Patient-reported outcomes on the trajectory of hematological cancer

A multi-method study

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BY
MIA SOMMER

DISSERTATION SUBMITTED 2020

AALBORG UNIVERSITY
DENMARK

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ENGLISH SUMMARY

Background:. Patient-reported outcomes (PROs) applied to clinical practice have proven successful in providing patient-centered care in terms of increased patient involvement, improved provider-patient communication and as support to shared decision making. Patients with hematological cancer report unmet supportive care needs throughout their experience with the disease. These unmet needs are associated with impaired health-related quality of life (HRQoL) expressed as impairment of physical, physiological and social functioning as well as increased symptom burden. Thus, these patients face a variety of challenges along the disease trajectory, which are not fully meet today, underpinning the importance of investigating if PROs have the potential to enhance patient-centered care and quality of care in patients with hematological cancer.

Aim: The overall aim of this PhD thesis was to examine the potential of PROs among patients with hematological cancer along the disease trajectory and to determine if PROs could facilitate patient-centered care and contribute to increased quality of care in this population.

Method: This PhD thesis incorporates a multi-method research design consisting of three studies. In Study I, the feasibility of a shared care follow-up initiative for patients with B-cell disease was tested. The shared care follow-up initiative was based on alternating in-hospital physician visits and nurse-led telephone consultations based on PRO data. The study involved a survey of the patients' acceptability towards completing PROs as part of follow-up. Study II involved qualitative interviews exploring patients' experiences with participating in the shared care follow-up initiative. Study III was a longitudinal observational HRQoL study investigating HRQoL patterns during one year in a cohort of patients with hematological cancer who had relapsed or progressive disease.

Results: In Study I, the shared care follow-up proved feasible, yielding high patient adherence and receptivity to completing PRO measures expressed as; a) increased involvement in treatment (48/56 [86%]); b) easier recollection of symptoms (50/57 [88%]), and c) improved communication with the health professionals (51/57 [90%]). Study II described five themes that the participating patients experienced in the shared care follow-up initiative, finding positives in more aspects of everyday life and a shift in focus during the consultations from disease and treatment to psychological issues. Most patients were positive towards completing PROs as part of follow-up;

however, a few patients found the questions to be irrelevant and that it was difficult to get the message across. Study III demonstrated that patients with relapsing or progressive hematological disease reported moderate or severe symptoms or functional problems at baseline and that some patients experienced deterioration in HRQoL in the first year after a relapse diagnosis. Furthermore, a statistically significant correlation between impaired role functioning and estimated survival ≤2 years was found (OR 0.14, CI: 0.02; 0.95, p=0.04).

Conclusion: Overall, this multi-method PhD thesis demonstrates that PROs are valuable on the trajectory of hematological cancer in terms of increased patient involvement, identifying health problems, and improving patient–provider communication and as a supporting role in shared decision making. Although divergent patient experiences suggest that a one-size-fits-all approach is undesirable, PROs seem to provide health professionals with a valid tool in the pursuit of providing patient-centered care.

Implications for clinical practice: PROs may have the potential to target and individualize survivorship care of patients with hematological cancer. Basing survivorship care on a multi-disciplinary approach may allow for a more holistic approach to a patient's supportive care needs. To address deterioration in HRQoL during relapse treatment, implementation of PROs in hematological clinical practice may offer the opportunity to address symptoms earlier and support patients in maintaining usual activities.

Future research: Development and implementation of PRO-based interventions should be preceded by qualitative research studies exploring patient needs and preferences for the intervention in question, ensuring a solid foundation for future PRO-based interventions. The results of this research indicated a large symptom burden as well as deterioration in HRQoL among patients with relapse or progressive disease. To address symptoms and supportive care needs during treatment for relapsed or progressive disease, further research should encompass symptom monitoring based on PROs during treatment of these patients to identify potential positive patient outcomes.

DANSK RESUME

Baggrund: Anvendelsen af PRO data (patient-rapported outcomes) har vist siga at være værdifuld i forbindelse med patient-centreret pleje og behandling i klinisk praksis. PRO data har blandt andet vist fordele i forhold til øget patientinvolvering, forbedret kommunikation mellem patient og sundhedsprofessionelle og som støtte til fælles beslutningstagning. Hæmatologiske kræftpatienter rapporterer om uopfyldte behov i forbindelse med håndtering af sygdommen og følger til sygdommen i løbet af deres sygdomsforløb. Uopfyldte behov for støtte er associeret med nedsat helbredsrelateret livskvalitet i form af forringet fysisk, psykisk og social funktion og øget symptombyrde. Hæmatologiske kræftpatienter oplever således adskillige udfordringer i løbet af deres sygdomsforløb, som på nuværende tidspunkt ikke fuldt ud bliver mødt. På den baggrund er det vigtigt at undersøge, hvorvidt PRO data potentielt kan understøtte patient-centreret pleje og behandling.

Formål: Det overordnede formål med dette Ph.d.-projekt var at undersøge PRO datas potentiale hos hæmatologiske kræftpatienter i løbet af deres sygdomsforløb og klarlægge, hvorvidt PRO data kunne facilitere patient-centreret pleje og behandling og bidrage til øget kvalitet af pleje og behandling hos denne patientgruppe.

Metode: Dette Ph.d.-projekt er designet som et multi-metode forskningsprojekt, der indeholder 3 studier. I Studie I blev gennemførbarheden af et tværfagligt opfølgningsforløb for patienter med B-celle sygdom undersøgt. Det tværfaglige opfølgningsforløb var baseret på skiftevis opfølgning hos patientens ansvarlige læge og telefoniske sygeplejerskekonsultationer baseret på PRO data. Inkluderet i studiet var en undersøgelse af patienternes villighed til at udfylde spørgeskemaer, som en del af opfølgningsforløbet. Studie II var et kvalitativt interview studie, der havde til formål at undersøge patienternes oplevelser med at deltage i det tværfaglige opfølgningsforløb. Studie III var et longitudinelt observationelt studie, der undersøgte mønstre i udviklingen af helbredsrelateret livskvalitet hos hæmatologiske patienter med relaps eller progressiv sygdom i løbet af det første år efter relapsdiagnosen.

Resultater: I Studie I blev det tværfaglige opfølgningsforløb fundet gennemførbart som resultat af høj patientdeltagelse og høj modtagelighed i forhold til at udfylde spørgeskemaer. Undersøgelsen af patienternes villighed til at udfylde spørgeskemaer viste, at 48/56 [86%] patienter oplevede øget involvering, 50/57

[88%] patienter huskede nemmere symptomer og 51/57 [90%] patienter oplevede forbedret kommunikationen med de sundhedsprofesionelle. Studie II beskrev fem temaer over patienternes oplevelser med at deltage i det tværfaglige opfølgningsforløb og fandt, at det tværfaglige opfølgningsforløb havde positiv indflydelse på flere aspekter af hverdagslivet, ligesom de oplevede et skift i fokus i under konsultationerne fra sygdom og behandling til psykologiske spørgsmål. De fleste patienter var positive i forhold til at udfylde spørgeskemaer, men nogle patienter fandt spørgsmålene irrelevante og svært at få sit budskab igennem. Studie III viste, at hæmatologiske patienter med relaps eller progressiv sygdom rapporterede moderate eller alvorlige symptomer og/eller funktionelle problemer ved baseline og at nogle patienter oplevede forværring af helbredsrelateret livskvalitet 12 måneder efter relapsdiagnosen. Derudover, viste Studie III en statistisk signifikant association mellem nedsat rollefunktion og estimeret overlevelse ≤2 år (OR 0.14, CI: 0.02; 0.95, p=0.04).

Konklusion: Samlet viser dette multi-metode Ph.d.-projekt, at PRO data er værdifulde i løbet af et hæmatologiske sygdoms- og behandlingsforløb i form af øget patientinvolvering, identifikation af sundhedsproblemer, forbedring af kommunikation mellem patient og sundhedsprofessionelle og som en understøttende rolle i fælles beslutningstagen. Selvom divergerende patientoplevelser antyder, at en enhedsløsning er uhensigtsmæssig, ser det ud til at PRO kan anvendes som et validt værktøj til patient-centreret pleje og behandling.

