who underwent life-prolonging treatment(s). In the second study, 16 men were interviewed about their perspectives when faced with a life-prolonging treatment. In the third study, 17 men participated in serial interviews (a total of 31 interviews) about their experiences of decision-making regarding their life-prolonging treatment. The fourth and last study of the thesis comprised 114 men who answered repeated questionnaires containing questions about their satisfaction with how the decision regarding life-prolonging treatment had been made, as well as questions about their experiences of the treatment, over the course of one year. Statistical analyses were then performed to explore potential relationships between how satisfied the men were with their treatment decision-making experience and how they experienced the treatment.

The results of this thesis show that once men with prostate cancer develop metastases, their quality of life, symptoms and function gradually deteriorates over time in comparison to men who do not develop metastases. Some decline in quality of life and symptoms over time was also seen in the group of men with non-metastatic disease, however far less so than in the group who developed metastases. When men with mCRPC are faced with starting a life-prolonging treatment, they were aware that the treatment would not cure their illness. They performed a careful trade-off between what the treatment would hopefully accomplish (prolonging their lives) and what the treatment could potentially cost them in terms of intrusive side effects. They also thought about what would happen if the treatment did not work as they had hoped and whether other treatments would be available to them if that were to happen. When treatment decisions were being made, the men had diverse experiences. They identified their physician as a key actor and also modified their own approach to, and actions related to, treatment decision-making depending on their physician. For some, this meant they felt compelled to take on a more driving role in the decision-making process than they really wanted. The men wanted personalised information to form a basis for treatment decisions and accessed a variety of sources to find helpful information. Their satisfaction with how the treatment decision had been made was also related to how they rated their wellbeing over time. The results of this thesis call for early monitoring of quality of life, symptoms and functioning among men with metastatic prostate cancer, especially since their deterioration commonly is gradual and stretches over time. It was also found that treatment decision-making at the most advanced stage of metastatic prostate cancer was twofold. Decision-making included both the treatment itself and what aspects the men considered when deciding to proceed with treatment or not, and how they had experienced the structure of decision-making and how the decision had been arrived at. Given that men with mPC

report a declining condition, and diverse experiences and wishes for treatment decision-making, integrating a palliative approach early in the disease trajectory could serve as a way to identify and address their unmet needs regarding information, continuity of care, communication and treatment decision-making.

ABSTRACT

Background: Participation in treatment decision-making (TDM) is important to patients with cancer and TDM experiences and preferences for how to make treatment decisions have been extensively studied in men with localised prostate cancer. Their preferences for how to partake in TDM are diverse and influenced by several factors. A significant proportion of men with localised prostate cancer, however, develop metastatic disease (mPC), after which the disease is considered incurable. The life-prolonging treatment possibilities at the most advanced stage of mPC, metastatic castration-resistant prostate cancer (mCRPC) have increased dramatically over the past decade, and far less is known about experiences and TDM in these advanced phases of the disease.

Aim: The overall aim of the thesis was to explore experiences, expectations and treatment decision-making in men with metastatic prostate cancer.

Methods: Studies I and IV were prospective, longitudinal cohort studies, study II was qualitative and study III had a qualitative, serial design. In study I, two matched groups of men with mPC (n=106) and non-mPC (n=211) were followed over 5 years with repeated questionnaires. Quality of life, symptoms and functioning were compared between the groups using independent samples Mann–Whitney U tests. The samples in studies II-IV comprised men with mCRPC who underwent life-prolonging treatment. In study II, 16 men were interviewed about their perspectives when faced with a life-prolonging treatment. Data was analysed using interpretive description. In study III, 17 men partook in serial qualitative interviews about their experiences of TDM and data was analysed with qualitative content analysis. In study IV, 114 men answered repeated questionnaires about satisfaction with TDM regarding the life-prolonging treatment and treatment experiences over the course of one year. Associations between satisfaction with TDM at baseline and treatment experiences and wellbeing at six and 12 months were explored using Spearman's rank correlation.

Results: Compared to men with localised prostate cancer, men with mPC report increasing symptoms and worsening quality of life and functioning over time once they develop metastases. TDM was twofold and contained both the desired treatment outcome and aspects of the structure of how the treatment decision was made. When men with mCRPC are faced with a life-prolonging treatment, they weigh the potential treatment benefits – prolonging life – against the possible treatment side effects and their intrusion on the men's everyday lives. Receiving personalised information was important to the men, and the treating physician was a key party in TDM to whom the men modified their TDM role and -actions. Their satisfaction with the TDM structure was also associated with their physical and emotional wellbeing over time.

Conclusion: TDM regarding life-prolonging treatment was found to be a complex, balancing act in which men with mPC face and manage a number of complex situations and have diverse experiences and preferences. Given that men with mPC report declining quality of life, symptoms and functioning and had unmet needs regarding information, continuity of care, communication and TDM, early integration of a palliative approach into the care of men with mPC could work as a way to identify and manage needs that need to be addressed.

SVENSK SAMMANFATTNING

Bakgrund: Delaktighet i behandlingsbeslut är viktigt för patienter med cancer och beslutsfattande kring behandlingar har studerats extensivt hos män med lokaliserad prostatacancer. Deras erfarenheter av, och preferenser för, delaktighet i behandlingsbeslut har visat sig variera och påverkas av flertalet faktorer. En betydande del av män med lokaliserad prostatacancer utvecklar dock metastatisk sjukdom (mPC), som därefter inte är möjlig att bota. Behandlingsmöjligheterna med livsförlängande behandling i det mest avancerade sjukdomsskedet, metastatisk, kastrations-resistent prostatacancer (mKRPC), har ökat dramatiskt det senaste decenniet, och det saknas kunskap om mäns upplevelser och erfarenheter av beslutsfattande i detta avancerade sjukdomsskede.

Syfte: Avhandlingens övergripande syfte var att utforska upplevelser, förväntningar och behandlingsbeslut hos män med metastatisk prostatacancer.

Metod: Studie I och IV var prospektiva, longitudinella kohortstudier, studie II var kvalitativ och studie III hade kvalitativ, seriell design. I studie I matchades två grupper av män med mPC (n=106) och icke-mPC (n=211) och följdes över 5 års tid med upprepade frågeformulär. Livskvalitet, symtom och funktionsnivåer jämfördes mellan grupperna med hjälp av Mann-Whitney U-tester. Urvalsgrupperna i studie II-IV bestod av män med mKRPC som genomgick livsförlängande behandling. I studie II intervjuades 16 män om sina perspektiv när de ställdes inför livsförlängande behandling. Data analyserades med tolkande beskrivning (interpretive description). I studie III deltog 17 män i upprepade kvalitativa intervjuer om sina erfarenheter av behandlingsbeslut, och data analyserades med kvalitativ innehållsanalys. I studie IV besvarade 114 män upprepade frågeformulär om tillfredsställelse med beslutsfattande rörande livsförlängande behandling samt om erfarenheter av behandling under ett års tid. Spearmans rank-korrelationer gjordes för att utforska samband mellan tillfredsställelse med beslutsfattande rörande behandling och erfarenheter av behandling samt välbefinnande efter sex och 12 månader.

Resultat: Jämfört med män med lokaliserad prostatacancer rapporter män med mPC ökande symtom samt sjunkande livskvalitet och funktionsnivåer över tid efter att de utvecklat metastaser. Beslutsfattande rörande behandlingar visade sig vara tudelat och omfattade både det önskade behandlingsutfallet och strukturen för hur beslut fattas. När män med mKRPC står inför livsförlängande behandling väger de möjliga vinster med behandlingen – förlängande av livet – mot risken för behandlingsbiverkningar och deras påverkan på det dagliga livet. Personligt anpassad information var viktigt för männen och den behandlande läkaren hade en central roll i beslutsfattande rörande behandling, till vilken männen även modifierade sin egen roll och sina handlingar i relation till beslutsfattande. Det fanns även ett samband mellan deras tillfredsställelse med strukturen för beslutsfattande och deras fysiska och emotionella välbefinnande över tid.

Slutsats: Beslutsfattande kring livsförlängande behandling visade sig vara en komplex balansakt där män med mPC står inför, och hanterar, komplexa situationer och där deras erfarenheter och preferenser varierar. Eftersom män med mPC rapporterar minskande livskvalitet och funktionsnivåer och ökande symtom, samt hade behov rörande information, vårdkontinuitet, kommunikation och beslutsfattande, skulle tidig integrering av ett palliativt förhållningssätt kunna vara ett sätt att identifiera och hantera behov som behöver adresseras.

LIST OF SCIENTIFIC PAPERS

I. Doveson, S., Holm, M., Fransson, P., & Wennman-Larsen, A. (2022). Identification of early symptoms and changes in QoL and functioning among men with primary localized prostate cancer who later develop metastases: A matched, prospective study. *Palliative and Supportive Care,* 1-9. doi: 10.1017/s1478951522000074

II. Doveson, S., Holm, M., Axelsson, L., Fransson, P., & Wennman-Larsen, A. (2020). Facing life-prolonging treatment: The perspectives of men with advanced metastatic prostate cancer - An interview study. *European Journal of Oncology Nursing, 49,* 101859. doi: 10.1016/j.ejon.2020.101859

III. Doveson, S., Wennman-Larsen, A., Fransson, P., & Axelsson, L. (2022). Men's experiences related to decision-making in life-prolonging treatments of metastatic castration-resistant prostate cancer: a wish for a process adapted to personal preferences – a prospective interview study. *Submitted to journal.*

IV. Doveson, S., Fransson, P., Axelsson, L., & Wennman-Larsen, A. (2022). Associations between experiences of treatment decision-making and treatment experiences during the first year of life-prolonging treatment among men with metastatic castration-resistant prostate cancer. *In manuscript.*

CONTENTS

LIST OF ABBREVIATIONS

EORTC QLQ-C30	European Organisation of Research and Treatment of Cancer Quality of life Questionnaire
HRQoL	Health-related quality of life
IAHPC	International Association for Hospice and Palliative Care
mCRPC	Metastatic castration-resistant prostate cancer
mPC	Metastatic prostate cancer
PC	Prostate cancer
PCSS	Prostate Cancer Symptom Scale
PSA	Prostate-specific antigen
QoL	Quality of life
RT	Radiotherapy
TDM	Treatment decision-making

1 INTRODUCTION

When I was a little 8-year-old girl, I wrote in my diary that I wanted to become either an astronaut (deeply fascinated by space (still am)), dog breeder (adored dogs (still do)) or a researcher when I grew up to be an adult. I was not entirely sure what a researcher did, but I had a faint perception of what "science" was and figured it would probably be very exciting and important to work with. Fast forward 15 years, and I am working as a registered nurse at a specialised palliative care unit at the local hospital. Working there, I regularly met patients with cancer undergoing disease-directed life-prolonging treatments while simultaneously receiving palliative care. The question of whether to continue or terminate the disease-directed treatment would eventually come up as the patient's condition worsened, and I realised that the ways in which these discussions with the patients and their families unfolded were very diverse. Clearly, treatment decision-making at this late stage of cancer was a delicate process and not always as simple and straight-forward as one could maybe imagine. When I was offered the opportunity to join the research project as a doctoral student, accepting the offer was therefore one of the easiest things I have ever done. I was (and am!) very grateful for the opportunity to immerse myself in aspects of living with incurable prostate cancer and decision-making at the most advanced stage of the illness. My hope is for the results of this thesis to be helpful to healthcare professionals working in everyday clinical environments when supporting men with advanced prostate cancer who face complex treatment decisions.

2 BACKGROUND

2.1 TREATMENT DECISION-MAKING IN CANCER CARE

Patients' roles in treatment decision-making (TDM) have been shown to be important, none the least among patients with cancer. However, for various reasons decision-making does not always unfold in the way patients would like [1-5]. Barriers to shared decision-making regarding treatment could be patients' and/or families' unrealistic outcome expectations, unmet information needs as well as how treatment options are framed and presented by the treating physician [1]. Decision-making in cancer care is a complex process with several influencing factors, such as personal beliefs and values, along with previous experiences of both the treating physician and the patient. Availability of care has also been shown to influence the decision-making process [6]. Patients' perceptions of participation in cancer TDM may in turn be affected by several factors, e.g., the relationship with the treating physician, access to adequate information and their perception of hope. The desire for participation in TDM also tends to increase along the cancer disease trajectory, with patients describing increased decision-making competency and level of confidence [7] as well as a sense of there being more at stake the more advanced their illness becomes [8]. Since a large proportion of patients with cancer has been shown to want to be more involved in the decision-making process than they actually were [3-5], simply asking about the patient's preferred decision-making role could work as a facilitator for physicians to attain the patient's desired degree of participation [5, 9]. While research shows that patients with cancer want to partake in decisions regarding their own healthcare, there is also research indicating that patients with cancer wanted a less active role in decision-making than patients with non-cancer diagnoses [10]. Further, it has been shown that dissonance between the preferred degree of participation in TDM and the actual/perceived degree of participation in TDM has been associated with lower health-related quality of life (HRQoL) as well as poorer physical health and mood in patients with cancer [2]. The association was independent of the dissonance direction – indicating that patients who participated in decision-making to a greater extent than they had wished for also experienced lower HRQoL [2].

2.1.1 The concept of "patient participation"

A concept analysis of "patient participation" [11] identified four defining attributes that characterize the concept within the context of nursing practice: 1) an established relationship, 2) a surrendering of some power or control by the nurse, 3) shared information and knowledge, and 4) active mutual engagement in intellectual and/or physical activities. Halabi

et al (2020) performed a thematic analysis of "patient participation" in a review comprising 39 articles on the concept [12]. Attributes and dimensions of the concept are presented at three levels – micro (interpersonal), meso (organisational) and macro (societal/governmental). Patient participation was found to be influenced by individual characteristics, knowledge, skills and attitude of both the patients and healthcare professionals. Similarly to how Sahlsten et al (2008) [11] have described the concept, Halabi et al (2020) [12] found that within the patient- and healthcare professional relationship, both parties need to share information and knowledge as well as power, leadership and responsibilities with one another, all of which seem to be prerequisites for shared decision-making to occur. The patient- and healthcare professional relationship required time to develop towards what is called "partnership care" – a relationship that is characterized by trust, an open dialogue, mutual agreement over the goals of treatment, active mutual engagement and a mutual understanding of roles and responsibilities [12].

When patients were asked to describe "patient participation", the results display a view of the concept that goes beyond just being involved in decision-making. Instead, patient participation was described as "being involved in a life situation", with the patient as a holder of knowledge rather than a recipient of information, as well as interaction with healthcare staff [13]. Aside from being informed and having knowledge [13], conditions for participation in healthcare, as reported by patients, also include being regarded as an individual, receiving the care one finds necessary and partaking in planning. Utilising one's knowledge to make decisions about healthcare and performing self-care are also important dimensions of participation in healthcare [14].

2.1.2 Theoretical models for decision-making

There are three distinct theoretical models for medical decision-making in the literature – the paternalistic-, the informed- and the shared decision-making models [15]. In the paternalistic decision-making model, the physician holds the dominant role and suggests an option they believe would be the best for the patient following assessment of the patient's situation. The patient's role encompasses consenting to, or rejecting, the suggested option. The informed decision-making model unfolds in the opposite way, with the patient gathering information and then making the decision themselves [15]. It has even been argued that this model views the patient as more of a consumer, a recipient of the commodity that is information, who is then responsible for making a decision on their own based on that information [16]. Lastly, there is the shared decision-making model, where the patient and physician work together and

come to a joint decision [15]. The shared decision-making model is described more in-depth below.

2.1.3 Shared decision-making

It has been shown that shared decision-making is preferred by many patients, as opposed to paternalistic or informed decision-making [17]. Further, voices advocating shared decision-making as the path forward for treatment decisions have long been heard, none the least via the Salzburg Statement on shared decision-making from 2011 [18]. The statement calls for clinicians and patients to take a number of steps to facilitate shared decision-making, e.g. a two-way sharing of information and concerns about the decision that is to be made. Shared decision-making has even been argued to be "the pinnacle of patient-centred care" (Barry et al., 2012, page 781), as it engages the patient and considers their individual treatment preferences and needs in the decision-making situation [19]. Even earlier, a model for shared decision-making was developed by Charles et al (1997), who described four characteristics of shared decision-making: 1) At a minimum, both the physician and patient are involved in the treatment decision-making process, 2) both the physician and patient share information with each other, 3) both the physician and the patient take steps to participate in the decision-making process by expressing treatment preferences, and 4) a treatment decision is made and both the physician and the patient agree on the treatment to implement. The model elaborates further on the decision-making process by acknowledging the possibility, and the roles, of additional parties in the decision-making process, such as family or friends of the patient. Further, the model underlines that shared decision-making is a two-way street, with mutual power and responsibilities of the patient and the physician, and concludes that shared decision-making can only occur if it is not only desired, but also allowed, by both of them [15].

Based on the principles of shared decision-making, Elwyn et al (2012) developed a model for achieving shared decision-making in clinical practice [20]. The model describes a movement from initial talk about what choices there are, to a deeper joint exploration of the different options, to considering preferences and what the patient feels matters most to them. Finally, a decision is reached. Again, the two-way sharing of information, questions and concerns are described as important for shared decision-making to be facilitated [20]. Much like Elwyn et al (2012), Politi et al (2012) depicts shared decision-making as a motion in their model for facilitating shared decision-making in oncological practice [21]. It is described as a process that moves from identifying a situation where shared decision-making would be feasible, via

exploring risks and benefits of the different options to eliciting patient preferences and ultimately reaching a decision. They specifically address the challenges associated with decision-making in an oncological setting, such as how to treat patients with complex illnesses and/or comorbidities, how to support patients who feel compelled to make a treatment decision quickly or how to reason regarding side effect-intense treatments in patients with advanced incurable cancer who may be approaching end of life [21].

Shared decision-making as a concept has also been explored by interviewing patients and building a conceptual definition based upon their perceptions [22]. The definition is fourfold and describes the process leading up to the decision: 1) both physician and patient share information, 2) both are openminded and respectful, 3) patient self-advocacy, and 4) personalised physician recommendation [22]. Similarly to the theoretical shared-decision making models presented by Charles et al (1997) [15] and Elwyn et al (2012) [20], the mutual exchange of information and joint efforts of the patient and the physician towards shared decision-making are emphasised [22].

2.1.4 Patient expectations in cancer care

A model of the forming of health expectations by Janzen et al (2006) describes how they develop over time and are formed in relation to goals and behaviours [23]. Expectations are influenced by prior beliefs, understanding and experiences and are formed in a cognitive process utilising one's sense of probability (the likelihood of something occurring), causality (one action or outcome recognisably seen as a result of a previous one) and temporality (future events can be predicted using information from past events). Further, the perceived value of whether an event was to occur alongside one's sense of self-efficacy is an important component in developing a goal, that in turn leads to the development of an outcome expectation [23]. Patient expectations have been studied in the context of cancer. Patients with incurable glioblastoma and metastatic colon cancer have been shown to sometimes overestimate the survival benefits of life-prolonging treatment [24] and a substantial proportion of patients with advanced, incurable lung- and colorectal cancer, despite the palliative and life-prolonging intent of the treatment, might not have understood that the chemotherapy was unlikely to cure their cancer [25]. Treatment expectations do not only concern treatment outcome or intent, they may also encompass side effects of cancer treatment; where associations between response expectancies and patients' experiences of side effects of cancer treatment have been shown [26, 27], indicating that patients who expect

certain side effects from the treatment are also more likely to experience them during treatment.

