Treating patients with incurable cancer: costs, quality of life, and cost-effectiveness of a specialized palliative care intervention

Applicant:

Henriette Tind Hasse, RN, MHS, Oncological dept. OUH, Denmark

Main supervisor:

Søren Rud Kristensen, Associate professor, DaCHE, SDU and senior lecturer, Imperial College London.

Co-supervisors:

Trine Kjær, Professor, DaCHE, SDU.

Thea Otto Mattsson, MD, Post Doc, Ph.D. Department of Oncology, OUH.

Katrine Rahbek Schønnemann, MD, Ph.D. Clinical Associated Professor, department of Oncology, OUH

Introduction

Cancer treatment is under constant development, new treatments are continuously introduced increasing both the number of available drugs and combinations of treatments (1). This, combined with the fact that an increasing number of cancer patients live longer (2), facilitate the possibility of continuing treatment for longer. Hence, should the first choice of treatment prove ineffective, or cause non-acceptable adverse effects, other options are available (3-6). This puts a strain on the scarce resources allocated to the healthcare sector. Recent studies show that treatment given at the end-of-life has little or no effect on both overall survival and quality of life (QoL) and may cause more harm than good (5-8). Most cancer treatments given to patients with local advanced or metastatic cancer where curative therapy is no longer an option, are life-extending, implying a prolongation of the disease state, which can be very poor (5, 9, 10). In addition to the high cost of treatment, this implies that cancer treatment given late in life often has very poor cost effectiveness, and thus may not be the most optimal usage of public health care resources. Furthermore, results from a large international survey indicate that only a minority of people would prioritize life-prolonging treatment over quality of life (QoL) at the end of life (11, 12).

In recent years patient involvement has been recognized as a key component in clinical practice guidelines. This has led to the development of shared decision-making tools, as well as the measurement of patient reported outcomes (PRO) at point of care (13-16). In oncology, recent studies point towards Specialized Palliative Care (SPC) as a way to minimize the amount of antineoplastic treatment (cancer directed treatment) given late in life in accordance with patient preferences (17, 18). This is in line with recommendations by The Lancet commission (19), that point towards integrated SPC as a means to secure both high quality care and reduce costs in oncology. The commission concludes that integrated SPC and an earlier onset of SPC has a positive effect on the patient perceived quality of care and patient reported QoL – in addition to offering a reduction in; length of stay at hospital, chemotherapy given at the end of life, and the frequency of home deaths (19, 20). Despite the increased evidence on the positive effects of SPC, several issues remain unresolved including comprehensive cost analysis and understandings of the underlying variation in treatment effects. The commission highlights that more studies are needed to better secure that extra resources allocated toward SPC to patients with cancer result in cost savings. Integrated SPC will introduce extra patient consultations, which may result in extra costs in some areas, but due to a spillover-effect SPC may still be cost-effective. May and colleagues (21) point out the lack of studies of SPC that consider both patient QoL and cost in the same study and call for cross-sector collaboration to better interpret multiple sources of data. A Danish register study (22) showed significantly lower risk of receiving antineoplastic treatment in the last 14 days of life in patients receiving SPC compared with patients not receiving SPC. However, the study did not report potential costs savings relating to the reduction in antineoplastic treatment (22). Another area of concern is equality in access to health care. Some studies point toward a social inequality in the access to SPC, as well as other courses of treatment, with patients in lower socio-economic strata being underserved (23, 24). These studies suggest problems with securing equal access to health care in Denmark, despite free health care at the point of access, and the Danish health act that state that all must be secured equal access to health care (25).

Aim and research questions

The project aims to 1) explore differences in healthcare utilization among incurable cancer patients the last year of life 2) evaluate quality of life among patients with oncological cancer in a course of medical cancer treatment and 3) assess the cost effectiveness of SPC. Given the unique Danish registers, this project will be able to investigate patterns in healthcare utilization across sectors for the complete cancer population at a given time. Our analyses will include comparison of costs across patients with different disease paths, including the analysis of the consequences of receiving antineoplastic treatment at end-of-life. By prospectively collecting QoL data in patients with cancer further enrichment to our data enable us to analyze the quality of life among both curable and incurable cancer patients whilst being treated with medical cancer treatment, in the time up to death and to compare these findings with the health care utilization for certain specified sub-groups. By comparing patients submitted to integrated SPC and patients receiving standard care, it will illuminate if overall costs are reduced and patients QoL is increased.

As a methodological contribution, this project will seek to explore different ways of measuring QoL in patients at the end of life, using both the QALY and Capability approach.