Implikationer for klinisk praksis: PRO data indeholder et muligt potentiale i forhold til at individualisere kræftopfølgning til patienter behandlet for hæmatologisk kræft og en multidisciplinær tilgang til opfølgning kunne bidrage til en forstærket holistisk tilgang til patienternes behov for støtte. Risikoen for forringelse af helbredsrelateret livskvalitet som følge af relaps eller progressiv sygdom kunne muligvis adresseres ved hjælp af PRO data i forhold til at danne basis for tidligere behandling af symptomer og støtte patienterne i fastholdelse af vanlige aktiviteter.

Fremtidig forskning: Udvikling og implementering af interventioner baseret på PRO data bør være forudgået af kvalitative forskningsstudier, der undersøger patienternes behov og præferencer i forhold til den planlagte intervention og som bidrag til et solidt fundament for fremtidige PRO-baserede interventioner. Derudover bør fremtidig forskning undersøge, hvorvidt symptommonitorering baseret på PRO data kan medvirke til at stabilisere eller forbedre helbredsrelateret livskvalitet hos patienter med relaps eller progressiv hæmatologisk kræft.

LIST OF PUBLICATIONS

Paper I

Sommer M, Frandsen L, Jensen P, Nielsen SR, Nielsen LB, Brøndum RF, Bøgsted M, Madsen J, Severinsen MT, Sørensen EE, Grønkjær M, El-Galaly TC. **Shared care follow-up of patients with B-cell neoplasms based on nurse-led telephone consultations and PRO-Data: A feasibility study from the North Denmark Region**, *Will be re-submitted before August 10., 2020 to* BMC Health Services Research *under the status of potentially accepted*

Paper II

Sommer M, Frandsen L, Jensen P, Bøgsted M, El-Galaly TC, Grønkjær M. **Hematological cancer survivors' experiences of participating in a shared care follow-up – an exploratory interview study**, *under peer-review* at Journal of Cancer Survivorship, *submitted March 23, 2020*

Paper III

Sommer M, Nielsen LK, Nielsen LB, Brøndum RF, Nielsen MM, Rytter AS, Vesteghem C, Severinsen MT, El-Galaly TC, Bøgsted M, Grønkjær M, Jørgensen, L. **The use of patient-reported outcomes in precision medicine and hematological patients with relapse or progressive disease: a longitudinal observational study**, *under peer-review* at Journal of Patient-reported Outcomes, *submitted July 3, 2020*

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Mia Sommer, July 2020

TABLES AND FIGURES

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LIST OF ABBREVIATIONS

PRO	Patient-reported outcome
HRQoL	Health-related quality of life
QoL	Quality of life
PCC	Patient-centered care
EORTC-QLQ-C30	The European Organization for Research and Treatment of Cancer QLQ-30
MPN-SAF	Myeloproliferative Neoplasm – Symptom Assessment Form
HADS	Hospital Anxiety and Depression Scale
PFF	Patient Feedback Form
CIT	Curative intent treatment
DLBCL	Diffuse large B-cell lymphoma
FL	Follicular lymphoma
CLL	Chronic lymphocytic leukemia
MZL	Marginal zone lymphoma
WAW	Watch and wait
SCFU	Shared care follow-up
FoC	Fundamentals of Care

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CHAPTER 1. INTRODUCTION

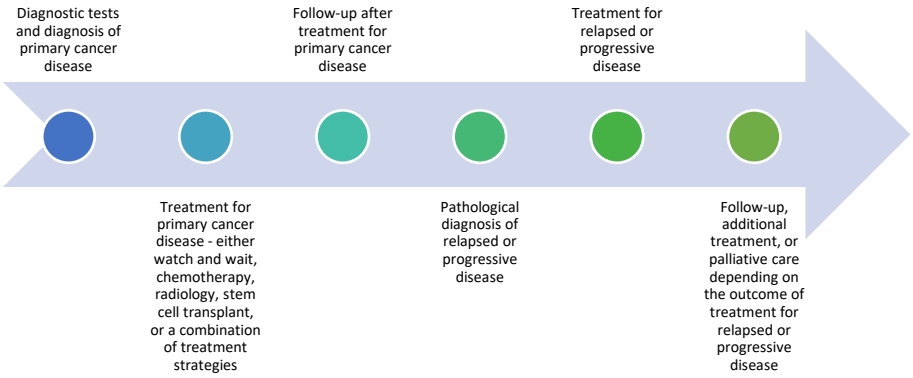
1.1. SETTING THE SCENE: HEMATOLOGICAL CANCER

Hematological cancers are a heterogeneous group of neoplasms defined by disease in the bone marrow and the lymph system. The main diagnostic categories are lymphomas, leukemias, and plasma cell neoplasms (1). Globally, incidence rates of hematological cancers have increased during the past decades, varying among continents and countries, with the highest rates in Australia, Western Europe, and high-income North America (2–4). The continuing increase in incidence rates is mainly the result of population growth, population aging, and changing population age structures (2). Studies indicate that more men than women are diagnosed with hematological cancer and that older adults are at higher risk of disease than younger people (2–4). Although survival has improved with the development of novel treatments (5), hematological cancer is often associated with high morbidity and mortality (2,3,6) and with secondary primary cancer (7). In 2018, approximately 4000 people were diagnosed with a malignant hematological disease in Denmark (8). Patients with hematological cancer are diagnosed, treated, and cared for at highly specialized hematological departments nationwide.

1.2. TRAJECTORY OF HEMATOLOGICAL CANCER

Hematological cancers follow an overall disease trajectory including diagnostic tests and diagnosis of primary disease, treatment of primary disease, and follow-up after primary disease. Some patients will experience relapse or progressive disease (9–13) for which they may receive treatement. After treatment, the patients may enter follow-up, receive additional treatment, or palliative care depending on the outcome of treatment for relapsed or progressive disease. Figure 1 illustrates the general hematological cancer trajectory.

Figure 1: Illustration of the general hematological cancer trajectory



In addition to the general disease trajectory, the individual disease trajectories offer a number of different scenarios because of the heterogeneity of hematological cancers. The disease trajectory varies according to the specific diagnosis, treatment, risk factors, patient characteristics, and number of relapses and episodes with progressive disease (9–13). Hematological cancers can be largely divided into two groups: disease with an often-aggressive pattern and a high chance of cure, e.g., aggressive lymphomas and acute leukemia (9,13); and diseases of a more chronic nature e.g., chronic leukemia, indolent lymphoma, and multiple myeloma, which are incurable and progress throughout a patient's life (10–12). For all diseases, diagnostic testing and primary disease identification are the first steps on the trajectory. During this time, staging and risk assessment are carried out. Following diagnostics, a patient may receive treatment with immunotherapy, chemotherapy, stem cell transplantation and/or radiation or enter an observational period (watch and wait) depending on individual diagnosis, staging, and risk assessment (14–17). After treatment for the primary disease, patients enter survivorship care, which focuses on relapse detection and monitoring of adverse events and long-term complications. Survivorship care is structured as regularly scheduled follow-up visits with physicians at the outpatient clinic, and the interval is based on diagnosis, individual risk assessment, and treatment outcome (9,10,12). In case of relapsed or progressive disease, the treatment goal is to reach cure or remission. In cases where this fails, a patient will be offered further treatment or referred to palliative care.

Hematological cancers and treatment pose various challenges for patients throughout the disease trajectory. The health-related challenges occur because of the nature of the disease and as a consequence of treatment, adverse events, and complications related to treatment (18). The literature indicates that physical, emotional, and social aspects of a patient's life are negatively affected. These consequences affect both newly diagnosed patients and patients experiencing relapse and can continue long into survivorship (19,20).

1.3. HEALTH-RELATED CHALLENGES ALONG THE DISEASE TRAJECTORY

Patients with hematological cancer face various challenges along the disease trajectory. From onset of treatment and into survivorship, these patients describe unmet supportive care needs. Research shows that psychosocial needs, fear of recurrence, and informational needs are among the needs that patients expect health professionals to recognize during the disease trajectory (21–25). Although unmet needs are reported throughout the trajectory, it seems that survivors of hematological cancer particularly experience them. One of the consequences of not being supported during the transition from active disease into survivorship has been described as living without a safety net after cancer diagnosis and treatment (22,26). In addition to the consequences of unmet needs, research has established an association between unmet needs and impaired quality of life (QoL) and various areas of functioning. Finally, unmet needs may cause emotional distress (27–29).