2.2 PROSTATE CANCER - A BRIEF OVERVIEW

Prostate cancer (PC) is one of the most common forms of cancer and causes of cancer-related death globally, accounting for 7.3 percent of the yearly cancer incidence with over 1.4 million new cases and over 375.000 deaths yearly (2020). It is the most frequently diagnosed type of cancer among men in over half of the countries of the world [28], with the majority of the cases appearing in developed countries. The incidence rate also varies globally, which is mainly attributed to differences between countries regarding the use of routine PC screening among the male population [28, 29]. The incidence in Sweden is over 11,000 men yearly (2019) with a crude rate of 213 new cases per 100.000 persons yearly [30]. The risk of developing PC increases with age [31, 32] and a family history of PC [32, 33]. Some men also appear to have a genetic predisposition for PC, making them susceptible to developing the disease [29]. A number of studies have also highlighted the greater risk of developing PC among men with African descent [32, 34, 35].

Eighty to ninety per cent of men who are diagnosed with PC are diagnosed with localised disease [36]. Some undergo curatively intended treatments with surgery (prostatectomy) or radiotherapy (RT), while others undergo active surveillance, meaning that their PC is being regularly monitored and more invasive treatments could be considered if the disease progresses further [32]. No significant differences has been found regarding 10-year PC-specific mortality between the treatment modalities [37] and since the treatment options differ regarding side effects, individual assessments and sharing the decision-making with the patient has been recommended [38]. Watchful waiting can be an option for patients who are frail or whose life expectancy is less than 10 years, in which the PC is monitored awaiting symptomatic treatment if needed [32].

2.2.1 Treatment decision-making preferences among men with localised PC

In the context of localised PC, previous research emphasises the need for the physician to adapt to the patient's preferred level of participation [7], much in line with the shared decision-making model by Charles et al (1997) [15]. Men's preferences for their own PC TDM role are diverse. A majority of men with localised PC prefer to make treatment decisions together with their physician in a collaborative, or shared [15], process [39-42]. The

vast majority of men with localised PC also report having had a shared decision-making experience [43, 44]. A proportion of men instead prefer a decision-making process that could be described as more paternalistic in character [15], where the patients leave the treatment decision up to the physician [39-42]. Finally, preferences for informed decision-making [15] have also been described [40, 42, 45]. Preferences for a more active role in TDM is reported to a greater extent by men who are younger [39, 46] and have low-risk disease [39], whereas another study shows that younger men and men with higher educational level instead report preference for informed decision-making over shared decision-making [47]. Preferred TDM role has also been shown to be associated with type of treatment in localised PC [43]. A review including studies on early-stage PC concludes that the patient's decisions regarding treatment could involve a careful weighing of possible treatment benefits against potential treatment side effects. With these side effects sometimes being both unpredictable and uncertain for each individual patient, the decision-making process becomes complex. The process is also described as dynamic, and can vary between patients and also over time [48]. Though previous research indicates that shared decision-making is desired to a greater extent than its occurrence by patients with cancer [3, 5, 7], a review highlighted that this is not always the case for patients with PC – which contrasts to other cancer diagnoses in that they instead may be involved to a greater extent than they desire [3].

2.2.2 Factors of importance in treatment decision-making in localised PC

The physician is described as a very important influential factor on the men's TDM in localised PC [45, 47, 49], where spending enough time with them [44] to develop a connection and a relationship has been described as important [49]. Trust in one's physician is also important [50] and a lack of trust in one's physician has been shown to cause men to assume a TDM role that is more active than they otherwise would have intended or wanted [51]. Other important factors in TDM for men with localised PC are the desired treatment outcome, where preferences for active treatment (surgery or RT) are reported when the men want to choose a treatment that they believe would provide a definite cure of the cancer [44, 52, 53]. Research on patients with localised PC indicate that these patients, while overestimating the survival benefits of curative treatment also tend to underestimate their life expectancy without treatment [54, 55]. Further, treatment side effects are also important aspects considered by men faced with a treatment decision related to their localised PC [44, 53, 56]. Especially concerning side effects are a lengthy recovery from treatment, erectile dysfunction, urinary incontinence [56, 57], a negative impact on work [44, 58] and surgery complications [59]. Decisional regret has been studied among men who underwent radical

prostatectomies for localised PC, where the vast majority of men reported no regrets over their treatment decision after one year [60]. The association between participation in treatment decision-making for localised PC and decisional regrets has also been studied. At short-term follow-up, the majority of men (94%) reported that they had assumed either an active or a collaborative role in treatment decision-making. Neither the type of treatment chosen nor their reported decision-making role were associated with treatment regrets [61]. Conversely, at long-term follow-up after treatment of localised PC, treatment regrets are expressed by a greater proportion of men who undergo more invasive treatments (radical prostatectomy or radiation therapy) than of those who undergo active surveillance as primary treatment [62].

In trying to decide which treatment to choose, men with localised PC access the Internet [45, 52, 53, 63-66], social networks [58], TV/radio [64] written resources [45, 47, 52, 53, 64, 66], other patients [45, 47, 64] or patient organisations/federations [64], family members [44, 45, 53, 64] and friends [44, 45, 53, 64, 67] as a complement to the information they obtain from their physician [53, 56, 58, 63, 64, 67]. Despite the fact that men with localised PC access and utilise a large variety of sources to paint a clear picture of their treatment options, their risks and benefits, a notable amount of them report feeling less informed about treatment options than desired [66, 68]. Further, they also report lacking the necessary means to utilise the information in the actual decision-making [68], which alongside a perceived lack of adequate time and discussions concerning treatment side effects is associated with significantly more difficulties in deciding on a treatment [52].

2.3 METASTATIC PROSTATE CANCER – THE PROGRESSION FROM CURABLE TO INCURABLE

A small proportion (10-20%) of men with PC have metastatic disease already at diagnosis [36], and 15-30 percent of the men diagnosed with, and treated for, localised disease eventually develope metastatic PC (mPC) [36, 69]. For men who did not have metastatic disease already at diagnosis, time from diagnosis to development of metastases has been shown to be a prognostic factor for overall survival, where metastases already at diagnosis are associated with significantly shorter overall survival in comparison with men who develop mPC later on [70]. Once PC has metastasised, it is considered incurable and, in this phase, most men undergo hormone treatment (surgical castration or androgen deprivation therapy) to suppress and inhibit the disease [71]. Since a few years ago, taxane chemotherapy is also

combined with androgen deprivation therapy to treat metastatic hormone-naïve PC [72-74]. However, patients undergoing castration will eventually become resistant to the treatment and develop metastatic castration-resistant PC (mCRPC)[71]. This advanced disease stage is defined by a disease progression, usually determined by rising Prostate-Specific Antigen (PSA) serum levels despite ongoing castration treatment.

2.3.1 Living with incurable mPC and mCRPC

There are a number of symptoms associated with mPC, where pain from skeletal metastases (particularly the pelvis and spine), fatigue and problems with urinary and sexual functioning are common [75]. Aside from the symptom burden at this stage, undergoing hormone therapy for mPC is also associated with unwanted side effects, such as hot flushes, loss of libido, erectile dysfunction and a decrease in bone mass and bone density [76]. The consequences of living through the natural history of mCRPC in terms of symptom occurrence and distress as well as effect on HRQoL and different aspects of functioning and everyday life, have been studied. As for symptoms, men with mCRPC experience a range of symptoms, with pain from skeletal metastases, fatigue [77], nausea and vomiting, dyspnea and appetite loss being reported as particularly prominent [78]. The prognosis for men with mCRPC is poor. The median survival time is less than 18 months and the HRQoL rapidly deteriorates once the disease becomes castration-resistant [78]. Skeletal metastases at risk of causing skeletal fractures or cord compression have also been shown to affect HRQoL and functional status in men with mCRPC negatively [79]. The construction of a conceptual framework of patient-reported outcome measures for mCRPC by Eton et al. (2010) [80] has added knowledge to the field through literature reviews, patient interviews, practitioner surveys and analyses of archived study data. Eighteen important outcomes were identified and divided into five domains: *specific physical symptoms of disease, specific physical side effects of treatment, physical symptoms of disease and side effects of treatment, specific psychological concerns,* and *general aspects of quality of life and wellbeing* (Figure 1) [80].

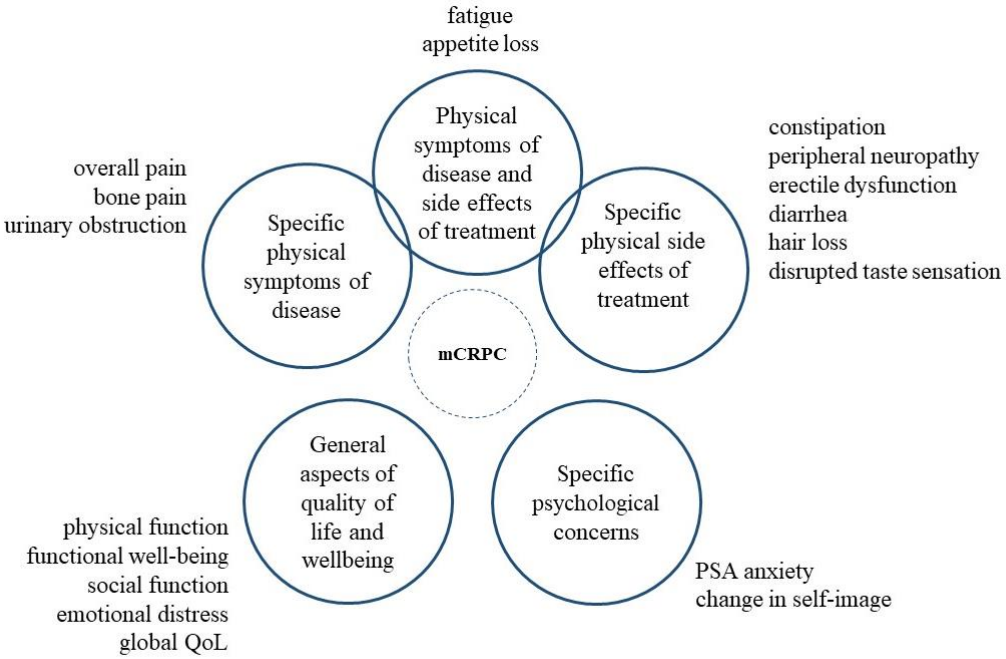

Figure 1. *Visual adaption of the conceptual framework of important patient-reported outcomes for men with mCRPC, by Eton et al (2010) [80]*

Though the symptom burden for men with mCRPC is severe, quality of life (QoL) and functioning have proven to be important as well, as seen in the framework [80]. It has also been shown that global issues might in fact be of even greater importance than single symptoms when rated by men with prostate cancer at different stages. A cross-sectional study on men with PC at different stages concluded that the same three global issues: *QoL, ability to perform normal activities* and *maintaining independence* were ranked as most important for men with PC regardless of disease stage. Even though pain as a single symptom was ranked as more distressing in the subgroup of men with mPC than in the groups with localised PC, these global issues were still ranked as more important than individual disease- or treatment-related symptoms [81].

2.3.2 Definitions of palliative care

Given that mPC is incurable, it could be argued that a palliative care approach would be feasible and potentially beneficial for men with mPC and mCRPC. Claims have also been made that a palliative care approach might be especially beneficial for men with PC already early on in their disease course [75, 82]. Palliative care is defined by the International Association for Hospice and Palliative Care (IAHPC) as "…the active holistic care of individuals across all ages with serious health-related suffering (suffering (…) associated with illness or injury of any kind. Health-related suffering is serious when it cannot be

relieved without medical intervention and when it compromises physical, social, spiritual, and/or emotional functioning) because of severe illness (…a condition that carries a high risk of mortality, negatively impacts quality of life and daily function, and/or is burdensome in symptoms, treatments, or caregiver stress) and especially of those near the end of life. It aims to improve the quality of life of patients, their families, and their caregivers" (Radbruch et al., 2020 page 22) [83]. It intends to neither hasten nor postpone death and assumes a holistic approach with consideration to the different dimensions of the patient and the patient's situation throughout the disease course. The definition also states that palliative care "is provided in conjunction with disease-modifying therapies whenever needed" (Radbruch et al., 2020 page 22) [83]. Also the Swedish National Board of Health and Welfare's definition of palliative care clearly states that palliative care is compatible with life-prolonging treatments early in a disease course [84]. The definition of palliative care is distinguished from that of palliative care at the end of life, that focuses solely on symptom alleviation and promotion of QoL when death is inevitable within a foreseeable future [85]. Neither definition [83, 84] provide limitations regarding specific diagnoses and where palliative care was once primarily practiced in the care of patients with cancer at the very end of life, palliative care has now come to include other illnesses, such as neurological conditions, heart failure and dementia [86]. A "palliative approach" is a concept related to palliative care that captures core values in palliative care but can be applied regardless of organisation or setting. It is a holistic approach that focuses on QoL [87]. The Swedish National Board of Health and Welfare has, in a similar way, emphasised that a palliative approach is holistic and should support the best possible wellbeing of the person [88]. Further, palliative care should rest on four cornerstones: symptom control, good communication with the patient and their family as well as within the team, multi-professional teamwork and support for families of the ill person [89].

2.3.3 Life-prolonging treatments of mCRPC

Before life-prolonging treatments became available for patients with mCRPC, life-prolonging chemotherapy had been proven to increase survival, improve QoL and relieve symptoms in patients with other advanced cancers, e.g. lung cancer [90]. The field of life-prolonging treatments of mCRPC had a breakthrough in 2004, when taxane chemotherapy (Docetaxel) in combination with steroids was shown to prolong overall survival [91, 92] and could also improve HRQoL and pain control [91] in comparison to treatment with Mitoxantrone and Prednisone [93, 94] that had been available at this stage up until then. However, the studies also reported adverse events, such as cardiovascular and gastrointestinal side effects [92],

during treatment with Docetaxel [91, 92]. Since then, the treatment landscape for mCRPC has developed and changed rapidly and continues to do so. Several different life-prolonging treatment options have been further refined and are now available alongside Docetaxel [95-99] Consecutive life-prolonging treatments have also become a possibility for patients whose disease continues to progress following first-line treatment [97, 98, 100, 101]. As the number of treatment options for mCRPC increase, so do the options for combining and sequencing them. With the rising number of options, sequencing treatments in an optimal way has proved to be a challenge as there are a lot of factors to consider, such as patient characteristics, functional level, previous PC treatments and their outcomes [73, 102, 103] as well as patient preferences [104].

2.3.4 Life-prolonging treatments within a palliative care context

Even though neither the IAHPC [83] nor the Swedish National Board of Health and Welfare [84] definitions of palliative care point towards any conflict between treatments with life-prolonging intent and a palliative care approach, balancing life-prolonging treatments against QoL within a palliative care context may be complex. Firstly, the transition from a curative to a palliative approach offers a variety of challenges for both patients and healthcare professionals regardless of diagnosis, with key issues concerning patient information and communication [105]. Implementing a palliative care approach earlier in the disease course could be beneficial for HRQoL when compared to standard cancer care for adults with advanced cancer. However, the importance of individualised interventions and decisions is also emphasised alongside the need to consider the patient's wishes when planning treatment [106]. Further, there are challenges associated with receiving life-prolonging treatments at the most advanced, incurable stages of cancer. The common standpoints and the disparities between life-prolonging chemotherapy and palliative care have been debated - discussing whether, and how, the two are compatible or not [107]. The treatment intention is a focal point when life-prolonging chemotherapy is given in the context of palliative care. Patients' perceptions of hope for a prolongation of life might make it difficult to assess the impact of the treatment on QoL, as the mere knowledge of the desired treatment outcome might cause patients to underestimate the negative impact or side effects of the treatment [108]. Treatment with non-curative chemotherapy at the very end of life might also be associated with unfavourable outcomes, such as shorter overall survival, more frequent hospital admissions and patients dying less often at home, making it imperative to make individual assessments of each patient to make decisions regarding initiation, continuation or cessation of chemotherapy at the end of life [109].

2.3.5 Decision-making in palliative care

When it comes to treatment decision-making at the end of life or in a palliative care context, deciding whether or not to proceed with certain treatments becomes complex due to the gravity of the patient's illness and the lack of definitive evidence or answers in complex decision-making situations [8, 107, 110]. Within the context of palliative cancer care, an observational study suggests that patient participation is constructed in dialogue and discourse in clinical encounters via particular arguments and strategies – "repertoires" – that influence the respective roles of patients and healthcare professionals in decision-making [110]. Exposing the uncertainty of the situation implied acknowledging the inability to fully foresee or predict whether or how a certain treatment would work or that there might not be an unambiguously superior option in a certain situation. In the co-construction of patient treatment preferences, patients and healthcare professionals addressed the options and explored e.g. the patient's previous experiences that might influence their current stance or preference for certain options. When working towards a decision, patient autonomy was affirmed by the healthcare professionals to ensure the patient knew their voice was the most important one when facing a decision. Finally, the authority of healthcare professionals was upheld by both patients and professionals acknowledging the superior medical competence of the professional. The repertoires are exercised by both patients and healthcare professionals, albeit in different ways, to justify patient participation in decision-making [110]. Even though patients with advanced cancer at the end of life seem to want their physician to partake in the treatment decision-making process and contribute with knowledge, experience and clinical expertise, their wishes also vary regarding who they want to take the lead in treatment decision-making. Their preferences range from wanting the physician to take responsibility for deciding, to wanting to be more decisive and to have the final say in the treatment decision. When looking ahead in time, the patients' view of their anticipated role in treatment decision-making was influenced by the aim of the treatment, which they also acknowledged would probably change along the disease trajectory. In a scenario where the goal of treatment was QoL, the patients wished to take on a more decisive role in treatment decision-making than in a scenario where the treatment goals would be continued life prolongation, where they instead preferred their physician to have a more decisive role [8].

2.3.6 Treatment decision-making among men with mPC

Research regarding patient perspectives on decision-making in the context of life-prolonging treatments of mPC is far scarcer than that on TDM in localised PC. The physician's treatment

recommendation has been shown to be the most important influencing factor on TDM among men with mPC [111]. A review of patient-reported outcomes in men with mCRPC undergoing life-prolonging treatment concluded that, given the severity of the disease, it is important not only to consider the specific treatment's desired positive effect on HRQoL but also its possible negative effects on HRQoL due to treatment side effects [112]. Controlling pain from skeletal metastases is shown to be important for men with mCRPC and, again, the benefits of treatment have to be weighed up against the costs -– where fatigue, memory loss and cognitive impairment were viewed as particularly concerning side effects of treatment [104]. QoL has been shown to be more important to men with mCRPC than extending life expectancy with the risk of being hampered by debilitating treatment side effects [113]. The same study evaluated a decision aid used for treatment decisions at this disease stage, and concluded that it could work as an enabling tool for greater understanding of the treatment options as well as a facilitator for interaction with physicians and nurses – who were perceived by the patients as important actors in the decision-making process [113]. Further, decisional regrets have also been studied in mPC, where 23 percent of men reported regrets about the treatment decisions made regarding their mPC. Men who expressed regrets also reported lower scores on measures of QoL. The same study also links regrets to the decision-making process, where men who expressed regrets were more likely to be unsatisfied with their decision-making role and how the treatment decision was arrived at [114]

3 RATIONALE

In summary, TDM has been shown to be important to patients with cancer, who generally want to be more involved in TDM than they perceived they were. However, this is not always the case for patients with PC, who instead sometimes report having been more involved in TDM than they would have wanted. Once PC becomes metastatic, it is considered incurable and treatments from here on out aim to inhibit the disease progression. For the men with the most advanced stage PC (mCRPC), the 2004 breakthrough of taxane chemotherapy for life-prolonging treatment of mCRPC offered the first real possibility to prolong survival at this advanced stage. Since then, the treatment possibilities for mCRPC, both treatment- and sequencing options, have exploded over the past decade. Today, there are several different life-prolonging treatment options, with diverse side effect profiles, available for men with mCRPC, both as a first-line treatment and consecutive treatments. The fast-changing treatment landscape offers complex challenges related to TDM, where QoL in an incurable disease phase must be balanced against the potential life-prolonging effect of treatment(s). The many treatment- and sequencing options may also make it difficult for both the man himself and the treating physician to assess and predict how each man will respond to and experience one or several life-prolonging treatment(s) and associated side effects. While different aspects of TDM have been studied extensively in men with localised PC, research on patient perspectives on experiences, expectations and TDM in men with mCRPC is far scarcer.