Specifically, the project seeks to answer the following three research questions;

1. *How do incurable cancer patients, receiving medical cancer treatment, rate their quality of life continuously over the course of one year, when measured using the QALY approach?*
2. *How is healthcare utilized in different population groups suffering from incurable cancer in their last year of life?*
3. *Dos integrated specialized palliation contribute to an increase in quality of life, a reduction in the usage of late oncological treatment, and a reduction in direct hospital costs in patients with incurable cancer?*

Theoretical background

When conducting prospective economic evaluations of a healthcare intervention the most commonly applied method is cost utility analysis (CUA) in which health outcome are measured in Quality Adjusted Life years (QALY) using instruments such as the EQ-5D(26, 27). The CUA method is requested by authorities in several countries, e.g. the National institute for Health and care Excellence (NICE) in England (28-30) and recently also in Denmark (31). QALY's are value based, i.e. QoL weights are derived according to individual preferences, and take into consideration that a life year in good health is not valued the same as a life year in poor health. The QALY is a two-dimensional metric in which a health care intervention is valued both according to the gain generated in terms of quality of life and length of life.

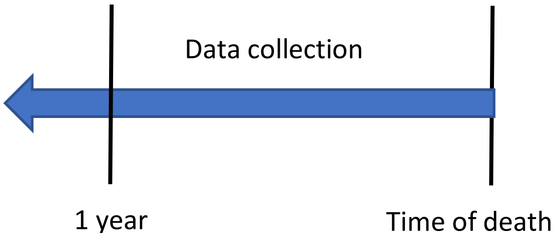
In cancer research the most frequently used QoL instrument is the EORTC-QLQ-C30 (EQC30). In contrast to the EQ-5D, the EQC30 is not preference-based and therefore it cannot be directly applied in economic evaluations. To overcome this, the EORTC-QLU-C10D (EQ-C10D) has been developed in which preference-based QALY weights have been derived. The EQ-C10D contains 10 dimensions (physical-, role-, social-, and emotional functioning, pain, fatigue, sleep, appetite, nausea, and bowel problems), with four levels in each (32). QALY weights for the EQ-C10D are currently available in e.g. the U.K., Australia, and Germany and other countries are underway (32-35). In Denmark preparations are underway for compilation of Danish weights (36).

Study I: ***Variation in utilization, costs, and quality of care the last 6 moths of life in Danish cancer patients. A national register-based study.***

Aim: To understand variation in healthcare utilization the last 6 months of life in patients with cancer.

Method: A retrospective cohort is created using the National patient registry, Danish cause of death registry, the Danish Cancer registry and the National Palliative registry. Sub-groups will be defined based on socioeconomic status, diagnosis, treatment choices and referral to SPC. Data is collected from day of death and one year back.

Participants: All adult (>18) patients who died from their cancer diagnosis in the years 2010 through 2020 are included. Persons diagnosed with cancer at the time of death, but with a different cause of death listed will be excluded.



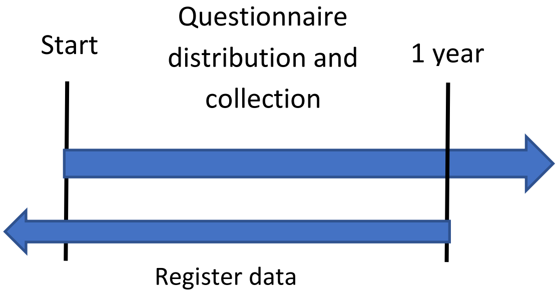
Outcome: Healthcare utilization analysis of all planned and acute contacts with hospital, general physician, costs and mortality. Furthermore, quality of care indicators are identified. Subgroup analysis are performed to identify potential differences in utilization patterns and costs

Implications: The knowledge gained in this study is valuable when assessing how healthcare services are allocated across i.e., socio-demographic groups, age and gender. This may influence the way we prioritize in healthcare, and in how healthcare is organized and distributed.

Study II: ***A longitudinal study of quality of life in oncological cancer patients undergoing medical cancer directed treatment, using both the EQ-5D-5L and the EORTC QLQ-C30D.***

Aim: To gain knowledge about self-rated QoL in patients suffering from cancer being treated with medical cancer treatment. Furthermore, to add to the sparse literature on appropriate measures of QoL for cancer patients at end-of-life. Prospectively collected data is combined with retrospectively collected registry data. This will result in a very complete and unique dataset.