It is well established that hematological cancers and their treatment have an overall negative effect on patient QoL throughout the disease trajectory (19,30–33). Various dimensions of QoL are affected, one of which is the physical dimension. Patients with hematological cancer suffer from physical symptoms such as pain, fatigue, and sleep disturbance. Furthermore, physical functioning, such as carrying out daily activities, is affected (19). Various degrees of anxiety and depression as well as social, cognitive, and role functioning have been detected as affected dimensions (34–37). Impaired QoL has been documented throughout the disease trajectory, from treatment for primary diagnosis to relapse situations to follow-up and long into survivorship (19,20,38,39). The literature makes it evident that hematological cancer particularly negatively affects survivors and patients who experience relapse. Hence, the following section contains a review of studies related to supportive care needs and

QoL within the context of survivors of hematological cancer and those who experience relapse.

CHAPTER 2. STATE OF THE ART

A systematic literature search was conducted to identify current scientific knowledge and potential gaps in the scientific literature in relation to unmet supportive care needs in survivors of hematological cancer and QoL in those who experience relapse. The literature search was carried out in cooperation with a research librarian. PubMed and CINAHL were searched using relevant search terms such as "Hematological Neoplasms," "Lymphoma," "Leukemia," "Multiple Myeloma," "Survivorship Care," "Patient-reported outcomes," "Quality of life," "Relapse," and "Recurrence."

2.1. SURVIVORSHIP CARE

The term "cancer survivor" is defined in a variety of ways, but the most widely used definition is that being a cancer survivor is a process that begins at diagnosis and continues through the balance of life (40). However, when reporting on cancer survivors, many authors choose a context-specific definition of survivorship based on the study sample (40). In the context of this PhD thesis, a cancer survivor is defined as a patient who has ended treatment for primary disease or relapse and entered follow-up as part of survivorship care, because these are the characteristics of the patients studied.

Patients with hematological cancer report unmet supportive care needs during the disease trajectory, with an emphasis on psychological needs (21–26,28,41–47). Psychological needs relate to a desire or requirement for help or support that underlies a person's emotional psychological well-being. The literature review makes it evident that fear of recurrence is among the most predominant unmet needs for patients with hematological cancer (21,22,24,48–50). Furthermore, these patients report unmet needs in relation to the transition from active treatment to survivorship care (26,47,51,52). This transition is described as *"living without a safety net"* and *"adjusting to a new normal"* after cancer diagnosis and treatment (22,52). Information related to prognosis, managing and coping with side effects, lack of clarity regarding treatment decision making, and uncertainty about the future have also been reported as areas of unmet needs (21,23,26,44,49–51,53). Hence, insufficient support presents patients with challenges in dealing with issues related to the disease and what happens after treatment ends. In addition, unmet supportive care needs are associated with an impairment in QoL. A Danish population-based study examined a mixed population of patients with cancer, including patients with lymphoma, and found that unmet needs were associated

with impaired QoL and increased psychological distress (27). These results are supported by those of Oberoi et al. (2017), who found that unmet supportive care needs during treatment in a group of patients with hematological cancer were associated with impaired QoL in terms of physical and emotional well-being (28,29). Based on the existing literature, current survivorship care appears to be unsuccessful in terms of meeting the needs of patients with hematological cancer.

2.1.1. NURSE-LED SURVIVORSHIP INTERVENTIONS

During the past decades, nurse-led interventions have been introduced to enhance the quality of survivorship care and address the psychosocial and informational needs of patients. Moreover, nurse-led interventions may contribute to ease the workload within busy outpatient clinics. A variety of nurse-led interventions have been developed and tested in a number of cancer populations (54–78). The most predominant cancer diagnoses within the literature in this area are colorectal (56,57,60,61,64,74,77), prostate (59,62,67,72,76), and breast cancer (69,73,78). Some interventions have been designed to provide alternating physician and nurse-led consultations(54,72), whereas others have replaced physician visits with nurse-led clinics, either substituting physician visits with nurse-led consultations or adding consultations to the usual care program (58,79). Some interventions have been set in-hospital, and others have been telephone-based. Most interventions have relied on patient interviews that elicit information about the patient's health. Studies show that nurse-led survivorship interventions are well-accepted by patients (80,81) and suggest that most patients find nurse-led telephone consultations convenient and personalized (82–84). Furthermore, nurse-led interventions have been found to meet cancer patients' psychological and informational needs (85). Although findings are mixed, nurse-led survivorship interventions may reduce cancer symptoms and emotional distress and improve health-related QoL (HRQoL) and self-care (81,86).

2.1.2. NURSE-LED INTERVENTIONS IN HEMATOLOGY

Although a comprehensive knowledge base on nurse-led survivorship interventions exists, few studies have been conducted in hematological settings. Taylor et al. (2019) conducted a pragmatic randomized controlled trial, assigning survivors of lymphoma to either usual care or a nurse-led lymphoma survivorship clinic (87). These authors found that the survivorship clinic group reported fewer unmet needs, less distress, and an increase in empowerment compared with the control group,

although the differences were not statistically significant (87). In a pilot study, Overend et al. (2008) tested a nurse-led telephone intervention in survivors of hematological cancer with indolent and chronic malignancies and found that nurse-led telephone consultations were safe and efficient and associated with a high level of patient satisfaction (88). Compaci et al. (2015) tested a model for an early trajectory survivorship follow-up of patients with lymphoma. Their findings suggested that alternating general practitioner visits and nurse-led telephone consultations was an efficient and patient-accepted alternative to standard follow-up (89). Finally, John et al. (2013) tested the feasibility of a nurse-led survivorship intervention for patients with lymphoma who were 3 years post-treatment and in complete remission. As an alternative to the usual in-hospital visits with physicians, the participants were offered 30-minute in-hospital visits with a nurse (79). These authors found that the patients were as satisfied or more satisfied with the nurse-led clinic than with usual care (79). Thus, nurse-led survivorship care may be feasible and well-accepted among patients with hematological cancer, and this alternative survivorship care model may meet patient needs and increase patient empowerment to a higher degree. However, two of the four studies were designed as in-hospital consultations, resulting in additional workload for nurses and additional scheduled in-hospital visits, which may not fit well with today's increasingly busy outpatient clinics. John et al. (2013) raised this point, noting that the intervention placed a significant strain on nurse workload and acknowledging that this model may not be feasible because of the growing number of outpatients (79). Furthermore, all four studies were based on interviews performed by the nurse with the aim of eliciting information about the patient's health state (79,87–89). However, the present health issues might be more efficiently approached if both patient and nurse were prepared before the consultation, and preparation might increase the efficiency of the use of the time while further enhancing the quality of the consultations. Research shows that use of patient self-report about self-perceived health status in terms of QoL, functioning, and symptoms —in other words patient-reported outcome measures (PROs) — can be beneficial when applied as a screening and dialogue tool in clinical practice (90). Thus, PROs may be valuable as a tool in the follow-up of patients with hematological cancer and may contribute to a more efficient and targeted consultation.

2.2. QUALITY OF LIFE

QoL is an important parameter in understanding the impact of cancer treatment and is increasingly used as clinical outcome in cancer trials (91). Using QoL as a clinical

outcome has come into focus during the last decades as healthcare systems and healthcare professionals increasingly have become aware of the importance of adding the patient perspective to clinical research (92,93). QoL is ill defined, and a uniform definition may be elusive because it means different things to different people (94). In the literature, there is a distinction between QoL and HRQoL. HRQoL has been defined as a patient's self-perceived health status and is argued to relate to the way health affects the overall QoL (95). Osoba et al. provided this often-used definition of HRQoL, writing that it " *… is a multidimensional construct encompassing perceptions of both positive and negative aspects of dimensions such as physical, emotional, social, and cognitive functions, as well as the negative aspects of somatic discomfort and other symptoms produced by a disease or its treatment"* (96).

Based on that argument and definition, I propose in this thesis that the role of HRQoL in the context of the primary aim of health professionals is to alleviate symptoms and care for patients in response to how the disease affects QoL and ultimately the patient's life (97).

2.2.1. HRQOL IN PATIENTS WITH HEMATOLOGICAL CANCER

Patients with hematological cancer experience impaired HRQoL during the disease trajectory (19,20). Numerous clinical studies have reported on HRQoL in patients with hematological cancer as a secondary or even tertiary endpoint with the aim of determining how drugs affect HRQoL (98–102). However, longitudinal observational and cross-sectional studies assessing HRQoL independent of treatment have established that patients with hematological cancer experience an overall negative effect on HRQoL at all disease stages (19,20,36,38,39,103,104). The physical dimensions of HRQoL are affected in terms of symptoms such as pain, fatigue, nausea, vomiting, insomnia (37,105), difficulties with concentration, and sleep disturbance (19,36), as well as in terms of reduced daily physical activity (106). Hematological disease also has been reported to negatively affect psychological dimensions (36,37,107) as well as role and social functioning in terms of relations and impaired functioning in daily activities (37).