4 AIMS

The overall aim of the thesis is to explore experiences, expectations and treatment decision-making in men with metastatic prostate cancer.

4.1 SPECIFIC AIMS

The specific study aims were:

I: To identify early symptoms and changes in QoL among men with primary localized PC who later develop metastases.

II: To explore the perspectives of men when facing life-prolonging treatment of mCRPC.

III: To describe men's experiences related to decision-making in life-prolonging treatments of mCRPC.

IV: To describe men's satisfaction with TDM and treatment experiences during the first year of a life-prolonging treatment of mCRPC.

5 MATERIALS AND METHODS

5.1 DESIGN

This thesis comprises studies with both a qualitative and a quantitative approach. Studies I and IV are both prospective cohort studies and studies II and III are qualitative interview studies. Studies II-IV derive from the same overall research project and is therefore presented in a partially joint and synthesised way in the methods section. A summary overview of the studies is presented in Table 1.

Table 1. *Overview of the studies*

	Study I	Study II	Study III	Study IV
Aim	To identify early symptoms and changes in QoL among men with primary localized PC who later develop metastases	To explore the perspectives of men when facing life-prolonging treatment of mCRPC	To describe men's experiences related to decision-making in life-prolonging treatments of mCRPC	To describe men's satisfaction with TDM and treatment experiences during the first year of a life-prolonging treatment of mCRPC
Design	Prospective cohort study	Qualitative interview study, inductive approach	Qualitative interview study, inductive approach	Prospective cohort study
Sampling	Consecutive	Purposeful	Purposeful	Consecutive
Participants	Two matched groups of 211 men with localised PC and 106 men with PC who developed metastases	16 men with mCRPC undergoing life-prolonging treatment	17 men with mCRPC undergoing life-prolonging treatment	114 men with mCRPC undergoing life-prolonging treatment
Data collection	Repeated questionnaires (EORTC QLQ-C30, PCSS), medical data, socio-demographic data	Qualitative interviews (n=16)	Qualitative serial interviews (n=31)	Repeated questionnaires (FACT-G, study-specific instrument on satisfaction with TDM), medical data, socio-demographic data
Data analysis	Descriptive statistics, independent samples Mann-Whitney U tests, repeated measures ANOVA	Interpretive description	Qualitative content analysis	Descriptive statistics, Spearman's rank correlation

5.2 STUDY I

5.2.1 Procedure and participants

The participants of this study were a subsample from a larger, prospective study comprising 3.885 men who were diagnosed with primary localised prostate cancer. Inclusion criteria for the study were men with newly diagnosed non-metastatic PC (tumour stages T1-T2) who were scheduled to undergo RT with curative intent as primary treatment. The participants received information about the study, and in conjunction with the start of primary RT were asked consecutively by a nurse at the RT department if they wanted to participate. The participants in this study were included between the years 1991 and 2008. For study I, a subsample of 107 participants who developed metastatic disease (mPC group) at some point during the follow-up time in the study were included. The study focuses on palliative care needs, which is why another inclusion criteria for the mPC group was that the participants had died during the follow-up time in the larger study. The participants in the mPC group were matched (1:2) with 214 participants who did not develop metastases (non-mPC group) during their time in the study. The mPC and non-mPC groups were matched on the following criteria: tumour stage at diagnosis, primary treatment (RT) and time for the last follow-up in the study. Upon inclusion, the participants received their first study questionnaire. This was then followed by repeated questionnaires at predetermined time-points over the course of up to five years in this study. The time-points baseline, treatment completion, three months, one year, two years, three years and five years were used in this study.

5.2.2 Measurements

The study questionnaire comprised a compilation of well-validated instruments to measure QoL, symptoms and functioning. *The European Organisation of Research and Treatment of Cancer Quality of life Questionnaire version 3.0* (EORTC QLQ-C30) [115] was used to measure QoL, functioning and symptoms and *The Prostate Cancer Symptom Scale* (PCSS) [116] was used to measure PC-specific symptoms.

The EORTC QLQ-C30 [115] is a 30-item scale, out of which the global health/overall QoL subscale, the five subscales that measure functioning (physical, role, emotional, social and cognitive) and four different symptom scales (pain, fatigue, nausea/vomiting and dyspnoea) were chosen for this study. The four response alternatives are the same for all functioning and symptom scales and range from “not at all” to “very much”. The global health/QoL questions have numerical response alternatives ranging from 1 (very poor) to 7 (excellent). All scores were either calculated by item or by scale, whereafter they were transformed to a number on a

scale ranging from 0 to 100 [115]. Higher values on the 0-100 scale indicate either better QoL/functioning or worse symptoms. The EORTC QLQ-C30 instrument has been tested and found to have good validity for self-assessment of HRQoL among patients with cancer [117] and prostate cancer [118]. Both clinically relevant changes [119] and clinically important threshold values [120] have been identified for the EORTC QLQ-C30 instrument. Clinically relevant changes mean changes in score that would be deemed significant from a clinical point of view. A 5-10 step change in score is the equivalent of "little change", 10-20 steps indicate "moderate change" and a >20-step change indicates "very much change" [119]. The clinically important threshold values are scores on the 0-100 scale that would indicate QoL, a symptom or level of functioning poor enough to require the attention of a clinician [120]. In the QoL and functioning scales, a score under the threshold score is considered to be clinically important and conversely, a score above the threshold score is considered to be clinically important for the symptom scales [120]. The PCSS instrument has been validated in a Swedish context [116]. It is a 43-item scale that uses a modified 10-step linear analogue response scale, with the responses ranging from 0 (meaning "no problem"/"very good function") to 10 (meaning "many problems"/"very bad function"). Three single items (urinary problems, bowel problems and sexual problems) were chosen from the instrument for this study.

5.2.3 Data analysis

Differences between the mPC group's and the non-mPC group's background characteristics were calculated using Student's *t*-test for the continuous variables and X^2 tests for the categorical variables [121]. Due to non-even group sizes, non-parametric tests (independent samples Mann–Whitney U tests) [121] were used to explore differences between the groups regarding QoL, symptoms and functioning. To explore whether the development of metastases in the mPC group could potentially explain the differences between the mPC group and non-mPC group, a sensitivity analysis was performed. The participants in the mPC group who developed metastases during the five years in the study (n=35) were removed from the sample at the follow-up where they had verified metastases and then removed from all subsequent follow-ups. Their corresponding matches (n=70) in the non-mPC group were removed at the same follow-up and beyond. Again, independent samples Mann–Whitney U tests [121] were used to explore differences in QoL, symptoms and functioning between the groups at each follow-up.

Further, a repeated measures analysis of variance (ANOVA) [122] was conducted to explore the changes in QoL, symptoms and functioning within the groups over time between the follow-ups. The analysis was chosen since each participant was present at all the included follow-ups, meaning each participant was present in all groups compared in the analysis of each outcome. The time-points baseline, three years and five years were included in the analysis in order to still include as many participants as possible since only participants who were present in all time-points for each outcome are included in the ANOVA. To determine between which time-points the differences arose, Bonferroni *post-hoc* tests were performed [122]. Also, age was added as a confounding factor in the analysis of differences over time within the groups. A significance level of $p<0.05$ was chosen to be statistically significant in all analyses. All statistical analyses were performed using the software *IBM SPSS Statistics version 26* (IBM, Armonk, NY, USA).

5.3 STUDIES II-IV – THE PROCEED PROJECT

Studies II-IV of this thesis are part of the overarching project named **PRO**state **C**ancer – **E**xperiences and **E**xpectations **D**uring treatment - PROCEED. The execution of the PROCEED project was inspired by the conceptual framework presented by Eton et al., (2010) [80]. Below follows a description of the project design and its inclusion and exclusion criteria, whereafter each of the individual studies II-IV are presented more in-depth.

5.3.1 Overall design and setting

The PROCEED project is a prospective, multisite cohort study with the overall aim to describe how men with one or more consecutive life-prolonging treatments for mCRPC perceive that they would like, and are allowed, to participate in discussions and decisions regarding care and treatment, what expectations they have on the treatment and what impact this has on how they feel during and after it. The PROCEED project is carried out at four different oncology clinics located in both urban and rural regions in Sweden. One hundred and fifty-four men who had been recently diagnosed with mCRPC were included in the research project as they were about to start a life-prolonging treatment at either one of the four study sites. All men in the project are followed with repeated questionnaires over the course of two years, the first year of which provided data for study IV of this thesis. A subsample of 17 participants was asked to participate in qualitative interviews, which provided data for studies II and III of this thesis (Figure 2).

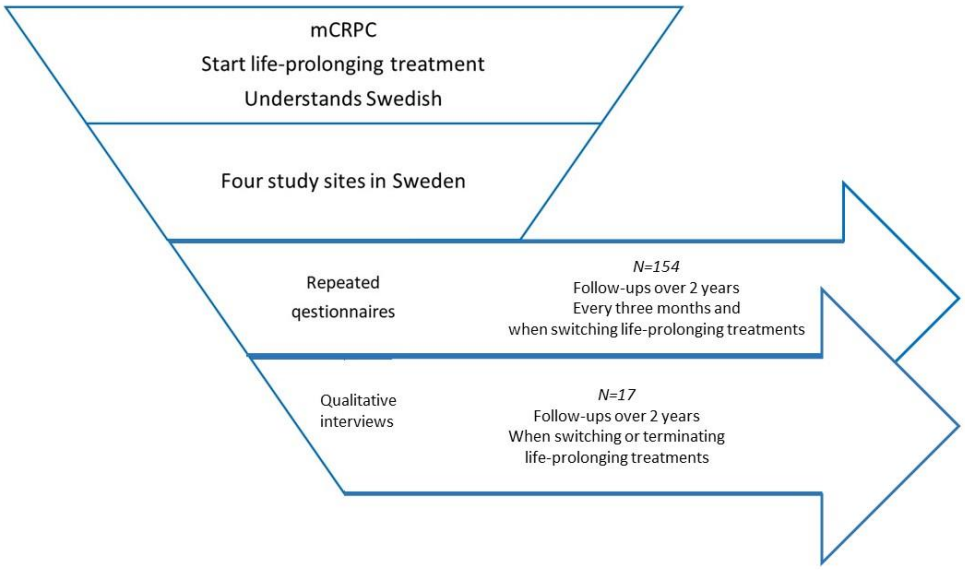

Figure 2. *Overview of the PROCEED project*.

5.3.2 Inclusion- and exclusion criteria in the PROCEED project

Inclusion criteria:

- Men who have metastatic PC and have been diagnosed with castrations-resistant disease (mCRPC).
- Men who will start their first life-prolonging treatment, regardless of previous treatments during their prostate cancer trajectory.

Exclusion criteria:

- Men who are not able to understand and express themselves in Swedish.

5.3.3 Sampling and participants in study II and III

A subsample of 17 participants from the overarching PROCEED participated in serial interviews, of which 16 of the baseline interviews constitute the data for study II and the entire interview series constitutes the data for study III. Since a joint sampling procedure was applied for both studies, a description of the process for both studies follows below. A purposeful sampling strategy [123] was used in an endeavour to include participants who had various experiences and perspectives, similar to a heterogeneity sampling [123]. In doing so, variation in background characteristics, such as place of residence, age, relationship status, educational level and planned first life-prolonging treatment, was sought after in the sampling process. After being included in the overarching PROCEED project, the participants in these studies were asked by a research nurse/study coordinator if they were interested in

participating in serial research interviews. After consenting to share their contact information, they were thereafter contacted via telephone by a researcher from the research project. After the participants received additional information and were given the opportunity to ask any further questions, a first interview was scheduled with those who wished to participate.

5.3.4 Study II - data generation

Data for this study was generated via 16 qualitative interviews [124] with 16 men. The interviews were conducted as the participant was either about to start, was undergoing or had undergone their first life-prolonging treatment after being diagnosed with mCRPC. The interviews were conducted in the place of the participant's choosing, which could be either in their own home, a secluded room at the oncology clinic or in a conference room at the researcher's workplace. Three participants preferred the interview to be done over the telephone instead of face-to-face. An open-ended approach was applied in the interviewing [123], meaning no pre-determined set of questions was utilised. This approach was chosen due to of the lack of research and knowledge about perspectives, expectations and TDM among men with mCRPC undergoing life-prolonging treatments. Instead, a thematic interview guide (Figure 3) that contained an opening question and three key topics to be covered was developed and used during all interviews.

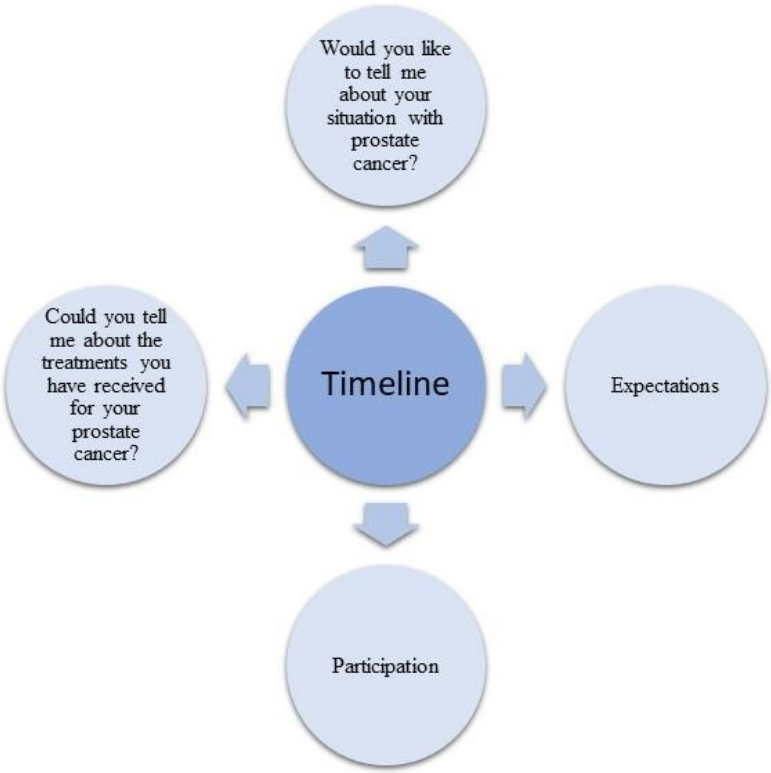

Figure 3. *The interview guide.*

All interviews commenced with the question: "*Would you like to tell me about your situation with prostate cancer?*" after which the participant was encouraged to narrate freely around the topics that emerged naturally. I tried to interrupt the narration as little as possible but sometimes asked probing and follow-up questions to get a clearer understanding of what was being told or to encourage the participant to elaborate further on something that was mentioned. Brief notes were taken during all interviews to keep track of questions and matters the interviewer wanted to return to or probe further. All face-to-face interviews were audio-recorded. Fourteen of the interviews were conducted by me and the median interview length was 56 minutes (range: 22-160 minutes).

5.3.5 Study II - data analysis

The interview data was analysed with an inductive approach [123] using interpretive description [125]. Interpretive description is an approach to research that does not stem from a tradition of theorising, but is instead sprung from an endeavour to generate findings and knowledge that would be easily "translatable" and applicable in the field of nursing and other disciplines facing everyday challenges when working in healthcare. A hallmark of interpretive description is the use of the researcher's forestructure - the prior knowledge about and understanding of the studied problem or question – that is seen as an inevitable part of scaffolding and conducting research studies. In analysis, the forestructure serves as a "lens" to be utilised and through which data is being analysed [125]. The analysis began with verbatim transcription of the interviews. The transcripts were then validated against the audio recordings to make sure everything in the recordings had been transcribed. To acquire a starting sense of the data in its entirety, the interviews were then both read and listened to several times. The aim of the study guided the continued analysis and was kept closely in mind at all times during the analysis. Throughout the analysis process, I worked closely with my co-authors and discussed the interviews and the analysis process. Firstly, each interview was divided into segments based on the content of each segment. This was tentatively done in order to ensure that nothing that could be of relevance for the study was excluded prematurely. A segment of the interview was constituted by text that revolved around a certain topic or question, and was delimited by a change of topic in the interview. This meant some segments were only a few sentences short whereas more elaborate reasonings rendered segments of up to a few hundred sentences. The segmenting was inclusively done to make sure the surrounding context was included in each segment. Each segment then received a content-based label that captured the core content of the segment in a few words or a short

sentence. Since human narratives are often intertwined and complex by nature, and in order to preserve that complexity in the best way possible, some segments received more than one label. Moreover, we made sure to keep moving back and forth between the segments and their wider context in the interviews to not lose the sense of the segments' context in the original text. After the entire data material had been segmented and labelled, the labels then functioned as tools to carefully begin looking at which segments could be relevant for the study's aim. Again, the initial inclusion of segments was generously done in order to not exclude potentially relevant segments prematurely. After having included all relevant segments, the labels worked as tools to start looking at patterns, similarities and differences in the data material. Tentative themes were formed and then finalised after reaching consensus among the authors.

5.3.6 Study III – data generation

Seventeen men who wished to participate in serial interviews constitute the sample for study III and a total of 31 qualitative interviews were conducted. The interview process for the baseline interviews is described in section 5.3.4. in this thesis. Prior to the follow-up interviews, I prepared myself by reading and listening to previous interviews and by making notes on aspects I wished to follow-up on since the last time I interviewed the participant. The follow-up interviews commenced with the question "*Would you like to tell me how you've been since we last saw each other?*" As in study II, I encouraged the participant to narrate freely and tried to interrupt the narration as little as possible. Therefore, brief notes were taken about matters to return to or probe further when an opportunity was given and a natural pause in the narration occurred. To encourage the participant to elaborate further on something, probing- and follow-up questions were also asked. All face-to-face interviews were audio-recorded. Twentynine of the interviews were conducted by me and the median interview length was 65 minutes (range: 22-160 minutes, total interview time: 32 hours and 19 minutes).

5.3.7 Study III - data analysis

Data was analysed using qualitative content analysis as described by Graneheim and Lundman (2004) [126]. Content analysis stems from quantitative roots in analyses of printed newspapers and communication in the early 1900s. The use has thereafter spread to other disciplines and qualitative approaches to content analysis emerged in the second half of the 20th century [127]. The intention of qualitative content analysis is to search for similarities and differences in the text and varying degrees of interpretation can be applied [126], which

is why it was chosen for this study. Since there is very limited knowledge of TDM among men with mCRPC, an inductive approach was used [123] to allow the participants' narratives to guide and steer the forming of the themes in the findings. The analysis followed the steps described by Graneheim and Lundman (2004) [126]. Firstly, all interviews were read and listened to several times to develop a sense of the data in its entirety. Similar to study II, the aim then guided the analysis and identification of meaning units. A meaning unit is a segment of text in which the content pertains to the study aim. After having identified meaning units in all the interviews, the meaning units were condensed. In the condensation, the meaning units were shortened to a more manageable length with their core content still preserved. The next step was coding, in which each condensed meaning unit received a code. A code captures the core content of each meaning unit in a single word or a short sentence. The codes were thereafter used as tools to search for similarities and differences in the data. Codes that contained and represented similar content were tentatively clustered together in the process of forming subthemes. Further, the aspect of time and how different matters and facets of the content had developed over time and subsequent interviews were continuously addressed and discussed in working with the subthemes. Lastly, the subthemes were finalised and gathered under overarching themes. Throughout the entire analysis, a close connection was always kept between the codes, meaning units and interviews to make sure neither codes nor meaning units got "lost in translation" and strayed from their original context in the interviews.