Method: A longitudinal prospective descriptive study of QoL in patients with local advanced or metastatic cancer receiving medical cancer directed treatment at an oncological out-patient department at a larger university hospital. Participants are identified by extracting all personal ID numbers (CPR nr.) on patients currently in a course of medical cancer treatment. The extraction of ID numbers is performed 2 to 3 times in 3-month intervals, this to insure enough participants. Patients eligible for participation are invited to complete both the EQ-5D-5L and the EQ-C30D questionnaire simultaneously. The information to the patients regarding the study will explain that the two different questionnaires contribute with valuable knowledge concerning different aspect of being ill and living with an illness that effect all aspect of the patient's life. The questionnaires are distributed electronically (through e-boks) from SDU. Follow up time is one year from enrolment, with an expected four questionnaires per patient. Information concerning performance status and stage of disease are collected in the EPC retrospectively, Furthermore, state of disease will be collected retrospectively to identify patients with incurable cancer. Thus, to perform subgroup analysis on this specific group of patients. The collected data is paired with register data for information as i.e. usage of healthcare services, income, social status, date of birth and date of death.



Participants: All patients receiving medical cancer treatment at the Department of Oncology at Odense University Hospital will be invited to participate. The enrolment procedure is repeated 2 to 3 times in 3-month intervals, giving a proximate of 2500 eligible patients.

Outcome: QoL measurements from both the EQ-5D-5Land the EORTC QLQ-C30D

Implications: This study provides knowledge of how patients asses their QoL when receiving medical cancer targeted treatment. This might lead to a change in the recommend treatment options in life-prolonging cancer care. The unique and valid registries in Denmark combined with QoL data will result in a very comprehensive knowledge concerning this patient group. Furthermore, this study will contribute with knowledge concerning how the different approaches, the EQ-5D-5L the EORTC, complement each other.

Study III: ***Health economic evaluation of integrated SPC intervention in patients with incurable cancer.***

Aim: To evaluate if need based SPC integrated into an oncological department is a cost-effective strategy and if SPC contributes to a change in PRO measured QoL in patients. Need based SPC is recommended by the Danish board of health:

"Identifying and assessing the patient's need for palliative intervention is based on a holistic approach and the individual patient's preconditions; happens as soon as possible - preferably at the time of diagnosis and systematically using the same and validated tools across sectors and repeated as needed".(37)

Method/study design: This study is completed concomitant to a need based integrated SPC intervention study (ISPCS). ISPCS is completed in collaboration between a department of oncology at a university hospital and a specialized palliative care service. Patients are systematically screened to evaluate the need of SPC, as recommended by the Danish board of Health (37). To evaluate ISPCS QoL assessment questionnaires are distributed at the time of eligibility and then continuously every 4 weeks for the duration of 12 week or until death occurs. Questionnaires are distributed electronically via e-boks. QoL is then compared between the two groups to see if there are differences in the measured QoL, and if differences occur immediately or over time within the 12 weeks follow up period. The perspective of the economic evaluation is the health sector perspective.

Participants: Precise criteria for inclusion are under development by the project owners. The case group in the economic evaluation consists of patients residing on the island of Fyn, who are eligible for screening to the integrated/need based SPC offer. The control group consists of patients, who are also eligible for screening to the need based integrated SPC offer, but reside in the remaining part of Denmark (mainly the region of Southern Denmark), and are thus not offered the intervention. All participants attend a cause of treatment at the Oncological department at OUH. Information about age, gender and cancer diagnosis are collected to enable matched controls and better secure that any difference detected is related to the intervention. Furthermore, information about hospitalization, oncological treatments, termination from the oncological department and date of death will be collected.

Outcome: Cost effectiveness analysis of need based integrated SPC, based on differences in QoL and resource use across case and control group.

Implications: Results of this study will help clarify whether SPC is a cost-effective strategy, and thereby inform policy.

Ph.D. plan

The Ph.D. project is expected to compose of at least three peer reviewed articles based on the studies outlined above. The articles will be submitted to high quality field journals such as Annals of Oncology, European Journal of Oncology Nursing, Journal of Palliative medicine, Journal of Public Health, Medical Decision Making and Health Economics. Furthermore, relevant international conferences will be attended, both within the clinical field and health economics possibly including the annual European Society for Medical Oncology (ESMO) congress, the International conference on Advancement in Palliative care and healthcare (ICAPCH), Society for Medical Decision Making Meeting, the Nordic Health Economic Study Group Meeting (NHESG), and the European Health Economic Association (EuHEA).