Patients with recurrent hematological disease seem to be more likely to experience impaired HRQoL compared to those with a recent diagnosis of primary disease (103–105). When these patients relapse, their situation worsens because potential treatment resistance poses a risk of overtreatment (108). This complex health challenge is being addressed as researchers seek to target treatment according to a

patient's genomic profile, known as precision medicine (109). Despite great progress in precision medicine, relapse continuously poses a challenge in clinical decision making, and physicians often cannot ensure a treatment effect, improvement, or stabilization in HRQoL. Thus, identification of patients who deteriorate as a result of relapse treatment would offer health professionals an evidence base for treatment decisions and patient guidance. However, the literature on HRQoL in patients with relapsing hematological disease is limited, so that evidence-based clinical decision making is challenging in terms of guiding patients toward the best treatment solution. Studies of HRQoL in patients with hematological relapse are either clinical studies, with highly selected study populations, making the results difficult to apply to population-based clinical practice (110–112), or are predominantly part of a combined investigation into HRQoL in patients in different hematologic disease states (103,104,113). Given these gaps, knowledge about HRQoL during relapse treatment is important for informing clinical decision making and optimizing treatment and care for patients experiencing relapse.

2.3. PATIENT-REPORTED OUTCOMES

In recent decades, PROs have been increasingly used in clinical practice and research because they have proven valuable in terms of introducing the patient perspective into healthcare (114,115). PRO is defined as a measurement based on *"any report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else"* (116). Thus, PROs represent the patient perspective on personal health status without outside interpretation and have been used extensively to elicit these perspectives (20,30,39). Although in clinical practice, PROs have the potential to enhance patient-centered care (PCC), their implementation needs to be carefully considered (114). A review of the options and considerations regarding this implementation noted that implementing routine PRO assessment involves a number of methodological and practical decisions such as identifying the goals for collecting PROs and determining relevant PRO measures (90,117).

2.3.1. PRO IN NURSE-LED CONSULTATION

PROs have been used as a screening tool during treatment and follow-up of cancer patients (118,119). Studies show that PROs have the potential to improve patient–clinician communication and to contribute to better symptom management

(117,120,121). Introducing PROs into survivorship care of patients with hematological cancer as a dialogue tool in combination with nurse-led interventions could be assumed to enhance quality of care. Furthermore, nurse-led survivorship interventions in combination with PROs could address the supportive care needs of patients in terms of psychological and informational needs, which are often not fully supported (21).

2.3.2. PRO TO MEASURE HRQOL OVER TIME

HRQoL is an important parameter in understanding the impact of cancer treatment, and assessment of HRQoL in patients with cancer is now conceptually viewed as an important complement to traditional objective evaluation measures such as survival and time to remission (122). Furthermore, identifying patients who are at risk of experiencing HRQoL deterioration during treatment may assist healthcare professionals in individualizing and targeting treatment and supportive care (123). Thus, applying PROs to measure HRQoL in patients with hematological disease may provide clinicians with the patient perspective of self-perceived health state, offering clinicians an important and central tool for providing patient–centered treatment and care (124).

2.4. PATIENT-CENTERED CARE

In recent decades, PCC has been a focus in western healthcare systems because of evidence that it can improve quality of care, patient outcomes, and cost effectiveness (125–127). PCC can be defined as: "*a partnership among practitioners, patients, and their families (when appropriate) to ensure that decisions respect patient's wants, needs, and preferences and that patients have the education and support they need to make decisions and participate in their own care*" (125,128).
As such, PCC is an approach to offering high-quality healthcare by inviting the patient to be an active partner in decision making about their health in ways that are consistent with the patient's needs and preferences (129,130).

In the context of this PhD thesis, providing PCC may help support patients with hematological cancer who have unmet supportive care needs and to target survivorship care towards the patient's individual needs. Additionally, measuring HRQoL at the group level using PROs may be considered within the frame of PCC as eliciting a patient's self-perceived health status to inform clinical practice. This

information may assist in providing better symptom management as well as in supporting patients managing functional problems. Thus, with the main objective of collecting information about patients' self-perceived health state, PROs may be considered a tool to facilitate PCC in patients with hematological disease.
In the literature, person-centered care and PCC are used seemingly interchangeably, and there are similarities; however, the term "person-centered care" is broader because the aim is to facilitate a meaningful life, whereas the aim for PCC is to reach a functional life (131). In this context, PCC is used here because the research encompasses patients with cancer who are linked to the health system by ongoing treatment and care.

2.5. RATIONALE FOR FURTHER RESEARCH

In summary, patients with hematological cancer report unmet supportive care needs and impaired HRQoL throughout the disease trajectory (20–23,30,106). These challenges pose a complex health problem for patients as well as health systems. Patients with hematological cancer are in a vulnerable and life-threatening position, and although health professionals work hard to treat and care for this patient group, research demonstrates that health professionals to some extent are unsuccessful in terms of meeting patient needs and ensuring patient HRQoL (21).

Research has established that nurse-led cancer survivorship interventions are feasible in terms of addressing the supportive care needs of patients, and these interventions are well-accepted by patients (80,81). Implementing PROs in clinical practice, i.e., as part of outpatient follow-up, has proved successful in facilitating targeted healthcare and promoting patient involvement (90,132). Thus, nurse-led interventions and PROs independently contribute to PCC by targeting unmet needs and involving patients in their treatment and care during the disease trajectory. However, it is not known whether the quality of cancer survivorship care to patients treated for hematological cancer could be improved by combining the two elements through nurse-led telephone consultations based on pre-collected PROs. This approach might have the potential to further target care and increase patient involvement. Assessing this potential requires the development and testing of interventions that address individual patient needs, as well as insight into the experiences of patients who participate in such interventions. Learning about their experiences may provide a deeper understanding of the aspects that are most

important to them, facilitating further development of interventions based on their experiences.

It is pivotal to address supportive care needs during survivorship because unmet need can lead to impaired QoL. Patients with hematological cancer experience impaired HRQoL throughout the disease trajectory, and those who experience relapse report worse HRQoL than newly diagnosed patients or cancer survivors (19). Because of the risk of treatment resistance resulting in overtreatment, the relapse situation is challenging in terms of clinical decision making and patient guidance. Moreover, physicians often cannot ensure stabilization or improvement in HRQoL during relapse treatment. Identifying patients who may deteriorate as a result of relapse treatment would be valuable in tackling this dilemma, informing shared decision making to facilitate PCC. Conclusively, there is a dearth in the literature regarding nurse-led survivorship interventions with survivors of hematological cancer and HRQoL research in patients with relapsed or progressive disease. Thus, this research is important and highly needed as patients with hematological cancer face a variety of challenges along the disease trajectory.

CHAPTER 3. THE OVERALL AND SPECIFIC AIMS FOR THIS PHD THESIS

The overall aim of this PhD thesis was to examine the potential of PROs among patients with hematological cancer along the disease trajectory and to determine if PROs could facilitate patient-centered care and contribute to increased quality of care in this population.

3.1. SPECIFIC AIMS

The PhD thesis consists of three studies that aimed to:

- investigated the feasibility of a shared care follow-up initiative based on alternating standard physician visits and nurse-led telephone consultations supported by PRO in patients with B-cell neoplasms. (Study I)
- to explore hematological cancer survivors' experiences of participating in a shared care follow-up based on alternating physician visits and nurse-led telephone consultations. (Study II)
- to identify patients who experienced deterioration in HRQL after relapse treatment and to investigate HRQL patterns in a cohort of hematological cancer patients with relapse or progressive disease. (Study III)

CHAPTER 4. RESEARCH DESIGN AND METHODS

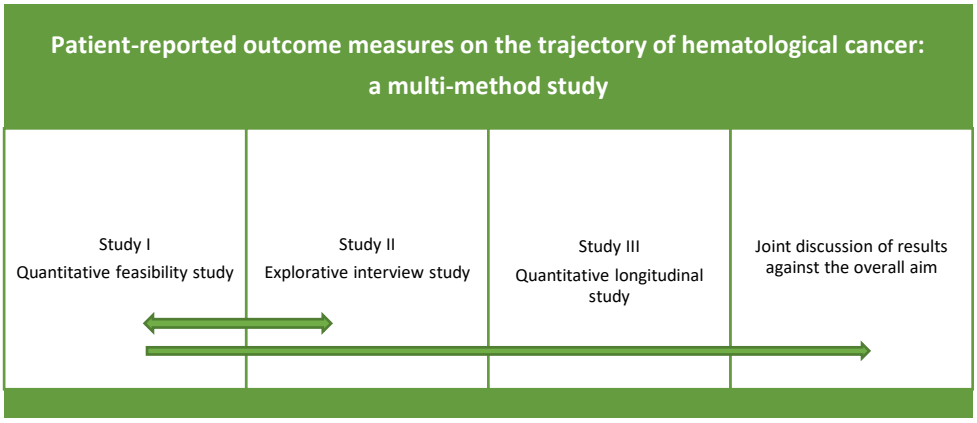
This chapter includes a description of the overall research design of the PhD thesis as well as a description of methods presented in paper I, II and III (133–135).