5.3.8 Study IV- Procedure and participants

The sample for study IV comprises the participants who started a life-prolonging treatment in the PROCEED project and then remained on the same treatment for one year. Participants on all types of life-prolonging treatments were included. All participants received a study baseline questionnaire upon inclusion in the study, in conjunction with the start of their first life-prolonging treatment. During their time in the study, they thereafter received study follow-up questionnaires approximately every three months.

5.3.9 Study IV - measurements

Both the baseline and follow-up questionnaires contain the validated *Functional Assessment of Cancer Therapy – General* (FACT-G) instrument [128] that measures different dimensions of QoL among patients with cancer. For this study, the physical and emotional dimensions were used since they related most to the study aim - TDM and treatment experiences.

Further, a two-part study-specific instrument was developed to measure: 1: satisfaction with TDM at baseline, and 2: experiences of treatments at all the subsequent follow-ups. The instrument has been tested for, and found to have, face validity [122] in think aloud interviews [129] prior to the start of study IV [130]. The satisfaction with TDM section consists of 27 questions that cover different aspects of satisfaction with TDM, communication, confidence, and trust. It uses a 4-step Likert-type response scale with responses that range from "No, not at all" to "Yes, as much as I wanted to". The items are divided into five subscales – *physician communication, treatment staff communication, technical competence, nurse communication* and *trust and confidence*. For this study, physician communication, treatment staff communication, nurse communication and trust and confidence were used. The follow-up questionnaire contains the second section of the study-specific instrument, that measures experiences of treatment. It consists of eight questions, of which four questions were selected for this study: "Do you think you are receiving the treatment that is right for you?", "Would you recommend this treatment to others with the same illness as you?", "Would you choose this treatment again?" and "As a whole, how would you rate this treatment?" The instrument uses a Likert-type response scale with 2-4 steps and responses ranging from "A lot worse/No, not at all/No/Bad" to "A lot better/Completely/Yes/Excellent". The items in this section are treated as single items in analysis.

Medical data (age, year of diagnosis, time from diagnosis to inclusion in the study, Gleason score at diagnosis, PSA at inclusion in the study and first life-prolonging treatment) was also extracted from the participants' medical records for the study.

5.3.10 Study IV - data analysis

Descriptive statistics are presented for participants' medical data at baseline. Descriptive statistics are also presented for each of the subscales pertaining to satisfaction with TDM at baseline, for each of the items pertaining to treatment experiences at all the follow-ups (3, 6, 9 and 12 months) and, finally, for physical and emotional wellbeing from baseline and at all follow-ups throughout the first year. Due to data skewness in most variables, medians and interquartile ranges are presented alongside means and standard deviations. Associations between satisfaction with TDM at baseline, treatment experiences and wellbeing at six and 12 months were explored using Spearman's rank correlations. A significance level of $p<0.05$

was chosen to be statistically significant in all analyses. All the statistical analyses were performed using the software *IBM SPSS Statistics version 27* (IBM, Armonk, NY, USA).

5.4 ETHICAL CONSIDERATIONS

All studies of this thesis have been granted approval by the Swedish Ethical Review Authority. Ethical permits for study I were granted by the Research Ethical Review Board in Umeå, Sweden; Dnr 02-054 and Dnr 95-163. Ethical permits for studies II-IV were granted by the Regional Ethical Review Board in Stockholm, Sweden; Dnr 2014/341-31/2, Dnr 2016/851-32 and Dnr 2016/2230-32.

Several ethical aspects are important to consider in this thesis project. Firstly, the study participants all have a severe, life-limiting illness, making it particularly important to consider potential risks of participating in the research project for the participants. Groups that could be viewed as especially vulnerable within nursing research have been identified, where people with severe illnesses and people with life-limiting or fatal illnesses are two especially vulnerable groups [122]. The fact that people belonging to these groups might not be able to protect themselves in the same way that people who are not ill or dependent on healthcare could, has been thoroughly discussed within the research group. On the other hand, one could also argue that *all* patients, or even families or relatives of patients, who participate in healthcare or nursing research should be considered especially vulnerable as long as they are dependent on the healthcare system in some way.

The weighing of potential benefits of the study versus the risks for the participants was extensively discussed in the initial phases of the project. We were aware that there are certain risks involved with participation in the study. The chances of the study results being of personal benefit to the participants are slim, especially since the study does not comprise interventions of any kind. However, it could be argued that participation alone in a study could serve beneficial as it gives an opportunity to tell one's story, address issues and bring to light matters that are important even if one does not participate in an intervention. For example, participating in an interview could be viewed as a positive experience in itself. Several participants in the study have made the point of communicating that they wanted to be in the study even though it would not benefit them personally but because they felt "it was important to do for future men with prostate cancer".

A core value has been emphasised regarding the voluntary nature of participating in the research project and the right to terminate participation at any given time. In the inclusion process, the patients who met the study's inclusion criteria were given information about the study either by their treating physician or a research nurse at the oncology clinic, after which they were asked whether they would be interested in participating. Given the dependent nature of their relationship with the clinic and the clinic staff, there was a risk that the patients would worry about their continued treatment if they declined and hence, felt coerced into participating in the study. To prevent this, the written information the patients were given about the study emphasised their rights and underlined that their care would not be affected by their choice to participate in the study or not, or if they chose to terminate their participation at some point during the study. This is also highlighted on the cover page of all study questionnaires they receive throughout the study. All patients were also given written information regarding the purpose of the research project, its execution and how the information they share via questionnaires, interviews or medical records is stored and handled. Written, informed consent was obtained from all participants upon inclusion in the study [131]. A subsample of men in the research projects was invited to participate in qualitative interviews. When being contacted by a researcher to receive information about the interviews, the voluntariness was again raised by the researcher via telephone. The participants' right to decline participation in subsequent interviews was also raised by the researcher when contacting the participants to invite them to additional interviews following the first one.

Given the gravity of their disease, we were aware early on of the risk that some participants would die during their follow-up time in the study, with the potential risk that a study questionnaire would be sent home to the relatives of a deceased participant. This was thoroughly discussed both within the research group and with the oncology clinics with whom the research group has collaborated. Study questionnaires were sent to all participants circa every three months or when they switched life-prolonging treatment to a new one. Since a lot can happen in three months, none the least in this late disease stage, a strategy for sending out questionnaires was developed where the research nurse/study coordinator always checked the participant's medical record before sending out a questionnaire. This was done not only to decide which questionnaire the participant was supposed to receive but also to make sure the participant was not deceased and was residing at home and not admitted to hospital for example.

Another risk that has been continuously discussed is the possibility of a participant experiencing malaise of some sort when participating in an interview or when filling out a study questionnaire. We were particularly aware of this risk when performing the research interviews, where we had the opportunity to meet with the participants either face to face or over the telephone and where there is a high possibility that sensitive or difficult topics might arise. If such a situation had occurred, the participant would have been encouraged to contact the treating oncological clinic, alternatively he would have been asked if it was all right for the researcher in the project to contact the clinic on his behalf. This was also made possible due the very close contact and cooperation with the clinics.

Prior to May 25th of 2018, the Swedish Personuppgiftslagen (1998:204) was followed to ensure that the participants' personal information and data were handled and stored correctly. The General Data Protection Regulation (GDPR) replaced Personuppgiftslagen on May 25th of 2018 and has thereafter been applied in the research project. All data generated or collected in the research project is stored and handled confidentially, meaning only persons who are involved in the project have access to the questionnaires, audio-recorded interviews/interview transcripts or data from the medical records. Every study participant received a numeric identification number upon inclusion, that is used to tag the study questionnaires and that functions as their identification number when data is entered into the study medical database. The identification numbers are noted by the research nurses at the clinics, making patient information available to the research group only on a need-to-know basis. Patient information (name and telephone number) has been accessed by members of the research group (for the qualitative interviews) via the research nurses only after the patient was contacted by the research nurse and asked specifically if they approved them sharing their name and telephone number with the researchers. Keeping the obtained patient-reported data (questionnaires and interviews) separated from the participation number key enables security in both directions, since we do not store patient information that could be linked to their individual data and the healthcare staff at the oncological clinics do not have access to individual data provided by their patients. As for storage and transfer of the data, only safe servers and connections are used to store data or transfer data in between research group members when necessary. To further protect the integrity of the participants, the results from this research project are presented in a way that ensures that single individuals cannot be identified through e.g. citations or circumstances.

6 RESULTS

Study I has a sample consisting of participants with metastatic and non-metastatic prostate cancer, whereas the samples in studies II, III and IV consist of participants with the more advanced disease stage mCRPC. Describing the situation for men with metastatic prostate cancer in study I laid the ground for the continued studies of experiences of men with mCRPC in studies II-IV. For this reason, the result section of this thesis commences with the results from study I, whereafter the results from studies II, III and IV are presented together in a synthesized way.

6.1 STUDY I

The final sample in study I consists of the 106 men in the mPC group and 211 men in the non-mPC group from which complete data was obtained. Both the mPC and non-mPC group generally reported low levels of symptoms and high levels of QoL and functioning. Significant differences started to occur between the groups at the three-year follow-up for a number of symptoms (pain, fatigue, dyspnoea, sexual problems), where the mPC groups scored significantly worse than the non-mPC group. As for QoL and functioning, a significant difference occurred in role functioning already at baseline and for social functioning at the two-year follow up, the mPC group scored worse on functioning than the non-mPC group. Significant differences were found for QoL and all functional scales except for cognitive functioning at the three-year follow-up, most of which remained significant also at five years. Compared to clinically relevant threshold values [120], the mPC group generally scored within the range for symptoms and functioning until the five-year follow-up, where a score above the threshold value (25) was reported for pain (mean 26.1 (SD 29.8)) and under the threshold value (83) for physical functioning (mean 82.4 (SD 23.2)). Their QoL started to deteriorate earlier and scores under the threshold value (70) were observed at treatment completion (mean 69.2 (SD 22.6)), three (mean 67.0 (SD 24.9)) and five (mean 60.4 (SD 26.6)) years. In summary, the mPC group gradually reported worsening QoL, functioning and symptoms over the five-year follow-up period, whereas the non-mPC group remained more stable over time.

In the sensitivity analysis, the participants in the mPC group who had developed metastases within the five-year time frame of the study (n=35) were removed from the sample alongside with their corresponding matches in the non-mPC group (n=70). On average, the participants in the mPC group who developed metastases did so after five years in the study. Upon renewed analysis, significant differences between the mPC and non-mPC

groups remained for role functioning at baseline and one year and for nausea/vomiting at three months, one and two years. No new significant differences were found and none of the previous significant differences between the two groups remained. Following the sensitivity analysis, both groups scored their QoL, symptoms and functioning within range of the clinically relevant threshold values [120] at all follow-ups.

Further analysis showed that differences also occurred over time within both the mPC and non-mPC groups. In the non-mPC group, QoL was found to significantly decrease between three and five years (mean difference -3.371, p=0.028) while fatigue significantly increased between baseline and five years (mean difference +5.352, p=0.011). In the mPC group, QoL (mean difference -17.949, p=0.001), pain (mean difference +14.966, p=0.010) and fatigue (mean difference +17.411, p=0.003) all worsened significantly between baseline and five years, QoL (mean difference -10.256, p=0.049) and pain (mean difference +13.675, p=0.008) worsened significantly between three and five years.

6.2 STUDIES II-IV

The samples in studies II, III and IV consisted of 16, 17 and 114 men with mCRPC respectively (Table 2). Their mean age was over 70 but the age of all participants had a wider range of 50-89 years. The majority of the participants were in a relationship and/or cohabitating with a partner and most were born in Sweden. Their educational level ranged from nine-year compulsory school to university-level studies. In studies II and III, the majority of the participants underwent chemotherapy (Docetaxel) as the first life-prolonging treatment, although hormone treatments (Enzalutamide and Abiraterone) were also represented in the sample. The proportions look somewhat different in the fourth study, where most participants instead underwent hormone treatments as their first life-prolonging treatment (Table 2).

Table 2. *Background characteristics of the participants in studies II-IV.*

	Study II	**Study III**	**Study IV**
Number of participants	16	17	114
Age, mean (range)	73 (60-82)	73 (60-82)	76 (50-89)
Relationship status			
In a relationship/cohabitating, n (%)	13 (81.3)	14 (82.4)	86 (75.4)
Not in a relationship/cohabitating, n (%)	3 (18.8)	3 (17.6)	17 (14.9)
Other/missing, n (%)	0 (0)	0 (0)	11 (9.6)
Place of birth			
Sweden, n (%)	16 (100)	17 (100)	98 (86.0)
Other Nordic country, n (%)	0 (0)	0 (0)	3 (2.6)
Other European country, n (%)	0 (0)	0 (0)	0 (0)
Country outside of Europe, n (%)	0 (0)	0 (0)	3 (2.6)
Missing, n (%)	0 (0)	0 (0)	10 (8.8)
Educational level			
9-year compulsory school, n (%)	3 (18.8)	3 (17.6)	42 (36.8)
High school, n (%)	5 (31.3)	6 (35.3)	35 (30.7)
University degree, n (%)	8 (50.0)	8 (47.1)	26 (22.8)
Missing, n (%)	0 (0)	0 (0)	11 (9.6)
First life-prolonging treatment			
Docetaxel	11 (68.8)	12 (70.6)	20 (17.5)
Cabazitaxel	0 (0)	0 (0)	2 (1.8)
Enzalutamide	4 (25.0)	4 (23.5)	69 (60.5)
Abiraterone	1 (6.1)	1 (5.9)	21 (18.4)
Radium-223	0 (0)	0 (0)	2 (1.8)

The results of studies II-IV have been synthesized into four domains (Figure 4) - *Weighing pros and cons of life-prolonging treatment when experiencing an incurable illness; Relating to healthcare professionals and the healthcare organisation; Seeking and obtaining personalised information relevant for TDM* and *Handling decisions to be made while on life-prolonging treatment.*

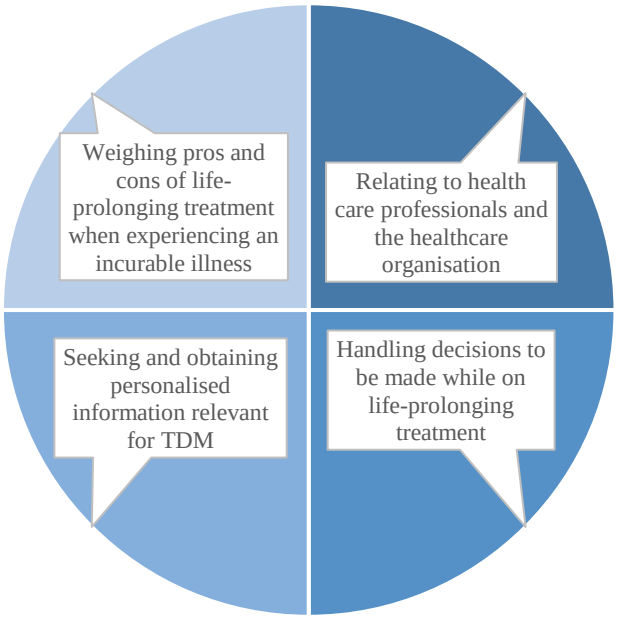

Figure 4. *The findings of studies II-IV.*

6.2.1 Weighing pros and cons of life-prolonging treatment when experiencing an incurable illness

All of the participants in studies **II**, **III** and **IV** had incurable prostate cancer – mCRPC – and the participants in studies **II** and **III** expressed an awareness that treatments from this point on would not cure their cancer but hopefully inhibit its progression (study **II, III**). For some, their prostate cancer had not presented with symptoms, nor had they experienced much – or any – symptoms throughout their disease trajectory. These participants found it peculiar that such a severe illness would act so quietly (study **III**). They had initially had their PSA-levels tested after being advised to do so by family members or friends or as part of regular health check-ups, and suddenly and unexpectedly had to make decisions about a severe illness due to the results of the PSA tests alone (study **III**). Knowing their disease was so advanced added dimensions to TDM and the participants in studies **II** and **III** mainly described now choosing between whether to start (study **II**) or continue (study **III**) life-prolonging treatment rather than choosing between different kinds of treatments. The men knew their life expectancy was limited due to the gravity of their illness and were also

aware that the life-prolonging treatment(s) would most likely be accompanied by side effects for which the degree of intrusion could range from light to debilitating. Hence, they were faced with trying to decide whether going through with a life-prolonging treatment would buy them enough additional time to make the treatment worthwhile in the end (study **II, III**). Side effects were initially described as a necessary price to pay for hopefully extending one's life expectancy (study **II, III**) but gradually became more worrying for the participants over time (study **III**). As for how the life-prolonging treatment could potentially affect various dimensions of the participants' everyday lives, study **IV** revealed that a substantial proportion (32.7-44.3%) of the participants had not had these conversations with healthcare professionals at all. In the light of their life-limiting illness and the prospect of undergoing life-prolonging treatment, study **II** also showed that the participants continuously thought about their mortality and reflected upon what the end of life and dying would be like even if they underwent life-prolonging treatment. While some described not being afraid of death and dying, uncertainty kept recurring in the participants' narratives when they talked about death and dying, and they described how there was no way of knowing how that time would evolve. Previous experiences of relatives or close ones who had died agonising deaths were painful and the participants described how these memories made them fear how their own end of life would be.

6.2.2 Relating to healthcare professionals and the healthcare organisation

Healthcare professionals played an important role, as shown in studies **III** and **IV**. In the interviews for studies **II** and **III**, the physician was highlighted as being an important source of information and a key figure in TDM, whereas registered nurses were mentioned mostly as the ones administering treatments and were seldomly talked about in relation to TDM or support. Instead, physicians seem to be the most important healthcare professional that men with mCRPC encounter before, during and after life-prolonging treatments in relation to TDM (study **III**). Study **IV** also showed that most men were satisfied with the physician communication at baseline, over 70 per cent reported the highest level of satisfaction in over half of the questions in this subscale. The questions with the highest reported level of satisfaction were whether they had had the opportunity to ask questions (90.2 % reported "yes, as much as I wanted to"), if they had sensed a genuine commitment from their physician (83.3 % reported "yes, as much as I wanted to") and whether the physician had respected their opinions (83.2 % reported "yes, as much as I wanted to"). Further, satisfaction with physician communication was also associated with how the participants rated the treatment as a whole at six months [correlation coefficient: 0.284,

p=0.032] and physical (correlation coefficient: 0.385, *p*=<0,001) and emotional (correlation coefficient: 0.458, *p*=<0,001) wellbeing at six months following start of life-prolonging treatment. An association was also found between physician communication and emotional wellbeing at 12 months following start of life-prolonging treatment (correlation coefficient: 0.462, *p*=<0.001) (study **IV**). Also in study **III**, the participants underlined how they wished for a physician who showed a genuine interest and commitment to them, and who was also knowledgeable and well updated. However, even though they generally reported high levels of satisfaction with physician communication (study **IV**), the participants wished for better physician continuity when it had been lacking (study **III**).