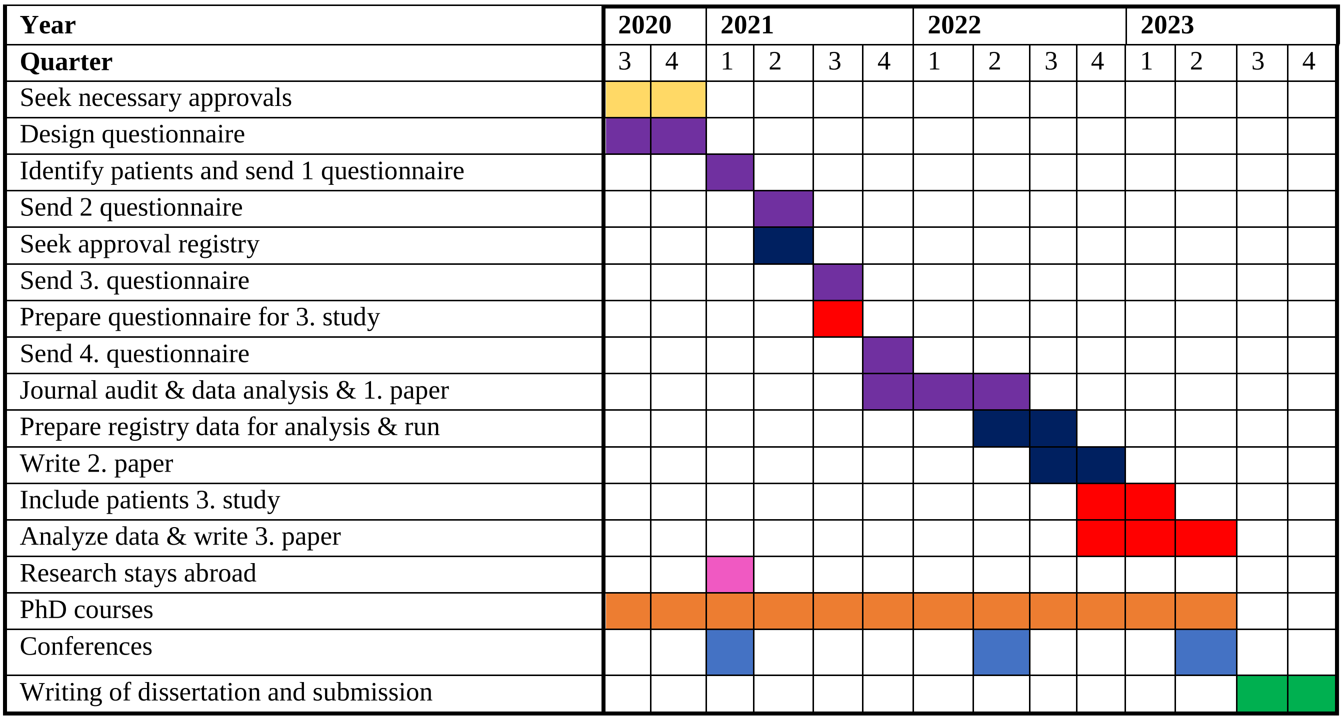
Study abroad

At least one international stay during the PhD period is planned. DaCHE, Danish Centre for Health Economics, has a strong international research network and will help arrange a stay at a relevant international institution. Furthermore, there are several international collaborative opportunities within both the oncological and palliative field.

Approvals and Ethical aspects

All necessary data approvals will be obtained from The Agency for Patient Safety and The Department of Oncology at Odense University Hospital. All patients invited to participate in the studies described in this protocol will have the right to decline, without it effecting their treatment. Furthermore, patients who do not wish to continue their participation are free to decline further participation at any time. All studies are done with respect for the individual patient and their QoL.

Time-schedule



Year	**2020**		**2021**				**2022**				**2023**			
Quarter	3	4	1	2	3	4	1	2	3	4	1	2	3	4
Seek necessary approvals	🟨	🟨												
Design questionnaire	🟪	🟪												
Identify patients and send 1 questionnaire			🟪											
Send 2 questionnaire				🟪										
Seek approval registry				⬛										
Send 3. questionnaire					🟪									
Prepare questionnaire for 3. study					🟥									
Send 4. questionnaire						🟪								
Journal audit & data analysis & 1. paper						🟪	🟪	🟪						
Prepare registry data for analysis & run								⬛	⬛					
Write 2. paper									⬛	⬛				
Include patients 3. study										🟥	🟥			
Analyze data & write 3. paper										🟥	🟥	🟥		
Research stays abroad			▨											
PhD courses	🟧	🟧	🟧	🟧	🟧	🟧	🟧	🟧	🟧	🟧	🟧	🟧		
Conferences			🟦					🟦				🟦		
Writing of dissertation and submission													🟩	🟩

Purple = paper one. Dark blue = Paper two. Red = Paper three. Pink = study aboard. Orange = PhD courses. Light blue = Conferences. Green = Dissertation writing.

Supervisors

Main supervisor: Søren Rud Kristensen, Associate professor, DaCHE, SDU and senior lecturer, Imperial College London.

Co-supervisors: Trine Kjær, Professor, DaCHE, SDU. Thea Otto Mattsson, MD, Post Doc, Ph.D. Department of Oncology, OUH. Katrine Rahbek Schønnemann, MD, Ph.D. Clinical Associated Professor, department of Oncology, OUH

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