4.1. MULTI-METHOD RESEARCH DESIGN

The overall research design of this PhD thesis is a multi-method design including three studies. Multi-method design is a research approach in which both quantitative and qualitative methods are used to answer the study questions (136,137). In this PhD thesis, multi-method research design was chosen because both quantitative and qualitative methodologies and data sources were needed to sufficiently investigate the potential of PROs during the hematological disease trajectory (136). The assumption was that this approach would generate a deeper understanding of the studied topic in terms of addressing the complex health situation in which patients with hematological cancer find themselves during treatment and survivorship. In addition, findings from each method were assumed to complement each other and strengthen the research to answer the overall aim.
The three studies and their interconnection are displayed in Figure 2. As indicated by the double arrow, Figure 2 shows how Study I and Study II are interconnected, investigating a shared care follow-up initiative by examining the feasibility and exploring patient experiences, thus eliciting knowledge from two perspectives using two research methods. The single arrow illustrates that the results from each study and their interconnection will be addressed in a joint discussion, comparing and contrasting the results with each other and in the context of existing research.

A multi-method approach offers advantages in terms of the potential to accentuate distinctive aspects of the studied field as well as eliciting a deeper understanding through use of quantitative and qualitative data sources (136,137). However, limitations of this research design also have been accentuated because applying both methods is time consuming and requires the researcher to have a certain level of expertise in both methods to generate robust results and findings (137).

Figure 2: Overview of the three studies and their interconnection in the framework of a multi-method research design



4.2. SETTING

All three studies were conducted at the Department of Hematology, Aalborg University Hospital, Denmark.

4.3. STUDY I

The description of Study I is based on the paper entitled, *"Shared care follow-up of patients with B-cell neoplasms based on nurse-led telephone consultations and PRO-Data: A feasibility study from the North Denmark Region"* (133).

4.3.1. DESIGN

Study I was a feasibility study with the aim to investigate the feasibility of a shared care follow-up initiative based on alternating standard physician visits and nurse-led telephone consultations supported by PRO in patients with B-cell neoplasms.

4.3.2. STUDY POPULATION AND RECRUITMENT

Patients receiving ongoing post-treatment follow-up after B-cell treatment were eligible for inclusion. The inclusion criteria were "(a) ≥18 years; (b) diagnosed with B-cell neoplasms (chronic lymphocytic leukemia and lymphomas); (c) disease in remission or stable without treatment initiatives for at least six months prior to inclusion; and (d) sufficient self-care to report new symptoms and willingness to return PRO measures on a regular basis". Exclusion criteria were a) conditions requiring close medical attention; b) conditions which compromised the comprehension of the study aim (e.g. dementia); and c) inability to complete questionnaires online (133). The patients were recruited during in-hospital routine follow-up visits with the attending physicians specialized in hematology and in B-cell disease particularly. The sample size was reached using a convienice sampling strategy including as many patients as possible during the recruitment period (133,138).

4.3.3. FOLLOW-UP STRUCTURE

The patients were assigned to alternating standard routine follow-up with their attending physician at the hematological outpatient clinic and nurse-led telephone consultations. The nurse-led telephone consultations were scheduled ad hoc replacing every second physician visit. Prior to all consultations, blood samples were taken and approved by the attending physician. The interval for the follow-up was individualized depending on diagnosis, time since treatment, disease-related risk

factors, and individual assessments made by each patient's responsible physician (133).

4.3.4. DATA COLLECTION

4.3.4.1 Data collection instruments

PRO data were collected using the European Organization for Research and Treatment of Cancer EORTC-QLQ-C30 (EORTC-QLQ-C30) (139), Myeloproliferative Neoplasm – Symptom Assessment Form (MPN-SAF) (140), Hospital Anxiety and Depression Scale (HADS) (141). The PRO measures are presented in Table 1.

Table 1: Description of patient-reported outcome measures used in a shared care follow-up initiative in patients with B-cell cancer (133)

Measure		Description
European Organization for Research and Treatment of Cancer - EORTC QLQ-C30 (139)	Health-related quality of life	30-item cancer-specific questionnaire consisting of 15 domains • one global quality of life (QoL) scale • five functional domains (physical, role, emotional, cognitive, and social functioning) • nine symptom domains (fatigue, nausea and vomiting, pain, dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties)
Hospital Anxiety and Depression Scale – HADS (141)	Anxiety and depression	14-item anxiety and depression questionnaire consisting of 2 scales • Anxiety (HADS-A) • Depression (HADS-D)
Myeloproliferative Neoplasm – Symptom Assessment Form MPN-SAF (140)	Symptoms	17-item symptom scale developed to measure symptom burden in patients with MPN constructed from • MPN • BFI • TSS ("worst fatigue" from the BFI plus nine items from the MPN-SAF – concentration, early satiety, inactivity, night sweats, itching, bone pain, abdominal discomfort, weight loss, and fever)

The MPN-SAF was chosen because no lymphoma-specific PRO measure was available in Danish at the time the study began. Four ad hoc questions were developed in collaboration with consultants specialized in B-cell cancer to cover lymphoma-specific symptoms (133). The ad hoc questions are presented in Table 2.

Table 2: Ad hoc questions added to the MPN-SAF to cover B-cell neoplasm–specific symptoms associated with recurrent disease (133)

Have you since last consultation:		
Noticed swollen lymph nodes?	Yes:	No:
Had infections that demanded antibiotic treatment?	Yes:	No:
Experienced the same symptoms as last time you were ill from your blood disease?	0 (No) 1 2 3 4 5 6 7 8 9 10 (Yes)	
Do you feel ill from your blood disease?	0 (No) 1 2 3 4 5 6 7 8 9 10 (Yes)	

The survey of the patients willingness to and perception of completing PRO measures as part of follow up was conducted using the Patient Feedback Form (PFF) (142,143).

4.3.4.2 Data collection procedure

The patients responded to electronic PRO measures prompted by email invitations sent 7 days before scheduled consultations, with a request to complete them 3 days before the appointment. The PRO data were collected through an online IT platform hosted by Dansk Telemedicin A/S.
The nurse-led telephone consultations were based on analysis of the collected PRO data. Prior to any consultation, the nurse analyzed the PRO data using the calculated scores as well as an assessment of any changes in scores between consultations (144–146). If needed, an in-hospital nurse consultation was arranged, or alternatively, the patient was offered a visit with the physician (133).

A cross-sectional survey of patient acceptability with completing PRO measures as part of the follow-up was conducted in between November 2018 and March 2019, inviting all included patients. Data was collected using RedCap, which is a secure web platform for building and administering surveys (147). The survey was conducted anonymously to prevent potential response bias (133,148).

4.3.5. STATISTICAL ANALYSIS

Descriptive statistics were used to assess the feasibility, calculating recruitment rate, response rate, dropout rate, and patient acceptability with completing PRO measures as part of clinical practice. (133).

4.3.6. ETHICS

Participation was voluntary, and the patients gave oral and written consent prior to inclusion. The study was approved by the national Data Protection Agency (jour. no. 2008-58-0028). According to Danish law, the study was exempt from formal ethical approval (133).

4.4. STUDY II

The description of Study II is based on the paper entitled, *"Hematological cancer survivors' experiences of participating in a shared care follow-up – an exploratory interview study* (134).

4.4.1. DESIGN

Study II was a qualitative interview study with the aim to explore hematological cancer survivors' experiences of participating in a shared care follow-up based on alternating physician visits and nurse-led telephone consultations.