Further, the participants emphasised that a clear and direct communication style was important for them in order to feel trust in the physician. A long-term relationship was described as an important factor to form a trusting relationship with one's physician, which in turned facilitated dialogue about one's unique situation, wishes and goals (study **III**). Even though physician continuity was described as both lacking and as a factor for trust in study **III**, the participants reported a high level of satisfaction also regarding trust and confidence in study **IV**. Four questions pertained to confidence and trust in study **IV,** and over 80 per cent reported the highest level of satisfaction in each of all four questions. Satisfaction with confidence and trust was also associated with emotional wellbeing (correlation coefficient: 0.246, *p*=0.032) at six months following the start of life-prolonging treatment. Further, the physician was an important factor in how the men chose to position themselves in the decision-making process. Some had experienced a collaborative decision-making process, whereas some had been presented with a single treatment option that the physician regarded as the best for them. Others had done some research of their own and suggested a treatment themselves. Regardless of how the treatment decision had been reached, the participants modified their own role and actions depending on the approach to decision-making their physician had, even if it meant taking on a more or less driven role than they would originally have wanted (study **III**).While registered nurses were seldomly mentioned in the interview studies **II** and **III**, study **IV** showed that the participants reported a high level of satisfaction also with nurse communication prior to starting their life-prolonging treatment. Nurse communication was also associated with whether the participants believed they were undergoing the treatment that was right for them (correlation coefficient: 0.291, *p*=0.037) and physical (correlation coefficient: 0.284, *p*=0.016) and emotional (correlation coefficient: 0.285, *p*=0.015) wellbeing at six months following start of life-prolonging treatment (study **IV**).

Recurring in the participants' narratives was their sense of the urgency of their situation and illness and how a perceived lack of efficiency in their healthcare had been a consistent bother throughout their prostate cancer trajectory (study **III**). The healthcare organisation was described as tardy and difficult to navigate, and several participants described feeling like they had to work around the system instead of waiting for the system to work for them. This could e.g., mean contacting physicians or clinics ahead of referral or accessing one's own medical records online to get a hold of test results when information or answers were delayed. The participants wished for a cohesive chain of care with cooperation between clinics and seamless handovers between clinics and physicians but when this did not occur, some instead felt like they themselves had to manoeuvre their healthcare situation (study **III**).

6.2.3 Seeking and obtaining personalised information relevant for TDM

Both before and after deciding to proceed with a (new) life-prolonging treatment, the participants in study **III** engaged in information seeking to form a basis for their treatment decision. They expressed beliefs about prostate cancer and its treatments, particularly chemotherapy, based on previous experiences of themselves or others (studies **II, III**). They believed chemotherapy to be particularly intrusive compared to other treatments (study **III**) and prepared themselves to deal with the treatment and its side effects in ways they found necessary (study **II**). Looking for, and obtaining, personalised information served as a way for the participants in study **III** to form a basis for their treatment decision and enabled them to partake in treatment decisions in the way they wanted. They wished for the information to be adapted to their own preferences regarding quality, quantity and timing, meaning some were adamant about learning everything there was to know about their cancer and all its possible treatments, while others instead preferred to obtain information at a slower pace and described that their questions arose gradually after some clinic appointments (study **III**). The participants generally reported high levels of satisfaction with the information they had received about the life-prolonging treatment (study **IV**), over 90 percent reported feeling fully satisfied with their opportunity to ask their physician questions. Further, over 90 per cent of the participants replied either "yes, almost as much as I wanted" or "yes, as much as I wanted" to the questions on whether the physician explained so that they understood; whether the physician had explained possible benefits of the treatment and whether the physician had explained potential risks and side effects of the treatment (study **IV**). By asking the physician questions and utilising online resources (e.g.

government healthcare service information and PC patient federations) they tried to fill in their knowledge gaps and paint a clear picture of their unique situation and conditions. The participants felt that it was bothersome when their information needs were not met, which was something that some participants had experienced regularly throughout their disease course (study **III**).

6.2.4 Handling decisions to be made while on life-prolonging treatment

While being on a life-prolonging treatment, the participants had to wait for their treatment to be evaluated (study **III**). Meanwhile, they were also thinking about the possibility that the treatment would not be successful and considered the consequences of such a scenario (study **II**). While being hopeful that the medical advancements in the prostate cancer field would make a new treatment available to them (study **II, III**), the participants also worried about what a new treatment would be like and how intrusive it could possibly be (study **II**). Finding out that the current treatment had failed meant being faced with yet another treatment decision about whether to proceed with a new treatment or not treat the cancer at all (study **III**). It also meant the participants knew that their prognosis and treatment chances had changed for the worse (study **III**). While the participants initially described the decision to treat as easy to make, these decisions gradually became more difficult over time as their vitality diminished and the treatment side effects became more likely to really take their toll on them. Some asked for a treatment hiatus themselves and others had life-prolonging treatment paused or terminated by their physician when the outcome was not as expected or hoped for or when the side effects became too severe. Some participants felt dissatisfied going on a treatment pause as they feared the pause would benefit the cancer, whereas others felt relieved they would get the chance to recuperate and regain some strength during the hiatus (study **III**).

7 DISCUSSION

7.1 DISCUSSION OF FINDINGS

This thesis aimed to explore experiences, expectations and treatment decision-making in men with metastatic prostate cancer. When faced with a life-prolonging treatment, men with the most advanced PC (mCRPC) perform a trade-off between the pros and cons of the treatment while knowing that it will not provide a cure for their illness but most likely come with intrusive side effects. The findings also show that men with metastatic PC already report a variety of symptoms that escalates over time. Their QoL and functioning was also found to diminish over time once their PC metastasised. Further, their physical and emotional wellbeing over time was associated with their satisfaction with TDM at the start of life-prolonging treatment. Their decision-making entails cooperation with healthcare staff, mainly their physician, to whom they also modified their TDM role and -actions. They wished for personalised information and utilised different sources in their search for adequate and helpful information. Even though many men reported and described being satisfied with their TDM experience, obstacles to TDM were still highlighted as being of concern. TDM among men with mCRPC was found to be twofold. Not only did it concern the content of the decision, implying the desired treatment outcomes and what is at stake, but also how the treatment decision was being made and its structure (Figure 5).

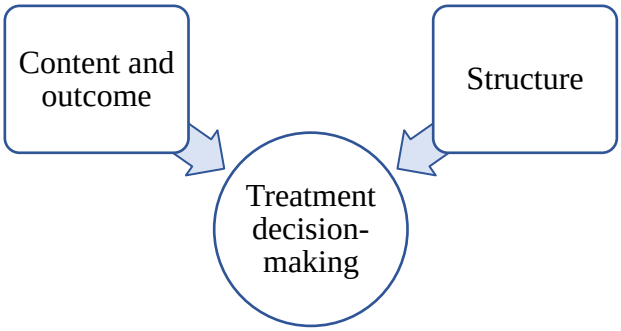

Figure 5. *Two dimensions of treatment decision-making among men with mCRPC.*

7.1.1 The content and outcome of the treatment decision

The results of this thesis show that men who are diagnosed with mCRPC and faced with potentially starting a life-prolonging treatment perform a careful trade-off between the desired treatment outcomes and the dreaded treatment side effects. They were initially sure that possibly trading quality of life for quantity of life would be worth it, but over time the quality of the remainder of their lives became increasingly more important to them than necessarily extending their life expectancy at any cost. With no guarantees of either the

desired outcome or the occurrence or distress of side effects, weighing benefits against risks becomes complex, none the least in this late disease stage. The complexity of balancing treatment benefits with risks has also been seen in previous research on localised PC [44, 53, 56]. Even if patients with localised PC tend to underestimate their life expectancy without treatment and overestimate their life expectancy with treatment [54, 55], the desired outcome of treatment may be more distinct, curing vs. not curing, while in this late phase the outcome is more uncertain, life prolongation, making the complexity even greater. Similarly, patients with other cancer types, at more advanced stages, have been found to overestimate the survival gain from life-prolonging treatment [24]. The results in this thesis showing that the men's perspectives on the treatment outcome changed over time are also interesting in relation to previous research on patients with stage I-IV cancers, that shows a discrepancy between healthcare professionals' and patients' treatment priorities. Regardless of cancer stage, the patients prioritised increased survival more often than healthcare professionals whereas health care professionals were more focused on QoL [132]. Seen in light of the already noted complexity of the trade-off between treatment benefits and risks among men with mCRPC in this thesis and previous research, the divergence in priorities further underlines the importance of exploring the patient's priorities and wishes as part of the treatment decision-making process.

The men in this thesis were all diagnosed with incurable PC. TDM for men with mPC and mCRPC could be viewed as taking place within a palliative care context due to the severity of the illness. When looking at both the IAHPC [83] and Swedish National Board of Health and Welfare [84] definitions, it seems evident that a palliative approach could be suitable for men with mPC and beyond. It has also been shown that men with PC could benefit from a palliative care approach already early on and then throughout the disease course [75, 82]. With the rapid development of the treatment landscape of mCRPC [71, 133], the survival for men with mPC has increased significantly, making the living-with-incurable-cancer-phase longer than it used to be. The results in this thesis show that men with mPC experience a range of symptoms and worsening QoL and functioning, that also escalates over time once their disease has become metastatic. Over the past two decades, it has been argued that an early palliative care approach might be especially beneficial to patients with PC, who often endure long disease trajectories that stretch over several years [75, 134] and whose symptoms increase over time [77, 78]. The disease-directed treatments these men undergo also commonly entails side effects, such as nausea/vomiting, diarrhoea [135], urinary incontinence and erectile dysfunction [136], that need to be addressed.

Despite the calls for an earlier integration of palliative care for men with PC, it has been shown that men with PC report a range of unmet needs throughout their disease course [137, 138]. Given that men with mPC experience a range of symptoms and worsening QoL as time passes, the potential benefits from a palliative care approach may seem obvious. However, there are barriers to integrating palliative care with standard oncology care [139-141]. A lack of systematics in identifying and referring patients that could benefit from palliative care services or -consultations has been found [139, 141]. Further, stigma associated with the very term "palliative care" among patients and families might also constitute a barrier to integration [139], alongside some oncologists' beliefs that palliative care is either incompatible with cancer therapy [139, 141] or that palliative care is already part of what they are doing and the care they are providing [139]. Finally, practical or organisational issues might also serve as barriers to integrating palliative care with oncology care [139, 141].The men in this thesis also identified organisational issues that have caused them problems. They had commonly experienced changing clinics at least once over the course of their illness and found the healthcare organisation to be difficult to navigate and sometimes somewhat tardy. Even though most of them did not change from oncology- to palliative care services specifically, the tight bulkheads between other clinics constituted a problem for the men.

The participants included in the studies in this thesis expressed an awareness that the treatment would not cure their PC, but instead hopefully prolong their lives. This contrasts to previous research showing that some patients with other incurable cancers misunderstand the treatment intent and believe the life-prolonging treatment to be curative [25]. It has also been shown that the treatment outcome is an important factor in TDM for men with localised PC, who are prone to choosing the treatment they perceive likeliest to cure their cancer [44, 52, 53]. Given the weight assigned to the treatment outcome by men already at the early stages of PC, awareness of and discussions about the intent of a treatment seem crucial at the most advanced disease stage when the cancer has become incurable. When revisiting the health expectations model by Janzen et al (2006) [23], awareness and an understanding of the treatment intention could be seen as important elements in forming an expectation. Understanding the intended and desired treatment outcome could potentially influence prior beliefs, the sense of probability and the perceived value of the outcome, as described in the model, which are all important components in forming a health expectation. It is perhaps not far-fetched to assume that an inadequate understanding of the treatment intent might lead to

unrealistic treatment expectations. This might, in turn, negatively affect the possibility for the patient to make an informed decision about whether to accept or decline a certain treatment.

7.1.2 The structure of the treatment decision

As for the other part of TDM experiences – the structure and how the decision was arrived at, the men in the studies of this thesis had had various experiences. The men's TDM experiences and preferences for their own decision-making role extends across all three theoretical models for decision-making (paternalistic, shared and informed) [15], much like treatment decision-making preferences [40-42] and experiences [43, 44] among men with localised PC earlier in the disease course. Further, previous research indicates that decision-making preferences among patients with cancer evolve over time [7, 8], whereas the men in this thesis were found to adapt and modify their own TDM role depending on the physician with whom they met and interacted. For some, this could sometimes lead them to assume a TDM role they had not originally wished for. Taking on a TDM role that deviated from what they had actually wanted was described as a negative experience, regardless of whether they felt obliged to take on more or less responsibility than desired. Similarly, a discrepancy between desired and actual TDM role has been shown to be associated with poorer HRQoL, physician health and mood in patients with cancer [2]. The results of this thesis also show that satisfaction with how TDM has unfolded is associated with how men with mCRPC experience the life-prolonging treatment over time. Satisfaction with TDM was also associated with their wellbeing at both six and 12 months following start of treatment. Relationships between TDM experiences and emotional wellbeing have also been found in patients with other advanced cancers [142], where satisfaction with TDM had a positive effect on emotional wellbeing.

This thesis has shown that continuity and a trusting relationship with one's treating physician were important for the TDM process among men with metastatic PC. The lack of staff continuity was bothersome for those who had that experience as it hindered the development of a trusting relationship to form between them and their physician. Also previous research underlines the importance of time to develop the patient-physician relationship and -connection [44, 49]. Trust in one's physician also links back to the preferred TDM role among the men in this thesis, who described that trusting one's physician facilitated dialogues about their life situation, priorities in life and treatment goals. Further, satisfaction with confidence and trust at the time for TDM was found to be associated with wellbeing over time. Similarly, trust has also been shown to be important in TDM among men with localised

PC [50], and lacking trust in one's physician can even influence the role men assume in TDM [51].

The physician was described as an important source of information that the men in this thesis utilised when trying to form a basis for the treatment decision ahead, much like previous research on men with localised PC [45, 47, 49]. Moreover, it was important to the men in the studies in this thesis that the information they wanted and needed was personalised regarding quality, quantity and timing. Similar to their TDM role preferences, the information preferences among the men also ranged over a large span, from wanting to know everything immediately to wanting to obtain carefully chosen information at a more moderate pace. Consequently, they tried to adapt and personalise the information landscape to accommodate their personal preferences during the TDM process. In doing so, they utilised a selected variety of sources of information, which is a strategy also used by men with earlier stage PC [44, 45, 52, 53, 63-66]. However, while the participants in study IV of this thesis reported having had a TDM experience they were generally satisfied with, the results from study III revealed that not all men felt they knew what they needed to know to make treatment decisions over time. Similar to previous research on localised PC [66, 68], they instead described how they had been consistently lacking adequate information about their treatment options and illness even now after reaching its most advanced stage. When adding what has been found in this thesis to what is already known about information seeking and management in men with PC, a desire for personalised information and dialogue about their illness and its treatments appear to run like a thread throughout the disease trajectory.

7.1.3 Interpreting the findings through the lens of a palliative approach

The findings of this thesis suggest there are unmet needs among men with mPC. Seeing as men with mPC live with an incurable illness, a palliative approach could serve as a basis to meet some of these men's needs. Below is a suggested model of application of a palliative approach in relation to the findings of the thesis, using the four cornerstones of palliative care [89] to understand the care of men with mPC (Figure 6).

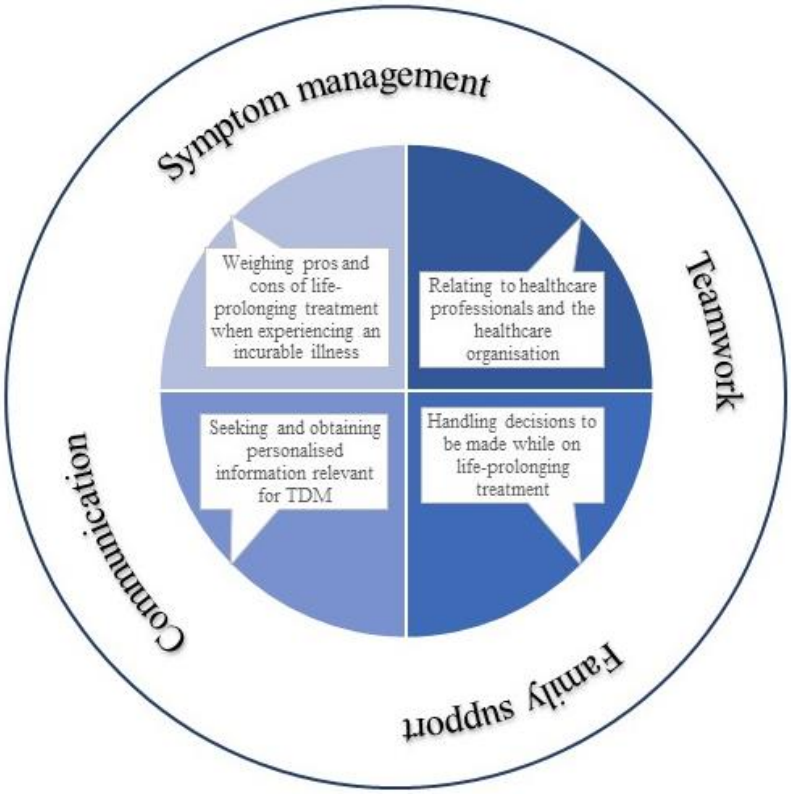

Figure 6. *A model of the application of a palliative approach to meet unmet needs among men with mPC based on the thesis results.*

Men with mPC experience a range of increasing symptoms and declining functioning and QoL once they develop metastases. Preservation of QoL is a focal point in a palliative approach [87] and by applying a palliative approach, worsening of symptoms and functioning could be addressed early on. Given that side effects of treatments can be seen as a sort of symptoms, the weighing of pros and cons of treatment could also benefit from a palliative approach where these issues are addressed and discussed already when the patient considers life-prolonging treatment. Healthcare professionals and the healthcare organisation were also crucial to men with mCRPC. In the cornerstones of palliative care [89], communication and multi-professional teamwork are seen as a way to facilitate dialogue and utilise the knowledge and skills of several professions to meet the needs of the patient and their family. It has also been argued that the patient (and their family) should be seen as an important, if not *the* most important, member of the team [143]. The participants in the studies of this thesis did mostly talk about the relationship they had with their physician, despite that multi-professional teamwork is described as vital in both oncology [144] and palliative care [89]. They also expressed very diverse needs regarding information quality, quantity and timing.

Given the complexity of men's situation at this advanced stage PC, it seems reasonable to believe that there is much to gain from multi-professional teamwork in relation to symptom control, information exchange, treatment evaluation, support and navigation of the healthcare system. Lastly, a palliative approach is holistic [87], meaning it acknowledges and affirms multiple dimensions of a person – including physical, social, emotional and spiritual dimensions [83]. The vast majority of the men in the studies of this thesis were married/in a relationship and had children. In the qualitative interviews, they described that family members or friends were important in relation to information gathering and -management and that they discussed the treatment options with someone close to them. Experiences of someone close to them dying agonisingly made them fear for what their own death would be like. They also took care of practical matters to ease the burden of their future demise for their family members. It is apparent that the men live in a social context with family, relatives, friends and/or other close ones. If a palliative approach were to be applied in the care for men with mPC, it may be that the needs of the persons close to the patient would also be addressed.

7.2 METHODOLOGICAL CONSIDERATIONS

When conducting research studies, methodological strengths and limitations must always be considered in relation to the study results, so also in this thesis. The methodological considerations section is divided into two parts: the first discusses aspects of reliability and validity in the quantitative studies I and IV, and the second discusses aspects of trustworthiness in the qualitative studies II and III.

7.2.1 Reliability, internal- and external validity/generalisability

7.2.1.1. Design

The longitudinal design of studies I and IV is a strength, as it allowed for the following of the participants over a prolonged period of time. Prospective, longitudinal studies are also rare in this patient group, especially among men with the most advanced disease stage (mCRPC), as it was only recently their life expectancy increased to what it is now. However, attrition is a challenge associated with longitudinal designs [122] that poses a threat to the study's internal validity and that cannot be overlooked when planning and executing research studies. The risk of attrition in the longitudinal studies was acknowledged early on in the PROCEED project and is discussed more in depth in section 7.2.1.2. below.

7.2.1.2. Sampling and selection of participants

In studies I and IV, the intent was to ask all patients who met the inclusion criteria at the study sites to participate consecutively, until the required number of participants for the studies had been met. Consecutive sampling strategies were utilised as a way of counteracting sampling bias [122], for which the risk was deemed greater if for example a convenience sampling, snowball sampling or recruitment via patient federations had been used. However, the sampling did not work flawlessly, and the inclusion process took longer than expected for study IV given the size of, and expected patient flow at, the oncology clinics in the study. Even though the vast majority (87.5%) of the men who were asked to participate also chose to do so, not all eligible patients were asked to participate, which constitutes a risk of sampling bias [122] if e.g. the patients with the most symptoms or whose health was declining were not asked to participate out of concern for their wellbeing or energy levels.

An inclusion criterion in all four studies of this thesis was the participants' ability to understand and express themselves in Swedish, which constitutes a source of sampling bias. This criterion was established to protect the eligible patients' right to completely understand all relevant information about the study and hence, enable them to either consent or decline participation fully informed. However, the Swedish population is steadily becoming more linguistically diverse and notwithstanding the intent of this criterion, it is possible that inclusion also of non-Swedish-speaking participants would have added to the results of this thesis and increased its generalisability.

The men in these studies had advanced stage PC and a certain attrition due to worsening condition and death of participants was to be expected. Consequently, when planning the PROCEED project, a certain attrition was accounted for in the power calculations to determine the sample size. This was handled by a degree of over-inclusion of participants, where the number of participants slightly overshot the upper level of participants required to achieve a statistical power of 80 per cent with a significance level of 95 per cent using the FACT-G instrument [128]. Some attrition did occur in the longitudinal studies over time, which might be considered a limitation of the results of this thesis. The greater part of the attrition in study IV was, as expected, due to participant deaths. The proportion of participants who chose to terminate their participation did so either due to their declining condition or without providing a reason. There is an obvious risk for attrition bias [122] in studies I and IV of this thesis, where the participants with, most likely, the most severe

illness die or drop out since they find participation too demanding as their condition worsens. This could in turn affect the internal and external validity [122] of the studies negatively.

7.2.1.3. Measurements

The instruments used in studies I and IV of this thesis will be discussed based on the concepts validity and reliability [122] – pertaining to the "what" and the "how" of instrument evaluation and quality assessment. The validity of an instrument refers to whether the instrument measures what it is intended to measure, meaning "is the instrument measuring the right thing?". An instrument's reliability instead refers to the accuracy and consistency of the instrument used, meaning "is the instrument measuring this in the right way?" A strength in studies I and IV is the use of instruments that have been tested for reliability and validity [115-118, 128] and been found to be reliable and valid. However, the treatment landscape has rapidly evolved for patients with advanced PC which means they live longer than they used to, and the group of patients with mCRPC who live on for years with their illness is growing. This presents challenges related to measuring QoL, symptoms and functioning that cannot be overlooked when interpreting the results of studies I and IV. None of the above instruments have undergone psychometric testing specifically with a sample of men with mPC or mCRPC in a Swedish context, which might be considered a limitation that weakens the validity of the instruments in this sample and the internal validity of the studies.

A study-specific instrument was used to measure satisfaction with TDM and treatment experiences in study IV. At the time of the commencement of the PROCEED project, there were no instruments that measured satisfaction with TDM available in Swedish, which is why a study-specific one was developed. The validated QLQ-INFO25 instrument from EORTC [145] was considered as an option, but was discarded for this study as it does not properly cover satisfaction with TDM or treatment experiences. The study-specific instrument has not undergone formal psychometric testing, which is a weakness that affects the study's internal and, in turn, external validity negatively. The instrument was, however, tested for face validity [122] prior to the data collection in this study [130]. Men with mCRPC were interviewed used think aloud methodology [129] as they filled out and reacted to a questionnaire comprising the study-specific instrument. The instrument was found to have face validity, which indicates that the content of the instrument appeared to be relevant to this sample of the intended patient population, and no alterations to it were

made. Another concern that arose was what might be a ceiling effect [122] in the satisfaction with TDM and treatment experiences questions, where data in most variables was found to be skewed. This could relate to issues of how the instrument questions and response alternatives were constructed and formulated, and negatively influences the ability to identify changes in scores over time [122]. To be useful in further studies, the instrument would have to undergo proper psychometric testing in order to determine its reliability and content validity.

7.2.1.4. Data collection

Strengths of the data collection in studies I and IV link back to the longitudinal design of both studies, that allowed for multiple data collection points at follow-ups over time. This way, the development of QoL, symptoms, functioning (study I) and treatment experiences and wellbeing (study IV) could be followed over the course of one to five years. There are also challenges associated with longitudinal data collection, one of them being the risk of attrition [122]. A more in-depth discussion of the risks associated with attrition in studies I and IV has been conducted in section 7.2.1.2. of this thesis. Longitudinal studies in a PC population could be seen as especially intricate given how the treatment options for mCRPC have exploded since 2004 [133]. Data collection for study IV started almost a decade after life-prolonging treatments of mCRPC was approved and implemented, and data was collected over a shorter period of time. Data collection for study I, on the other hand, started and extended over the years prior to, during and following the 2004 treatment breakthrough for mCRPC. Consequently, the treatment options were more of a level playing field for the participants in study IV than in study I. It is possible that treatments that were not yet available to the men included early in the study might have affected the levels- and development of symptoms, QoL and functioning among men who were included later in the study and for whom newer treatments had become available.

7.2.1.5. Data properties and analysis

In study I, significant difference between the mPC and non-mPC group in PSA levels was found at baseline, which could imply a more aggressive or advanced disease in the mPC group. Proceeding by examining the Gleason scores in each group and comparing them would have been the natural next step to detect a potential difference between the groups in disease aggression at baseline. However, the Gleason scoring system in its current form was not used until post year 2000 [146] and hence, the study lacks data on Gleason scores and no such comparison could be done. PSA levels were initially considered as a matching

criterion to counteract potential differences in disease aggression between the groups but were eventually excluded in the matching process due to not being able to successfully match enough participants. Not being able to account for a possible difference in disease aggression/Gleason score, affects the generalisability of the study negatively. There was not complete data on secondary treatments the participants might have undergone post their primary RT in study I, and likewise there was no data on whether the participants in the mPC group had been diagnosed with mCRPC and undergone associated treatments. Consequently, it is possible that e.g., side effects from such treatments could have affected the QoL-, symptom- and functioning scores in the mPC group, which negatively affects internal validity and generalisability of the study. The satisfaction with TDM and treatment experience variables in study IV were, upon exploration, found to be skewed and a possible ceiling effect was discovered. This could be attributed to the design and reliability of the study-specific instrument, which is discussed more in-depth in section 7.2.1.3.

Even though longitudinal studies in this population are much needed and the opportunity to follow the participants over lengthy periods of time holds great value, the data analysis must ultimately depend on the data properties. Data analyses were chosen carefully in the work with studies I and IV in this thesis, and the properties of the study data were considered in relation to basic assumptions of the analysis options. Non-parametric, instead of parametric, tests were used for comparison of groups in study I and for exploration of correlations in study IV. Non-parametric tests are less powerful and do not rely on the same strict assumptions as parametric tests [122]. While being less powerful, they are, however, more appropriate when basic assumptions for a parametric test are not met.

7.2.2 Trustworthiness

Aspects of trustworthiness in studies II and III will be discussed based on the Lincoln and Guba (1985) framework for developing trustworthiness in qualitative research [147]. *Credibility* pertains to the "truth" of the findings - whether they reflect what was really conveyed by the participants and whether participants who have experience of the studied problem have been selected, *dependability* refers to the consistency and stability of the findings, *confirmability* pertains to the degree of influence by the researcher on the findings, and *transferability* refers to whether the findings could be applicable in other contexts than that of the study.

7.2.2.1. Design

Studies II and III of this thesis had a qualitative descriptive design with an inductive approach [123, 124]. Given the scarcity of previous research, the inductive approach strengthened the credibility of the studies as the findings were derived from the participants' narratives, as opposed to a deductive approach where a set of predetermined premises guides the execution of the study. The longitudinal design of study III, which entailed a prolonged engagement in the study [147] for both myself and the participants, also enhanced the credibility of the study.

7.2.2.2. Sampling and selection of participants

The sampling in studies II and III was purposeful [123], and credibility was strengthened by the recruitment of participants from the PROCEED project which was diverse with regards to background characteristics. The intent was to generate rich narratives that captured various experiences of TDM and being faced with life-prolonging treatment. The sampling size was guided by the concept of information power [148] rather than data saturation [149] - that is an otherwise common way of determining sample size in qualitative research. Initially, the sample size for the qualitative interviews was tentatively set at 20-25 participants for studies II and III respectively. Thereafter, the sample size was continuously evaluated during the data generation process based on the sample specificity and the richness and depth of the dialogue/interviews [148]. Applying the data saturation concept to data generation may work well on many occasions and determining that data saturation has been achieved may also in many cases mean that all dimensions of the studied phenomenon have actually been discovered and explored. However, since life-prolonging treatments of mCRPC is a relatively young field and knowledge about men's experiences relating to the study aims is limited, it was deemed likely that a lot of new information would emerge during the interviews. Consequently, the data saturation principle would have been less applicable for these studies since determining when saturation had been reached would most likely have been very difficult. It would plausibly have required a significantly larger sample size to determine, thus, resulting in a probable overflow of data that could have been problematic to manage and do justice in the analysis. Since a sample with dense specificity and dialogues of high quality was attained, thus enhancing information power with rich and deep data [148] the sample size was taken down to 16 and 17 participants for studies II and III respectively during the data generation process.

7.2.2.3. Data generation

Data for studies II and III was generated through qualitative interviews [124], which was considered a way to capture the experiences of the participants via their narratives [123]. A topical interview guide (Figure 3) was developed, that covered the topics related to the study aims. A strength of studies II and III is the choice to approach the interviews in an open-ended way [123], as opposed to performing e.g. semi-structured interviews [124] following a more extensive and detailed interview guide. The choice of this interview approach was grounded in the lack of knowledge about how men with mCRPC experience their treatments and TDM and allowed for the participants to narrate more freely and bring forth what was important or urgent to them, thus strengthening the credibility of the study. This approach to interviewing proved to be successful during the data collection, as all the interviews yielded rich data and all the participants were eager to share their story and appeared to find the interview situation comfortable. Of course, there are also challenges and risks associated with this interview approach; the main concern being the skills and experience of the interviewer [123]. A more conversational interview requires greater flexibility and interpersonal skills and for the interviewer to be able to "think on their feet". Starting out as an interviewer in study II, I was a novice and did not have previous experience of research interviewing aside from the think aloud interviews I conducted to test the study-specific instrument for face validity prior to the data collection for study IV of this thesis [130]. It cannot be ruled out that personal biases, beliefs or preconceptions may have affected how the interviews unfolded or negatively affected the dependability or credibility of the study. Therefore, I endeavoured to be careful and agile in my interviewing, trying to ensure that it was the participant's narrative leading the way through the interview. Further, I continuously asked them to explain and elaborate on the matters raised to avoid premature assumptions or personal interpretations of mine. I tried to be open to unexpected turns of events in the participants' narratives and was early on aware that interviewing certainly is co-creation of data rather than collection of data. Moreover, as part of increasing reflexivity [123], reflecting upon and evaluating the execution of the interviews has been an ongoing process within the research group throughout the data collection.

The data generation in study III was designed to follow each participant's disease trajectory and the life-prolonging treatments that coincided, meaning each individual disease course and treatment sequence could not be predicted when they were first asked to participate in the interviews. It turned out that the majority of the participants did not proceed to new

treatments post their first one and hence, the follow-up interviews are fewer than the baseline ones. However, like the baseline interviews, the follow-up interviews were still rich in data and provided elaborate narratives of the men's experiences over time. Nevertheless, it is possible that follow-up interviews also with the participants who remained on the same treatment could have added other perspectives on TDM.

7.2.2.4. Data analysis

Interpretive description [125] was applied for analysis in study II and qualitative content analysis [126] was used to analyse data in study III. Due to the study aims, an inductive approach was applied in both analyses to increase credibility. Throughout the analysis process in both studies, I worked in close collaboration with at least one other member of the research group. This way, dependability was [147, 150] strengthened as the interviews and the analytical decisions were always discussed among at least two researchers. As a way to enhance credibility and dependability, what could be viewed as researcher triangulation was then performed when the remaining co-authors joined the analytical process periodically and reviewed the material with "fresh sets of eyes". Further, these discussions served to address and manage the pre-understandings of all researchers involved in the study. It was also a way to enhance reflexivity [123], as my perceptions of the data and the results were regularly challenged and sometimes overturned in favour of new ideas and perspectives. To increase confirmability, credibility and to create a basis for assessment of transferability, quotations were used generously in both studies. Though it might be tempting to choose quotations that are especially touching or to emphasise certain matters or points, each quotation was carefully considered and chosen to be illustrative of and reflect central aspects of each theme to enhance credibility, confirmability and transferability. Moreover, emphasis was placed on methodological transparency of the studies in order to enhance credibility, confirmability and basis for the reader's assessment of transferability to other contexts [147, 150].

Further, a new set of criteria to enhance and evaluate credibility of a qualitative study using interpretive description (study II) has been suggested [125], some of which will be discussed in relation to study II of this thesis. Representative credibility of the study pertains to whether the sampled participants of a research study are likely to have experiences that are relevant to the study aim and if data was collected in such a way that the research question could be answered. Seeing as the concept somewhat overlaps with the concept of credibility as described by Lincoln and Guba (1985) [147], measures to enhance

credibility of the study has been discussed in sections 7.2.1.-7.2.4. Further, the study must be morally defensible and of disciplinary relevance [125]. Even though the participants of study II all belong to a group of people who could be viewed as especially vulnerable due to their severe, incurable illness, as discussed in “ethical considerations” in this thesis, the study is still morally defensible. The field of life-prolonging treatments is relatively new, and more needs to be known about the experiences of men who are faced with these treatments. Although there were no obvious personal benefits from partaking in the study, the vast majority of the men who were asked decided to participate, which could be an indication of the urgency of these matters from their perspective. Moreover, measures were taken to assure the safety and integrity of all participants throughout the study, as discussed in “ethical considerations” of the thesis. The study is considered to be of high disciplinary relevance. Its origin is sprung from an oncology clinic and healthcare professionals working daily with patients with mCRPC undergoing life-prolonging treatments. After a research gap in the field of life-prolonging treatments of mCRPC had been identified, the research study was designed. Further, results from study II (as well as the other studies of this thesis) will be reported back to and presented at the oncology clinics which were involved in the research project. Attention was also placed on presenting data in such a way that it would be feasible to translate into clinical practice and make use of in everyday contact with men with mCRPC undergoing life-prolonging treatment.

8 CONCLUSIONS

This thesis aimed to explore experiences, expectations and treatment decision-making in men with metastatic prostate cancer. The thesis adds to the knowledge and understanding of what TDM entails at the most advanced stage of PC, and reveals a complex balancing act in which men with mPC try to navigate and handle a variety of difficult and complex situations. TDM was found to be twofold and the men's experiences of and preferences for both content and structure were found to be diverse. This goes to show that "not one size fits all" regarding TDM in men with metastatic PC, and that open and honest discussions about the patient's life situation, priorities in life, the treatment outcome and in what way the patient would like to partake in TDM should be initiated already when life-prolonging treatment first becomes an option. Given that QoL, symptom and functioning deteriorate over time in men with mPC once they develop metastases, and that men with mCRPC have been found to have unmet needs relating to information, continuity of care, communication and TDM, early integration of a palliative approach could serve as a way to detect needs that need to be addressed.

9 FUTURE RESEARCH

This thesis could hopefully constitute a basis for further research in the field of advanced prostate cancer.

Such work could include:

- perspectives on treatment decision-making among men who receive an mCRPC diagnosis but do not undergo life-prolonging treatment.

- treatment experiences and perspectives on treatment expectations among men with mCRPC who undergo consecutive life-prolonging treatments over several (>2) years.

- associations between type of life-prolonging treatment and satisfaction with treatment decision-making among men with mCRPC who undergo life-prolonging treatment.

- perspectives on priorities, treatment expectations and treatment decision-making among relatives and families of men with mCRPC undergoing life-prolonging treatment.

10 ACKNOWLEDGEMENTS

There are a lot of people without whom this thesis would not have been possible, and to whom I would like to extend my deep and sincere gratitude.

To **all the participants** in the studies of this thesis. I am beyond humbled and deeply grateful that you took the time and effort in your lives to fill out questionnaires and sit down to do interviews with me. Thank you for your trust and for sharing your experiences, hopes and fears with me, I sincerely hope I have done them justice. I will cherish the meetings I have had and the things I have learned from you. Without all of you, this thesis project would not have been possible.

Thank you to **the Sophiahemmet Foundation**, the **Swedish Prostate Cancer Federation**, the **Sjöberg Foundation**; **The Kamprad Family Foundation** and the **Ulrica Croné Foundation** for financial support of this project.

Agneta Wennman-Larsen, my main supervisor, for recognizing and encouraging my interest in research back at the very beginning when I started off in the PROCEED project. I would never had dared taking this on without you! Thank you also for always sharing all your knowledge, wisdom and experience over the years, your generosity has been very (!) valuable to me and I truly learned a lot from you. You have always made sure to make yourself available for questions, discussions and reflections, all of which I have greatly appreciated. Thank you also for always challenging me, it has made me grow as a researcher and for that I will always be grateful. It began here!

Lena Axelsson, my co-supervisor, for the many interesting and fun hours we have spent reading and discussing interviews and manuscripts and everything else! Your patient guidance and sharing of knowledge and insights in many domains have been immensely appreciated. Thank you for your endless and genuine support in many ways and for always believing in me - whenever I was in doubt, you were never.

Per Fransson, my co-supervisor, for so generously sharing your expertise and profound experience of prostate cancer research and for bringing much valued clinical insights and perspectives to our discussions. And even though we are 735 kilometres apart (Yes, I checked!) in Nyköping and Umeå, you were always just an e-mail or phone call away and eager to help with any questions I had!

The late **Olav Lindqvist**, who was my co-supervisor up until his sudden and unexpected death in early 2018. I wish you could have been here. For many reasons that go beyond me or my thesis, but one of them being for you to see what has become of the research project and the interviews we worked on together. Thank you for everything that you taught me, you took on your role as my supervisor with the utmost patience and always made me feel like there wasn’t a stupid question in the world. This day is not the same without you.

My mentor **Ulrika Kreicbergs**, even before you agreed to be my mentor, I thought of you as an academic role model - skilled, knowledgeable, empathetic and passionate about what you do. Thank you for being my mentor over the years and for always providing very sound and helpful advice. Thank you also for all the much-appreciated words of encouragement when I needed them the most.

My dear friend and long-time colleague **Maja Holm,** also in the PROCEED project with me. I believe you already know that you were (and still are!) a great inspiration to me when you started your doctoral education. All of a sudden, I knew a researcher! You always answered my questions patiently and were then one of my biggest supporters when I decided to go for it myself. Thank you for always making me feel included and inviting me to research seminars already when I was just at the very beginning of my education. Thank you for always being there to "lend me an ear" and for your many words of encouragement and wisdom over the years!