4.4.2. STUDY POPULATION AND RECRUITMENT

Eligible participants for Study II had participated in the feasibility study. In total, 12 patients were included, and the study population was sampled based on the concept of purposeful sampling to ensure maximum variation (149). Maximum variation was chosen "*to capture a wide range of perspectives and elicit common patterns across the patient experience"* (134). Sampling was based on patient characteristics such as age, sex and diagnosis. Furthermore, the participating patients had undergone at least two nurse-led telephone consultations, meeting a certain level of experience with the shared care follow-up. The patients were recruited by telephone, and written information and consent forms were forwarded by email or postal service (134).

4.4.3. DATA COLLECTION

Data were collected through one-on-one interviews based on a semi-structured interview guide (150). This guide was chosen to elicit the patient experience and allow for a dynamic yet systematic approach to the interviews (134,150).

4.4.3.1 Data collection instrument

The semi-structured interview guide was developed based on the seven phases of an interview study, as presented by Kvale and Brinkmann (151). The interview guide covered the research topics in question, such as experience of the shift from regular follow-up to shared care follow-up, completing PRO measures as part of follow-up, and the patients' perception of talking to a nurse as part of follow-up (134).

4.4.3.2 Data collection procedure

The interviews were conducted face-to-face at the patients' homes and at Aalborg University Hospital research facilities. The interviews lasted 45–90 minutes, were recorded on a mini-recorder, and were subsequently transcribed. It was estimated that interviewing 12 patients would be sufficient to meet the point of data saturation, defined as the point at which further data collection would not lead to further new knowledge (134,152). The interview guide is presented in Appendix E.

4.4.4. DATA ANALYSIS

Thematic analysis was used to analyze the data (153). Initially, the transcribed data were openly coded using descriptive coding to elicit common codes throughout the dataset. Next, the data were re-coded with the intention of identifying categories and themes across the dataset (154). The reliability of the analysis process was established through repeated dialouge among the authors. The data set would be re-consulted in case of divergence and until general agreement was reached (134,154). Furthermore, validity was pursued by presenting positive as well as discrepant data derived from the data material (155). The analysis was aided by NVivo qualitative analysis software (156).

4.4.5. ETHICS

Prior to the interviews, the patients signed a written consent form. During data analysis and reporting of findings, the patients were identified and thereby anonymized by project identification numbers to secure potential identification of the patients. The study was approved by the Danish Data Protection Agency (jour. no. 2008-58-0028). Approval from the National Ethics Committee was not required according to Danish legislation (134).

4.5. STUDY III

The description of Study III is based on the paper entitled, *"The use of patient-reported outcomes in precision medicine and hematological patients with relapse or progressive disease: a longitudinal observational study"* (135).

4.5.1. DESIGN

The study was a longitudinal, observational population-based study with the to identify patients who experienced deterioration in HRQL after relapse treatment and to investigate HRQL patterns in a cohort of hematological cancer patients with relapse or progressive disease.

The study was a sub-study of a prospective, non-interventional population-based clinical study with the aim "*to describe genetic alterations in tumors from hematologic relapse patients and hence explore the potential of precision medicine*" (ProGen/ProSeq) (108,109,135). The clinical study has been ongoing at the Department of Hematology, Aalborg University Hospital, since 2016.

4.5.2. STUDY POPULATION AND RECRUITMENT

Eligible patients were recruited by study nurses connected to ProGen/ProSeq. The details of recruitment and workflow have been reported in detail by Bødker et al. (2020) (108). The study population consisted of patients age ≥18 years with hematological cancer and with pathologically verified relapsed or progressive disease. Patients were excluded in case of non-response to the baseline questionnaire and subsequent relapse during the study period.

4.5.3. DATA COLLECTION

The data collection was carried out using PRO measures and extraction of clinical data from electronic health records.

4.5.3.1 PRO measures

The PRO data were collected using the EORTC-QLQ-C30 and HADS (141,157). These PRO measures were described in detail in Section 4.3.4.1.

4.5.3.2 Data collection procedure

The time points for PRO data collection were set to baseline and 3, 6, 9, and 12 months, respectively, and baseline was defined as the point of verification of diagnosis of relapsed or progressive disease. The PRO measures could be completed either online or in hard copy. Online PRO measures were administered via REDCap survey tool (147) and links to the online PRO measures were sent via email. In case of non-response to the PRO measures, a reminder was sent after 7 days and subsequently after 14 days in case of continuous non-response. If the patients chose to complete the PRO measures in hard copy, they would receive the PRO measures by post including a pre-stamped return. No reminders were sent because postal delivery time taken into account would affect the real-time data collection (135).

4.5.4. ANALYSIS

Descriptive statistics were used to describe patient characteristics, response, and dropout rates. Patients were categorized based on treatment strategy: curative-intent treatment (CIT) and non-CIT. HRQoL domain scores were scored according to developers' guidelines (144,146), and missing data in EORTC-QLQ C30, were managed according to developers' guidelines (144), and for HADS, guidelines by Bell et al. (2016) were applied because no guidelines are available from the developers (135,158).

The PRO data were analyzed on the patient level to identify the proportion of patients reporting moderate and severe symptoms or functional problems at baseline and at 12 months of follow-up. The thresholds for severe and moderate symptoms and functional problems in the EORTC-QLQ-C30 were based on thresholds

defined in existing research in patients with hematological cancers (37,39). For HADS, presence of anxiety or depression was based on the thresholds presented by the developers (146). A responder analysis was carried out to identify the number of patients experiencing either improvement or deterioration in HRQoL domains assessing each patient's individual score change from baseline to 12 months of follow-up (159). Finally, Fischer's Exact test was used to test potential correlations between baseline characteristics and deterioration in HRQoL domains (135) .

At the group level, the baseline mean scores for EORTC-QLQ-C30 and HADS (160) were calculated, and the difference from baseline to 12 months for each HRQoL domains was calculated, fitting the HRQoL scores as linear mixed models (161). Finally, clinically relevant differences from baseline to the 12-month follow-up, were calculated using Cocks' guidelines for interpreting change in scores for the EORTC-QLQ-C30 were (162), and the threshold for clinically meaningful change in HADS was based on distribution-based minimum important differences of standard errors of measurement (163). The significance level was set to 95%. The statistical analyses of the PRO data were carried out in R (135,164).

4.5.5. ETHICS

The patients signed a consent form before entering the study. The study was approved by the Danish Data Protection Agency (Jour. No. 2008-58-0028) as well as the Ethical Committee of North Denmark (N-20150042) (135).

CHAPTER 5. RESULTS

The results are presented in relation to each study, and the study aim is presented to optimize readability. For further elaboration on the results, please consult Paper I, Paper II, and Paper III (133–135).

5.1. STUDY I

Aim: to investigate the feasibility of a shared care follow-up initiative based on alternating standard physician visits and nurse-led telephone consultations supported by PRO in patients with B-cell neoplasms.

Results (133)**:** Between February 2017 and June 2018, we included 80 patients with B-cell disease. The inclusion process is illustrated in Figure 3. The baseline characteristics of the patient population including age, diagnosis, time since treatment, and number of nurse-led telephone consultations are presented in Table 3.