Ulrika Rönningås, my friend and PROCEED colleague. Working with you in the project has been great! You brought so much valuable knowledge and experience as a research nurse to the group, and I have learnt so much from you. (I think all of us in the PROCEED group have!) Thank you for sharing the highs and the lows of doctoral student life with me, for all the mails at weird hours and for all the talks about anything and everything!

Lars Beckman in the PROCEED group. Thank you for believing in the value of the PROCEED project and for your invaluable help in getting the study started and running at one of our study sites! Thank you also for sharing your knowledge and for bringing very important clinical perspectives to the discussions in the group.

Karolinska Institutet and everyone at the **Division of Insurance Medicine**, especially **Emilie Friberg** and **Kristina Alexanderson**. Thank you for making me feel welcomed and for many appreciated learning opportunities at seminars and other activities throughout my PhD journey!

Ewa Englund Lindgren, the late **Jan Åke Lindgren** and the late **Pernilla Hillerås,** thank you for seeing a promise in me and hiring me at **Sophiahemmet University** as a doctoral student and a teacher. Thank you **Johanna Adami** and **Cecilia Larsdotter** for continued employment and support!

Eva Skillgate and **Ingela Rådestad** at Sophiahemmet University for very helpful advice and support!

The **staff at Sophiahemmet University**, for uplifting chats, laughs and words of encouragement!

A massive thank you to all the staff at "our" oncology clinics for all your hard work getting the research project up and running at the time and then following our study participants over

the years! **Anna-Maria Hasselgren-Häll, Eva af Trampe** and **Michael Szeps** at Aleris Christinakliniken; **Katrin Fines Hamrin, Pia Rajapakse, Hanna Emanuelsson, Anna-Karin Dinwiddie, Khairul Majunder, Chunde Li** and **Marie Hjälm-Eriksson** at Karolinska University Hospital; **Heléne Lind, Carina Eliasson** and **Christine Näslund** at Länssjukhuset Sundsvall-Härnösand; **Vivian Brännström** at Norrland's University Hospital. You rock!

The **members of the "Living with complex life-limiting health conditions" research group** at Sophiahemmet University, for creating a constructive, open and fun environment for seminars and exchange of knowledge and research experience. Thank you for all the valuable input I have received on manuscripts, texts and presentations over the years and thank you for allowing me to also read your work and learn from it!

The staff at the **KI Library** and **Sophiahemmet University Library** for excellent and friendly help with books, articles, data bases and reference management over the years!

Spiros Lukas, Joakim Lehnström and **Jimmy Rydén** att Sophiahemmet University. You have my deepest gratitude for always coming to my rescue whenever my computer and "technical stuff" malfunction. Whether it be SPSS licenses, product recommendations for a home office setup or trying to salvage a destroyed dataset, you are always eager to help. Thank you!

Alexandre Beckman and **Kseniya Hartvigsson,** current and former educational administrators at the Department of Clinical Neuroscience at Karolinska Institutet, for all of your swift, kind and professional help with all sorts of questions I have sent to your inbox!

The **student administrative department** at Sophiahemmet University, thank you for providing excellent help and support with all kinds of practical things that go with being a doctoral student and a teacher.

My colleagues **in the SPPA teacher team**, thank you for sharing my interest in palliative care and for being such role models in practicing student-centred teaching!

All of the **doctoral students** at Sophiahemmet University, both current and alumni, whom I had the pleasure to work alongside. Thank you for many refreshing and fruitful discussions about methods, data, statistics, analyses, bias etc etc - the list is long ;) The best of luck to all of you who still have a bit left on the PhD journey!

Lina Lindqvist, for taking on the mountain of work transcribing some of my qualitative interviews and doing it swiftly and meticulously. Your help has been very much appreciated!

Sheila Macdonald-Rannström, for excellent help with reviewing my English. A manuscript left to you is in good hands, and as a bonus – I have learnt a lot (and hopefully improved) on the way!

Annika Evolahti, for swift and professional help with proofreading my “kappa”!

Jenny Doveson, for the beautiful cover illustration!

The warmest of thank yous also to all of my friends who have cheered me on over the years, especially:

The **Lindén family - Anna-Karin, Erik, Esmeralda** and **Emanuel –** my precious and dear friends. Without an ounce of hesitation, you were there for me when I needed it the most. Never once did you doubt me and just like family does, you always made sure I knew you had my back. I love you.

My dear friend **Amira Diallo**. Thank you for sticking by me through thick and thin and always believing in my abilities. Thank you for always being able to make me laugh, even at the darkest of times. Your sense of humour is amazing and no one but you has ever made me laugh to the point of literally falling over. You are truly one of the greatest people I know.

Jason Murphy, I am so happy and grateful I have gotten to know you and you have become very dear to me. Your rock-solid trust and belief in me are truly astonishing, thank you for always picking me up when I am down. Thank you for all of our discussions and for your valuable and wise input on ideas and texts. Thank you for always generously offering your time, whether it be driving somewhere, discuss a research matter or just talking.

Maria Billemark Öqvist, thank you for making me feel so welcome at my very first job as an RN. I knew right away that I liked you and you have since become one of my closest friends. Thank you for all the laughs and for your advice on all sorts of matters, you are one of the wisest people I know. Thank you also for always being genuine and honest and for your bravery in taking on the most difficult of conversations.

Therese Hallberg, on my first day at ward 4 you showed me around and you made sure I got the locker next to yours in the staff changing room. Over the next few years followed a sticky note locker correspondence thus far unmatched :) Thank you for all the five-hour phone calls about nothing and everything and for always bringing light to my darkness and self-doubt. Throughout our entire friendship, you have never stopped believing in me or encouraging me.

Louice Karlsson, my dear friend and fellow specialist nurse in palliative care. You have been a rock to me over the years since we got to know each other as students in the very first class of SPPA (then MAPA) at SHH! You are one of the kindest and most intelligent people I know, and our friendship is very precious to me <3

Jenny Rossen and **Anna Akselsson**, my dear friends and colleagues. Remember when our PhD journey began up in the doctoral student attic? How time flies! I am the last one up and your never-ending support and cheering has meant more to me than you both probably know. Thank you for all of our discussions and reflections and for sharing this special journey with me.

My friend **Anders Linde**. The hours we spent talking and laughing were true highlights of my PhD journey. Thank you for sharing the highlights and lowlights with me!

My dear friend **Ingegerd Jansson**, for being one of the most generous people I know, and for all the times you let me borrow your apartment when I had early trains to catch to do interviews! Thank you also for always believing in me and for all the words of encouragement and support throughout my life.

My friend **Malin Eneslätt**, the loss of our supervisor Olav was devastating, I am so grateful for your camaraderie at that time and afterwards. Thank you for all the conversations about life and death and for sharing the journey of doctoral studentship with me.

Katarina Holmberg, my friend and colleague, for always being able to see the humour even in the oddest of situations, it is refreshing and has lightened up my days on many occasions! I have greatly appreciated (and still do!) all of our conversations about research and teaching and everything else!

My friend and colleague **Carina Lundh Hagelin**, for all the heartfelt conversations (!) and laughs and for your continuous and genuine support over the years!

Slutligen vill jag tacka de personer som stått mig allra närmast under alla år, utan vars stöd, tid och kärlek inget av detta hade varit möjligt. Min familj.

Stort och innerligt tack till min svägerska **Sofia Kummel**, du är en av de godaste lyssnarna jag vet och får verkligen personer som möter dig att känna sig sedda. Tack för din omtänksamhet och att du alltid lyssnar och svarar med sådan klokhet och eftertanke. Stort och varmt tack också till min svåger **Håkan Lindholm Doveson** för din hjälpsamhet i såväl stort som smått. Tack också för alltid lika stimulerande och utmanande samtal och diskussioner. Tack till er båda två, Sofia och Håkan, för att ni alltid visat och uttryckt en övertygelse om att jag ska få ihop min avhandling till slut!

Min mormor, **May-Britt Kummel**, som ända sedan jag var liten hade en benhård tro på min förmåga att klara det jag tar mig för. Tack för att du alltid tyckte det jag gjorde var viktigt och att det gjorde skillnad. Tack för den kärlek du gav under hela ditt liv. Jag önskar att du hade kunnat vara med och fira att avhandlingen blev klar till slut.

Jenny Doveson, min allrakäraste lillasyster, och **Per Doveson Kummel**, min allrakäraste lillebror. Det har varit vi tre alltid, Knatte, Fnatte och Tjatte i 33 år nu ;) Tack för all lek och allt roligt vi alltid delat och fortfarande delar. Utan er hade livet tett sig ensamt och tomt. Tack för att ni alltid har lyssnat, peppat och trott på mig och intalat mig att ”men syster, du klarar det”. Och nu har jag ju faktiskt det. Jag älskar er. Och syster, nu får det bli lekparkshäng och promenader runt Brandholmen – jag längtar! Lillebror, det första vi ska boka nu är ett Naruto-maraton – nu måste vi bli klara med Chuunin exam-avsnitten och se avsnitt 101 (igen)!

Ruth Doveson Jurison, som redan hunnit bli 4 år och är den mest fantastiska stora lilla systerdottern man kan tänka sig. Din nyfikenhet och entusiasm över livet och världen är så oförstörda. Att få följa dig är en ynnest och när jag ser hur klok och omtänksam du redan är så sväller mitt hjärta av stolthet. Tack för den glädje du alltid bringar och för att du blåser liv även i min nyfikenhet och känsla av förundran över världen. Jag älskar dig!

Min mamma **Marie Doveson Kummel** och min pappa **Tommie Doveson**, som osvikligt har stått vid min sida under mina 35 år på jorden. Jag vet inte riktigt var jag ska börja. Genom allt har ni alltid gått bredvid mig. Tack för att ni alltid har trott på mig och älskat mig och velat mitt allra bästa. Tack för allt ni har lärt mig. Tack för alla skratt. Tack för att ni alltid vetat att den man är som människa, är så oändligt mycket viktigare än det man presterar. Tack för att ni alltid varit stolta över mig även under de stunder i livet när jag känt mig otillräcklig. Tack för att ni alltid lyssnar, för att ni alltid har tålamod och för ett stöd utan gränser. Mina ord räcker inte till för att uttrycka hur mycket jag älskar er.

11 REFERENCES

1. Belanger, E., C. Rodriguez, and D. Groleau, *Shared decision-making in palliative care: a systematic mixed studies review using narrative synthesis.* Palliat Med, 2011. **25**(3): p. 242-61.

2. Atherton, P.J., et al., *The relation between cancer patient treatment decision-making roles and quality of life.* Cancer, 2013. **119**(12): p. 2342-9.

3. Tariman, J.D., et al., *Preferred and actual participation roles during health care decision making in persons with cancer: a systematic review.* Ann Oncol, 2010. **21**(6): p. 1145-51.

4. Wang, Y., et al., *Influencing factors of lung cancer patients' participation in shared decision-making: a cross-sectional study.* J Cancer Res Clin Oncol, 2022.

5. Herrmann, A., et al., *Not asking cancer patients about their preferences does make a difference. A cross-sectional study examining cancer patients' preferred and perceived role in decision-making regarding their last important cancer treatment.* Eur J Cancer Care (Engl), 2018: p. e12871.

6. Tariman, J.D., et al., *Physician, patient, and contextual factors affecting treatment decisions in older adults with cancer and models of decision making: a literature review.* Oncol Nurs Forum, 2012. **39**(1): p. E70-83.

7. Thorne, S., J.L. Oliffe, and K.I. Stajduhar, *Communicating shared decision-making: cancer patient perspectives.* Patient Educ Couns, 2013. **90**(3): p. 291-6.

8. Brom, L., et al., *Patients' preferences for participation in treatment decision-making at the end of life: qualitative interviews with advanced cancer patients.* PLoS One, 2014. **9**(6): p. e100435.

9. Zucca, A., et al., *The first step in ensuring patient-centred quality of care: ask the patient.* Eur J Cancer Care (Engl), 2017. **26**(1).

10. Brom, L., et al., *Congruence between patients' preferred and perceived participation in medical decision-making: a review of the literature.* BMC Med Inform Decis Mak, 2014. **14**: p. 25.

11. Sahlsten, M.J., et al., *An analysis of the concept of patient participation.* Nurs Forum, 2008. **43**(1): p. 2-11.

12. Halabi, I.O., et al., *"Patient participation" and related concepts: A scoping review on their dimensional composition.* Patient Educ Couns, 2020. **103**(1): p. 5-14.

13. Eldh, A.C., I. Ekman, and M. Ehnfors, *A comparison of the concept of patient participation and patients' descriptions as related to healthcare definitions.* Int J Nurs Terminol Classif, 2010. **21**(1): p. 21-32.

14. Eldh, A.C., I. Ekman, and M. Ehnfors, *Conditions for patient participation and non-participation in health care.* Nurs Ethics, 2006. **13**(5): p. 503-14.

15. Charles, C., A. Gafni, and T. Whelan, *Shared decision-making in the medical encounter: what does it mean? (or it takes at least two to tango).* Soc Sci Med, 1997. **44**(5): p. 681-92.

16. Ishikawa, H., H. Hashimoto, and T. Kiuchi, *The evolving concept of "patient-centeredness" in patient-physician communication research.* Soc Sci Med, 2013. **96**: p. 147-53.

17. Kraetschmer, N., et al., *How does trust affect patient preferences for participation in decision-making?* Health Expectations: An International Journal of Public Participation in Health Care & Health Policy, 2004. **7**(4): p. 317-326.

18. *Salzburg statement on shared decision making.* BMJ, 2011. **342**: p. d1745.

19. Barry, M.J. and S. Edgman-Levitan, *Shared decision making--pinnacle of patient-centered care.* N Engl J Med, 2012. **366**(9): p. 780-1.

20. Elwyn, G., et al., *Shared decision making: a model for clinical practice.* J Gen Intern Med, 2012. **27**(10): p. 1361-7.

21. Politi, M.C., J.L. Studts, and J.W. Hayslip, *Shared decision making in oncology practice: what do oncologists need to know?* Oncologist, 2012. **17**(1): p. 91-100.

22. Shay, L.A. and J.E. Lafata, *Understanding patient perceptions of shared decision making.* Patient Educ Couns, 2014. **96**(3): p. 295-301.

23. Janzen, J.A., et al., *What is a health expectation? Developing a pragmatic conceptual model from psychological theory.* Health Expect, 2006. **9**(1): p. 37-48.

24. Brom, L., et al., *Challenges in shared decision making in advanced cancer care: a qualitative longitudinal observational and interview study.* Health Expect, 2017. **20**(1): p. 69-84.

25. Weeks, J.C., et al., *Patients' expectations about effects of chemotherapy for advanced cancer.* N Engl J Med, 2012. **367**(17): p. 1616-25.

26. Sohl, S.J., J.B. Schnur, and G.H. Montgomery, *A meta-analysis of the relationship between response expectancies and cancer treatment-related side effects.* J Pain Symptom Manage, 2009. **38**(5): p. 775-84.

27. Devlin, E.J., L.A. Denson, and H.S. Whitford, *Cancer Treatment Side Effects: A Meta-analysis of the Relationship Between Response Expectancies and Experience.* J Pain Symptom Manage, 2017. **54**(2): p. 245-258.e2.

28. Sung, H., et al., *Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries.* CA Cancer J Clin, 2021. **71**(3): p. 209-249.

29. Pernar, C.H., et al., *The Epidemiology of Prostate Cancer*. Cold Spring Harb Perspect Med, 2018.

30. *Statistics database*. 2022, The National Board of Health and Welfare: Stockholm.

31. Leitzmann, M.F. and S. Rohrmann, *Risk factors for the onset of prostatic cancer: age, location, and behavioral correlates.* Clin Epidemiol, 2012. **4**: p. 1-11.

32. Mottet, N., et al., *EAU-EANM-ESTRO-ESUR-SIOG Guidelines on Prostate Cancer-2020 Update. Part 1: Screening, Diagnosis, and Local Treatment with Curative Intent.* Eur Urol, 2021. **79**(2): p. 243-262.

33. Hemminki, K. and K. Czene, *Attributable risks of familial cancer from the Family-Cancer Database.* Cancer Epidemiol Biomarkers Prev, 2002. **11**(12): p. 1638-44.

34. Ben-Shlomo, Y., et al., *The risk of prostate cancer amongst black men in the United Kingdom: the PROCESS cohort study.* Eur Urol, 2008. **53**(1): p. 99-105.

35. Rebbeck, T.R., et al., *Global patterns of prostate cancer incidence, aggressiveness, and mortality in men of african descent.* Prostate Cancer, 2013. **2013**: p. 560857.

36. Felici, A., M.S. Pino, and P. Carlini, *A changing landscape in castration-resistant prostate cancer treatment.* Front Endocrinol (Lausanne), 2012. **3**: p. 85.

37. Hamdy, F.C., et al., *10-Year Outcomes after Monitoring, Surgery, or Radiotherapy for Localized Prostate Cancer.* N Engl J Med, 2016. **375**(15): p. 1415-1424.

38. Vanneste, B.G., et al., *Prostate Cancer Radiation Therapy: What Do Clinicians Have to Know?* Biomed Res Int, 2016. **2016**: p. 6829875.

39. Davison, B.J. and E.N. Breckon, *Impact of health information-seeking behavior and personal factors on preferred role in treatment decision making in men with newly diagnosed prostate cancer.* Cancer Nurs, 2012. **35**(6): p. 411-8.

40. Hoffman, R.M., et al., *Decision-making processes among men with low-risk prostate cancer: A survey study.* Psychooncology, 2018. **27**(1): p. 325-332.

41. Hurwitz, L.M., et al., *A prospective cohort study of treatment decision-making for prostate cancer following participation in a multidisciplinary clinic.* Urol Oncol, 2016. **34**(5): p. 233.e17-25.

42. Song, L., et al., *Who makes the decision regarding the treatment of clinically localized prostate cancer--the patient or physician?: results from a population-based study.* Cancer, 2013. **119**(2): p. 421-8.

43. Lehto, U.S., et al., *Patient experiences at diagnosis and psychological well-being in prostate cancer: A Finnish national survey.* Eur J Oncol Nurs, 2015. **19**(3): p. 220-9.

44. Wagland, R., et al., *'Very difficult for an ordinary guy': Factors influencing the quality of treatment decision-making amongst men diagnosed with localised and locally advanced prostate cancer: Findings from a UK-wide mixed methods study.* Patient Educ Couns, 2019. **102**(4): p. 797-803.

45. Ihrig, A., et al., *Treatment decision-making in localized prostate cancer: why patients chose either radical prostatectomy or external beam radiation therapy.* BJU Int, 2011. **108**(8): p. 1274-8.

46. Davison, B.J. and S.L. Goldenberg, *Patient acceptance of active surveillance as a treatment option for low-risk prostate cancer.* BJU Int, 2011. **108**(11): p. 1787-93.

47. Sidana, A., et al., *Treatment decision-making for localized prostate cancer: what younger men choose and why.* Prostate, 2012. **72**(1): p. 58-64.

48. Feldman-Stewart, D., M.D. Brundage, and C. Tong, *Information that affects patients' treatment choices for early stage prostate cancer: a review.* Can J Urol, 2011. **18**(6): p. 5998-6006.

49. Bellardita, L., et al., *Treatment decision-making process of men with newly diagnosed localized prostate cancer: the role of multidisciplinary approach in patient engagement.* Mediterranean Journal of Clinical Phychology, 2019. **7**(1): p. 1-11.

50. Orom, H., et al., *Quality of physician-patient relationships is associated with the influence of physician treatment recommendations among patients with prostate cancer who chose active surveillance.* Urologic Oncology, 2014. **32**(4): p. 396-402.

51. Renzi, C., et al., *A Qualitative Investigation on Patient Empowerment in Prostate Cancer.* Front Psychol, 2017. **8**: p. 1215.