Figure 3: Flowchart illustrating the inclusion process and number of excluded patients, grouped by reasons for exclusion (133)

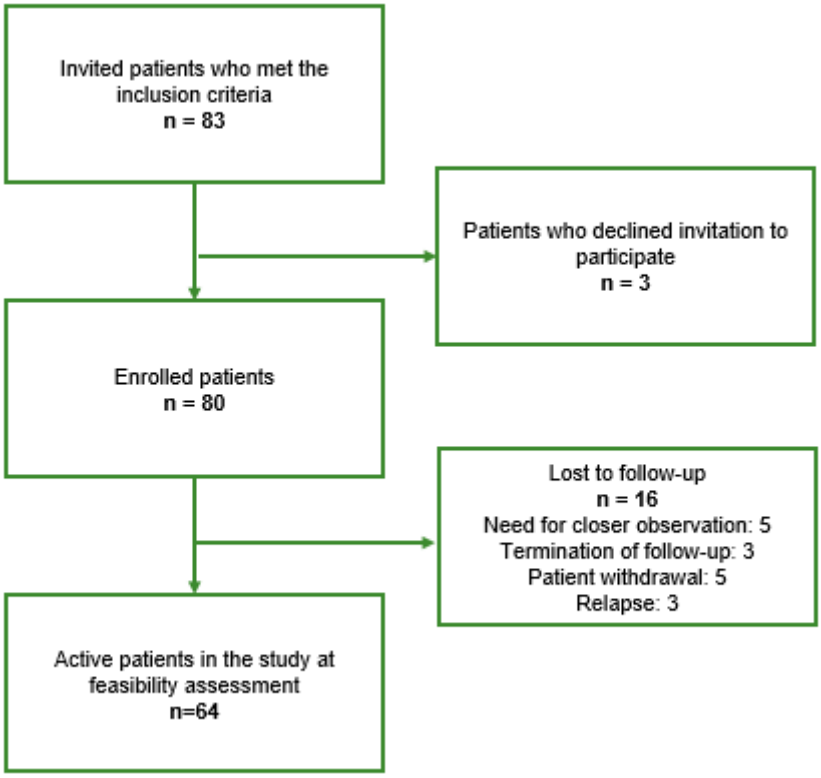


Table 3: Baseline demographic, treatment, and follow-up characteristics of patients with B-cell neoplasms and assessed as being in remission or stable without treatment initiatives 6 months prior to inclusion (n=80) (133)

	Curative lymphoma¶	Chronic lymphocytic leukemia§	Indolent lymphoma¥	Total
N	15	17	48	80
Female	8	3	27	38
Male	7	14	21	42
Age, median	70.0	69.0	68.0	68.0
Age, range	37.0–82.0	58.0–78.0	28.0–81.0	28.0–82.0
Number of visits at physician, median (range)	2.0 (0.0–4.0)	1.0 (0.0–2.0)	2.0 (0.0–4.0)	2.0 (0.0–4.0)
Number of nurse consultations, median (range)	2.0 (0.0–4.0)	1.5 (1.0–2.0)	2.5 (1.0–4.0)	2.0 (0.0–4.0)
Time since diagnosis median/y (range/y)	3.6 (2.0–16.6)	4.4 (2.0–20.2)	4.7 (1.1–16.8)	4.4 (1.1–20.2)
Time since last treatment (median/y)	3.2 (1.9–9.4)	3.6 (1.7–9.3)	4.0 (1.3–16.3)	3.4 (1.3–16.3)
Follow-up interval				
2-3 months	9.0	7.0	18.0	34.0
4-5 months	4.0	3.0	18.0	25.0
6 months	2.0	7.0	12.0	21.0
Number of treatment lines				
1	13.0	5.0	30.0	48.0
2	1.0	1.0	2.0	4.0
>2	0.0	0.0	4.0	4.0
No previous treatment (watch and wait)	0.0	10.0	12.0	22.0

¶Curative lymphoma: *diffuse large B-cell lymphoma; Hodgkin lymphoma;* ***§Chronic lymphocytic leukemia****);* ***¥Indolent lymphoma****: follicular lymphoma, lymphoblastic lymphoma, mantle cell lymphoma, marginal cell lymphoma, Waldenstrom macroglobulinemia*

5.1.1. PATIENT ADHERENCE

In total, 5 (5/80 [14.7%]) patients chose to leave the study, citing the following reasons: number of questions asked (n=1), impaired eyesight leading to difficulties reading PRO measures (n=1), and preference of regular hospital follow-up (n=3) (133). Furthermore, eight patients (8/80 [10%]) left the study because of relapse (n=3), mental health issues (n=1), infections unrelated to the hematological cancer (n=2), suspicion of relapsed disease (n=1), and terminal secondary cancer (n=1) (133).

5.1.2. NURSE-LED TELEPHONE CONSULTATIONS

In total, 129 nurse-led telephone consultations were carried out. Proportions of conducted consultations were distributed as follows (133):

- 46 patients (46/80 [57.5%]) received ≥1 nurse-led telephone consultation without additional intervention;
- 34 patients (34/80 [42.5%]) were discussed with the physician because of questions raised based by blood count or PRO measures;
- 5 (5/80 [14.7%]) patients were booked for an extra visit with their attending physician;
- No patients were booked to a nurse visit at the outpatient clinic; and
- 124 (124/129 [96.1%]) nurse-led telephone consultations took place, substituting for the same number of regular in-hospital visits

5.1.3. PATIENT ACCEPTABILITY SURVEY

In total, 59 (59/79 [75%] patients completed the Patient Feedback Form (one patient died before study start, so n=79). The survey study demonstrated that completing PRO measures as part of follow-up led to the following (133):

- It was easier for the patients to remember symptoms and side effects when speaking to healthcare professionals (50/57 [88%]);
- The communication with the healthcare professional improved as a result of completing PRO measures (51/57 [90%]); and
- The patients felt involved in their treatment (48/56 [86%]).

The proportions are based on the sum of the responses of “strongly agree” and “agree” in the patient feedback survey.

5.2. STUDY II

Aim: to explore hematological cancer survivors' experiences of participating in a shared care follow-up based on alternating physician visits and nurse-led telephone consultations.

Findings (134)**:** In total, 12 patients were recruited and interviewed. Patient characteristics are presented in Table 4 (134).

Table 4: Characteristics of patients with hematological malignancies included in the interview study of their experience with participation in a shared care follow-up based on alternating physician visits and nurse-led telephone consultations (134)

Characteristic	**N (%)**
Sex	
Male	6 (50)
Female	6 (50)
Age	
Median (range) 64 (53-79)	
Diagnosis	
DLBCL ŧ	2 (17)
FL ǂ	5 (42)
CLL §	1 (8)
MZL ¶	4 (33)
Treatment	
Chemotherapy	9 (75)
WAW ŧ	3 (25)
Marital status	
Living alone	4 (33.5)
Married/co-habiting	7 (58)
Married/co-habiting, with children	1 (8.5)
Job situation	
Employed	6 (50)
Unemployed/retired	6 (50)

ŧDLBCL – diffuse large B-cell lymphoma; ǂFL – follicular lymphoma; §CLL – chronic lymphocytic leukemia; ¶ MZL – marginal zone lymphoma; ŧWAW – watch and wait

5.2.1. THEMES AND KEY FINDINGS

The thematic analysis yielded in five themes: "*fewer visits to the hospital"*, *"feeling secure"*, *"the value of completing PRO measures"*," *nurse consultations"*, and *"using the telephone"* (134). The themes and findings are presented in Table 5.

Table 5: Themes and findings from the qualitative interview study with the aim of eliciting patient experiences of participating in a shared care follow-up program (SCFU) (134)

Themes	Findings
Fewer visits to the hospital	SCFU seemed to: • Offer convenience, • Entail less travel and less preparation, and • Lead to fewer encounters with other patients with cancer and this less experience of anxiety. For a minority of the patients, SCFU: • Did not lead to any a major change in their lives.
Feeling secure	SCFU seemed to uphold a sense of security because: • Patients saved time without compromising the feeling of security, • They always had the possibility of contacting the clinic or booking an extra visit, and • It was believed that the nurse would contact the physician if anything needed further investigation.
The value of completing PRO measures	Completing PRO measures as part of SCFU seemed to: • Increase the patients' focus on their health in new ways and • Facilitate tracking symptoms before they became too serious. For a minority of the patients, the PRO measures: • Were irrelevant to their situation and • Made it difficult to get the message across.
Nurse consultation	Introducing nurses into follow-up seemed to elicit: • An experience of being able to set the agenda and a feeling of being heard and taken care of, • A sense of more time, and • A space where patients would talk to the nurse about issues that they would not necessarily discuss with a physician. A minority of the patients stated that the switch in profession: • Made no difference.
Using the telephone	Introducing telephone consultations seemed to • Elicit discussions of a more sensitive nature than face-to-face meetings and • Create a personal space for discussion of health-related concerns.

In summary, for most patients, a shared care follow-up program seemed to contribute to easing their everyday lives in terms of alleviating practical, disease-related, and emotional concerns connected with hospital visits, whereas for others, the initiative led to no significant changes in their lives. Patient accounts suggest that their feeling of security was not compromised by participating in the shared care follow-up initative, but the possibility of extra consultations was important to the patients. As a part of intitiative , the patients were asked to complete a PRO measures and it seemed that introducing PRO measures into follow-up contributed to increased self-monitoring of health status. However, some patients found the PRO measures to be irrelevant, which led to frustration. Another new element introduced in the shared care follow-up program was the nurse-led telephone consultation. Based on patient accounts, introducing nurses into follow-up seemed to facilitate an open dialogue and a shift from disease-related topics to topics of a more psychosocial nature. Furthermore, patients seemed more ready to discuss topics that they normally would not bring up with a physician. The patient narratives suggested that telephone consultation provided an undisturbed room for dialogue, where concerns of all kinds could be addressed (134).