52. Dogan, C., et al., *Patient Decision Making Prior to Radical Prostatectomy: What Is and Is Not Involved.* Am J Mens Health, 2017. **11**(1): p. 108-115.

53. O'Callaghan, C., et al., *'What is this active surveillance thing?' Men's and partners' reactions to treatment decision making for prostate cancer when active surveillance is the recommended treatment option.* Psychooncology, 2014. **23**(12): p. 1391-8.

54. Mohan, R., et al., *Patients' survival expectations before localized prostate cancer treatment by treatment status.* J Am Board Fam Med, 2009. **22**(3): p. 247-56.

55. Xu, J., et al., *Patients' Survival Expectations With and Without Their Chosen Treatment for Prostate Cancer.* Ann Fam Med, 2016. **14**(3): p. 208-14.

56. Hall, J.D., et al., *Why patients choose prostatectomy or brachytherapy for localized prostate cancer: results of a descriptive survey.* Urology, 2003. **61**(2): p. 402-7.

57. Song, L.X., et al., *Who makes the decision regarding the treatment of clinically localized prostate cancer-the patient or physician?* Cancer, 2013. **119**(2): p. 421-428.

58. Xu, J., et al., *Men's perspectives on selecting their prostate cancer treatment.* Journal of the National Medical Association, 2011. **103**(6): p. 468-478.

59. Mazur, D.J. and D.H. Hickam, *Patient preferences for management of localized prostate cancer.* West J Med, 1996. **165**(1-2): p. 26-30.

60. Davison, B.J., A.I. So, and S.L. Goldenberg, *Quality of life, sexual function and decisional regret at 1 year after surgical treatment for localized prostate cancer.* BJU Int, 2007. **100**(4): p. 780-5.

61. Davison, B.J. and S.L. Goldenberg, *Decisional regret and quality of life after participating in medical decision-making for early-stage prostate cancer.* BJU Int, 2003. **91**(1): p. 14-7.

62. Hoffman, R.M., et al., *Treatment Decision Regret Among Long-Term Survivors of Localized Prostate Cancer: Results From the Prostate Cancer Outcomes Study.* J Clin Oncol, 2017. **35**(20): p. 2306-2314.

63. Fowler, F.J., Jr., et al., *Decision-making process reported by Medicare patients who had coronary artery stenting or surgery for prostate cancer.* J Gen Intern Med, 2012. **27**(8): p. 911-6.

64. Lehto, U.-S., et al., *Patient experiences at diagnosis and psychological well-being in prostate cancer: A Finnish national survey.* European Journal of Oncology Nursing, 2015. **19**(3): p. 220-229.

65. Sinfield, P., et al., *Patient-centred care: What are the experiences of prostate cancer patients and their partners?* Patient Education and Counseling, 2008. **73**(1): p. 91-96.

66. Xu, J.P., et al., *Patient Perspective on Watchful Waiting/Active Surveillance for Localized Prostate Cancer.* Journal of the American Board of Family Medicine, 2012. **25**(6): p. 763-770.

67. Cegala, D.J., et al., *Information seeking and satisfaction with physician-patient communication among prostate cancer survivors.* Health Communication, 2008. **23**(1): p. 62-69.

68. Davison, B.J. and E. Breckon, *Factors influencing treatment decision making and information preferences of prostate cancer patients on active surveillance.* Patient Educ Couns, 2012. **87**(3): p. 369-74.

69. Alva, A. and M. Hussain, *The changing natural history of metastatic prostate cancer.* Cancer Journal (Sudbury, Mass.), 2013. **19**(1): p. 19-24.

70. Frees, S., et al., *The impact of time to metastasis on overall survival in patients with prostate cancer.* World J Urol, 2018.

71. Cornford, P., et al., *EAU-EANM-ESTRO-ESUR-SIOG Guidelines on Prostate Cancer. Part II-2020 Update: Treatment of Relapsing and Metastatic Prostate Cancer.* Eur Urol, 2021. **79**(2): p. 263-282.

72. Botrel, T.E., et al., *Efficacy and Safety of Combined Androgen Deprivation Therapy (ADT) and Docetaxel Compared with ADT Alone for Metastatic Hormone-Naive Prostate Cancer: A Systematic Review and Meta-Analysis.* PLoS One, 2016. **11**(6): p. e0157660.

73. Shore, N., A. Heidenreich, and F. Saad, *Predicting Response and Recognizing Resistance: Improving Outcomes in Patients With Castration-resistant Prostate Cancer.* Urology, 2017. **109**: p. 6-18.

74. Markowski, M.C. and M.A. Carducci, *Early use of chemotherapy in metastatic prostate cancer.* Cancer Treat Rev, 2017. **55**: p. 218-224.

75. Rabow, M.W. and M.X. Lee, *Palliative care in castrate-resistant prostate cancer.* Urol Clin North Am, 2012. **39**(4): p. 491-503.

76. Shah, J., S.J. Khaksar, and P. Sooriakumaran, *Management of prostate cancer. Part 3: metastatic disease.* Expert Review Of Anticancer Therapy, 2006. **6**(5): p. 813-821.

77. Lindqvist, O., B.H. Rasmussen, and A. Widmark, *Experiences of symptoms in men with hormone refractory prostate cancer and skeletal metastases.* Eur J Oncol Nurs, 2008. **12**(4): p. 283-90.

78. Sullivan, P.W., et al., *Quality of life findings from a multicenter, multinational, observational study of patients with metastatic hormone-refractory prostate cancer.* Qual Life Res, 2007. **16**(4): p. 571-5.

79. Saad, F., et al., *Skeletal-related events significantly impact health-related quality of life in metastatic castration-resistant prostate cancer: data from PREVAIL and AFFIRM trials.* Prostate Cancer Prostatic Dis, 2017. **20**(1): p. 110-116.

80. Eton, D.T., et al., *Constructing a conceptual framework of patient-reported outcomes for metastatic hormone-refractory prostate cancer.* Value Health, 2010. **13**(5): p. 613-23.

81. Msaouel, P., et al., *Key issues affecting quality of life and patient-reported outcomes in prostate cancer: an analysis conducted in 2128 patients with initial psychometric assessment of the prostate cancer symptom scale (PCSS).* BMJ Support Palliat Care, 2017. **7**(3): p. 308-315.

82. Sanford, M.T., K.L. Greene, and P.R. Carroll, *The argument for palliative care in prostate cancer.* Transl Androl Urol, 2013. **2**(4): p. 278-80.

83. Radbruch, L., et al., *Redefining Palliative Care-A New Consensus-Based Definition.* J Pain Symptom Manage, 2020. **60**(4): p. 754-764.

84. National Board of Health and Welfare, *Definiton of "palliative care"*. 2011 2022-10-05]; Available from: http://termbank.socialstyrelsen.se/?TermId=471&SrcLang=sv.

85. National Board of Health and Welfare, *Definition of "palliative care at the end of life"*. 2011 2022-10-05]; Available from: http://termbank.socialstyrelsen.se/?TermId=474&SrcLang=sv.

86. Clark, D., *To comfort always - A history of palliative medicine since the nineteenth century*. 2016, Oxford, UK: Oxford University Press.

87. Touzel, M. and J. Shadd, *Content Validity of a Conceptual Model of a Palliative Approach.* J Palliat Med, 2018. **21**(11): p. 1627-1635.

88. National Board of Health and Welfare, *Definition of "Palliative approach"*. 2011 2022-10-15]; Available from: https://termbank.socialstyrelsen.se/?TermId=467&SrcLang=sv.

89. Ministry of Health and Social Affairs, *Döden angår oss alla - värdig vård vid livets slut (SOU 2000:6)*, G.o.o. Sweden, Editor. 2000, Government offices of Sweden: Stockholm, Sweden.

90. Pfister, D.G., et al., *American Society of Clinical Oncology treatment of unresectable non-small-cell lung cancer guideline: update 2003.* J Clin Oncol, 2004. **22**(2): p. 330-53.

91. Tannock, I.F., et al., *Docetaxel plus prednisone or mitoxantrone plus prednisone for advanced prostate cancer.* The New England Journal Of Medicine, 2004. **351**(15): p. 1502-1512.

92. Petrylak, D.P., et al., *Docetaxel and estramustine compared with mitoxantrone and prednisone for advanced refractory prostate cancer.* The New England Journal Of Medicine, 2004. **351**(15): p. 1513-1520.

93. Tannock, I.F., et al., *Chemotherapy with mitoxantrone plus prednisone or prednisone alone for symptomatic hormone-resistant prostate cancer: a Canadian randomized trial with palliative end points.* J Clin Oncol, 1996. **14**(6): p. 1756-64.

94. Kantoff, P.W., et al., *Hydrocortisone with or without mitoxantrone in men with hormone-refractory prostate cancer: results of the cancer and leukemia group B 9182 study.* J Clin Oncol, 1999. **17**(8): p. 2506-13.

95. Parker, C., et al., *Alpha emitter radium-223 and survival in metastatic prostate cancer.* N Engl J Med, 2013. **369**(3): p. 213-23.

96. Beer, T.M., et al., *Enzalutamide in metastatic prostate cancer before chemotherapy.* N Engl J Med, 2014. **371**(5): p. 424-33.

97. de Bono, J.S., et al., *Abiraterone and increased survival in metastatic prostate cancer.* The New England Journal Of Medicine, 2011. **364**(21): p. 1995-2005.

98. de Bono, J.S., et al., *Prednisone plus cabazitaxel or mitoxantrone for metastatic castration-resistant prostate cancer progressing after docetaxel treatment: a randomised open-label trial.* Lancet, 2010. **376**(9747): p. 1147-54.

99. Fizazi, K., et al., *Abiraterone acetate for treatment of metastatic castration-resistant prostate cancer: final overall survival analysis of the COU-AA-301 randomised, double-blind, placebo-controlled phase 3 study.* Lancet Oncol, 2012. **13**(10): p. 983-92.

100. Scher, H.I., et al., *Increased survival with enzalutamide in prostate cancer after chemotherapy.* N Engl J Med, 2012. **367**(13): p. 1187-97.

101. Harland, S., et al., *Effect of abiraterone acetate treatment on the quality of life of patients with metastatic castration-resistant prostate cancer after failure of docetaxel chemotherapy.* Eur J Cancer, 2013. **49**(17): p. 3648-57.

102. Lorente, D., et al., *Optimal Treatment Sequence for Metastatic Castration-resistant Prostate Cancer.* Eur Urol Focus, 2016. **2**(5): p. 488-498.

103. Handy, C.E. and E.S. Antonarakis, *Sequencing Treatment for Castration-Resistant Prostate Cancer.* Current Treatment Options in Oncology, 2016. **17**(12): p. 64.

104. Eliasson, L., et al., *Patients' Preferences for the Treatment of Metastatic Castrate-resistant Prostate Cancer: A Discrete Choice Experiment.* Clin Ther, 2017. **39**(4): p. 723-737.

105. Harrington, S.E. and T.J. Smith, *The role of chemotherapy at the end of life: "when is enough, enough?".* Jama, 2008. **299**(22): p. 2667-78.

106. Haun, M.W., et al., *Early palliative care for adults with advanced cancer.* Cochrane Database Syst Rev, 2017. **6**: p. Cd011129.

107. Baszanger, I., *One more chemo or one too many? Defining the limits of treatment and innovation in medical oncology.* Soc Sci Med, 2012. **75**(5): p. 864-72.

108. Daneault, S., et al., *Hope and noncurative chemotherapies: which affects the other?* J Clin Oncol, 2010. **28**(13): p. 2310-3.

109. Nappa, U., et al., *Palliative chemotherapy during the last month of life.* Ann Oncol, 2011. **22**(11): p. 2375-80.

110. Bélanger, E., et al., *Patient participation in palliative care decisions: An ethnographic discourse analysis.* Int J Qual Stud Health Well-being, 2016. **11**: p. 32438.

111. Oswald, L.B., et al., *What Do Men with Metastatic Prostate Cancer Consider When Making Treatment Decisions? A Mixed-methods Study.* Patient Prefer Adherence, 2020. **14**: p. 1949-1959.

112. Nussbaum, N., et al., *Patient experience in the treatment of metastatic castration-resistant prostate cancer: state of the science.* Prostate Cancer Prostatic Dis, 2016. **19**(2): p. 111-21.

113. Jones, R.A., et al., *Understanding Advanced Prostate Cancer Decision Making Utilizing an Interactive Decision Aid.* Cancer Nurs, 2018. **41**(1): p. 2-10.

114. Clark, J.A., N.P. Wray, and C.M. Ashton, *Living with treatment decisions: regrets and quality of life among men treated for metastatic prostate cancer.* J Clin Oncol, 2001. **19**(1): p. 72-80.

115. Aaronson, N.K., et al., *The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology.* Journal Of The National Cancer Institute, 1993. **85**(5): p. 365-376.

116. Fransson, P., B. Tavelin, and A. Widmark, *Reliability and responsiveness of a prostate cancer questionnaire for radiotherapy-induced side effects.* Support Care Cancer, 2001. **9**(3): p. 187-98.

117. Groenvold, M., et al., *Validation of the EORTC QLQ-C30 quality of life questionnaire through combined qualitative and quantitative assessment of patient-observer agreement.* J Clin Epidemiol, 1997. **50**(4): p. 441-50.

118. Arraras Urdaniz, J.I., et al., *The eortc quality of life questionnaire QLQ-C30 (version 3.0). Validation study for Spanish prostate cancer patients.* Arch Esp Urol, 2008. **61**(8): p. 949-54.

119. Osoba, D., et al., *Interpreting the significance of changes in health-related quality-of-life scores.* J Clin Oncol, 1998. **16**(1): p. 139-44.

120. Snyder, C.F., et al., *Using the EORTC-QLQ-C30 in clinical practice for patient management: identifying scores requiring a clinician's attention.* Qual Life Res, 2013. **22**(10): p. 2685-91.

121. Campbell, M.J., D. Machin, and S.J. Walters, *Medical statistics - a textbook for the health sciences*. 4th ed. 2007, Chichester, West Sussex, England: John Wiley & Sons Ltd.

122. Polit, D. and C. Beck, *Nursing research - Generating and assessing evidence for nursing practice*. 11th ed. 2021, Philadelphia, PA, U.S.A.: Wolters Kluwer.

123. Patton, M.Q., *Qualitative Research & Evaluation Methods*. 3 ed. 2002, Thousand Oaks, CA, U.S.A.: SAGE Publications.

124. Kvale, S. and S. Brinkmann, *Interviews - Learning the craft of qualitative reseach interviewing*. 3rd ed. 2014, Thousand Oaks, CA, USA: Sage Publications Inc.

125. Thorne, S., *Interpretive Description - qualitative research for applied practice*. 2nd ed. 2016, New York: Routledge.

126. Graneheim, U.H. and B. Lundman, *Qualitative content analysis in nursing research: concepts, procedures and measures to achieve trustworthiness.* Nurse Educ Today, 2004. **24**(2): p. 105-12.

127. Krippendorff, K., *Content analysis - An introduction to its methodology*. 4th ed. 2019, Thousand Oaks, CA, U.S.A.: SAGE Publications, Inc.

128. Cella, D.F., et al., *The Functional Assessment of Cancer Therapy Scale: Development and validation of the general measure.* Journal of Clinical Oncology, 1993. **11**(3): p. 570-579.

129. Fonteyn, M.E., B. Kuipers, and S.J. Grobe, *A Description of Think Aloud Method and Protocol Analysis.* Qualitative Health Research, 1993. **3**(4): p. 430-441.

130. Doveson, S., *Experiences of living with, and undergoing treatment of, metastastic, castration-resistant prostate cancer - A qualitative study*, in *Sophiahemmet University*. 2014, Sophiahemmet University: Stockholm, Sweden.

131. WMA. *Declaration of Helsinki by World Medical Association*. 2013 [cited 2018 2018-10-25]; Available from: https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/.

132. de Araujo Toloi, D., et al., *Living better or living longer? Perceptions of patients and health care professionals in oncology.* Ecancermedicalscience, 2015. **9**: p. 574.

133. Sumanasuriya, S. and J. De Bono, *Treatment of Advanced Prostate Cancer-A Review of Current Therapies and Future Promise.* Cold Spring Harb Perspect Med, 2018. **8**(6).

134. Kaya, E. and D. Feuer, *Prostate cancer: palliative care and pain relief.* Prostate Cancer Prostatic Dis, 2004. **7**(4): p. 311-5.

135. Sonnek, F.C. and E. van Muilekom, *Metastatic castration-resistant prostate cancer. Part 2: helping patients make informed choices and managing treatment side effects.* Eur J Oncol Nurs, 2013. **17 Suppl 1**: p. S7-12.

136. Brawley, S., R. Mohan, and C.D. Nein, *Localized Prostate Cancer: Treatment Options.* Am Fam Physician, 2018. **97**(12): p. 798-805.

137. Paterson, C., et al., *Identifying the unmet supportive care needs of men living with and beyond prostate cancer: A systematic review.* Eur J Oncol Nurs, 2015. **19**(4): p. 405-18.

138. King, A.J., et al., *Prostate cancer and supportive care: a systematic review and qualitative synthesis of men's experiences and unmet needs.* Eur J Cancer Care (Engl), 2015. **24**(5): p. 618-34.

139. Kain, D.A. and E.A. Eisenhauer, *Early integration of palliative care into standard oncology care: evidence and overcoming barriers to implementation.* Curr Oncol, 2016. **23**(6): p. 374-377.

140. Kaasa, S., et al., *Integration of oncology and palliative care: a Lancet Oncology Commission.* Lancet Oncol, 2018. **19**(11): p. e588-e653.

141. Bennardi, M., et al., *Palliative care utilization in oncology and hemato-oncology: a systematic review of cognitive barriers and facilitators from the perspective of healthcare professionals, adult patients, and their families.* BMC Palliat Care, 2020. **19**(1): p. 47.

142. Sorensen von Essen, H., et al., *Shared decision making in high-grade glioma patients-a systematic review.* Neurooncol Pract, 2020. **7**(6): p. 589-598.

143. Johnston, B., *Introduction to palliative care: Overview of nursing development*, in *Palliative care - The nursing role*, J. Lugton and R. McIntyre, Editors. 2005, Elsevier Churchill Livingstone: London, UK.

144. Ministry of Health and Social Affairs, *En nationell cancerstrategi för framtiden (SOU 2009:11)*, G.o.o. Sweden, Editor. 2009, Government offices of Sweden: Stockholm, Sweden.

145. Arraras, J.I., et al., *An international validation study of the EORTC QLQ-INFO25 questionnaire: an instrument to assess the information given to cancer patients.* Eur J Cancer, 2010. **46**(15): p. 2726-38.

146. Epstein, J.I., et al., *Contemporary Gleason Grading of Prostatic Carcinoma: An Update With Discussion on Practical Issues to Implement the 2014 International Society of Urological Pathology (ISUP) Consensus Conference on Gleason Grading of Prostatic Carcinoma.* Am J Surg Pathol, 2017. **41**(4): p. e1-e7.

147. Lincoln, Y.S. and E.G. Guba, *Naturalistic Inquiry*. 1985, Newbury Park, CA: Sage.

148. Malterud, K., V.D. Siersma, and A.D. Guassora, *Sample Size in Qualitative Interview Studies: Guided by Information Power.* Qual Health Res, 2016. **26**(13): p. 1753-1760.

149. Morse, J.M., *The Significance of Saturation.* Qualitative Health Research, 1995. **5**(2): p. 147-149.

150. Graneheim, U.H., B.M. Lindgren, and B. Lundman, *Methodological challenges in qualitative content analysis: A discussion paper.* Nurse Educ Today, 2017. **56**: p. 29-34.