5.3. STUDY III

Aim: to identify patients who experienced deterioration in HRQL after relapse treatment and to investigate HRQL patterns in a cohort of hematological cancer patients with relapse or progressive disease.

Results (135): In total, 178 patients were eligible for the study. Of the 178 eligible patients, 104/178 (58%) were sent baseline PRO measures. Reasons for ineligibility and number of non-responses at baseline are illustrated in Figure 4. Patient characteristics are presented in Table 6. (135). A response rate to baseline of 14/104 (13%) and a dropout rate during the study period of 40/90 (44%) were found (135).

Figure 4: Flowchart illustrating the inclusion process and number of non-responses to baseline and loss to follow-up at each timepoint (135)

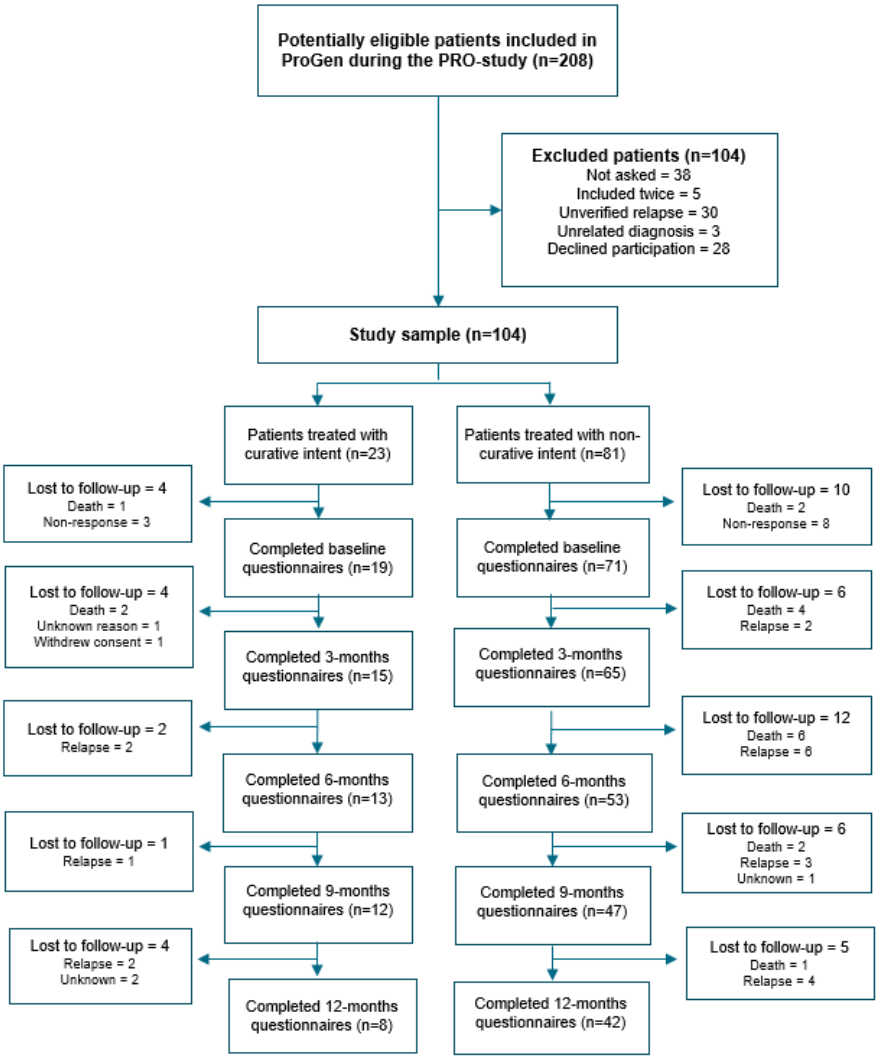


Table 6: Clinical and sociodemographic characteristics of patients with hematological cancer experiencing relapse (135)

Characteristics	Non-curative-intent treatment group, n (%)=71 (79)	Curative-intent treatment group, n (%)=19 (21)	Total n (%)=90 (100)
Sex			
Male	50 (70.4)	10 (52.6)	60 (66.7)
Female	21 (29.6)	9 (47.4)	30 (33.3)
Median age, years (range)	70.0 (34–93)	66.0 (44–88)	69.5 (34–93)
Age			
<50	1 (1.4)	2 (10.5)	3 (3.3)
50–59	8 (11.3)	3 (15.8)	11 (12.2)
60–69	23 (32.4)	8 (42.1)	31 (34.4)
>70	39 (46.5)	6 (31.6)	45 (43.3)
Diagnosis			
Aggressive lymphoma	11 (15.5)	13 (68.4)	24 (26.7)
Indolent lymphoma	22 (31.0)	2 (10.5)	24 (26.7)
Chronic leukemia	18 (25.4)	0 (0.0)	18 (20.0)
Acute leukemia	5 (7.0)	4 (21.1)	9 (10.0)
Multiple myeloma	15 (21.1)	0 (0.0)	15 (16.7)
Number of relapses			
1	38 (53.5)	17 (89.5)	55 (61.1)
2	16 (22.5)	2 (10.5)	18 (20.0)
≥3	15 (21.1)	0 (0.0)	15 (16.7)

¶Aggressive lymphomas include: Diffuse large B-cell lymphoma, Hodgkin lymphoma, Non-Hodgkin lymphoma, T-cell large granular lymphocytic leukemia, Angioimmunoblastic T-cell lymphoma. ǂ**Chronic leukemia include**: Chronic lymphocytic leukemia, Small lymphocytic leukemia, Chronic myeloid leukemia, Hairy cell leukemia. §**Indolent lymphomas include**: Follicular lymphoma, Maltoma, Mantle cell lymphoma, Nodal marginal zone lymphoma, Lymphoplasmacytic lymphoma, Waldenström's macroglubulinemia, Splenic marginal zone lymphoma, Peripheral T-Cell lymphoma **¥ Acute leukemia include**: Acute myeloid leukemia, Acute lymphoid leukemia, Myelodysplastic syndrome.

At baseline, the patients reported moderate and severe symptoms and functional problems in all HRQoL domains. The three most affected HRQoL domains were insomnia (moderate: 26 (29%); severe: 19 (21%); global health status (moderate: 41 (46%); severe: 19 (21%), and fatigue (moderate; 40 (44%); severe: 20 (22%)) (135). Furthermore, the patients reported both improvements and deterioration at the 12-month follow-up, with 16%–18% experiencing deterioration in fatigue, insomnia, diarrhea, and/or appetite loss as well as decreased role, emotional, and/or cognitive functioning (135). Rates of improvement and deterioration in HRQoL for the total cohort are presented in Table 7.

Table 7: Improvement or deterioration in health-related quality of life, anxiety, or depression from baseline to the 12-month follow-up for the total cohort (135)

Health-related quality of life domains	**Total (n=50)**	
	Deterioration, n (%)	Improvement, n (%)
EORTC-QLQ-C30		
Global health status	7 (14)	13 (27)
Physical functioning	5 (10)	8 (16)
Role functioning	8 (16)	14 (28)
Emotional functioning	8 (16)	8 (16)
Cognitive functioning	8 (16)	6 (12)
Social functioning	3 (6)	11 (22)
Fatigue	9 (18)	13 (26)
Nausea and vomiting	2 (4)	4 (8)
Pain	4 (8)	11 (22)
Dyspnea	5 (10)	7 (14)
Insomnia	9 (18)	12 (24)
Appetite loss	8 (16)	15 (30)
Constipation	6 (12)	5 (10)
Diarrhea	9 (18)	8 (16)
Financial difficulties	3 (6)	4 (8)
HADS		
Anxiety	5 (11)	1 (2)
Depression	1 (2)	1 (2)

N; number of patients, EORTC QLQ-C30; the European Organization for Research and Treatment of Cancer, HADS; the Hospital Anxiety and Depression Scale

When attempting to identify patient characteristics associated with deterioration in HRQoL at 12-months, a statistically significant correlation between impaired role functioning and estimated survival ≤2 years was found (OR 0.14, CI: 0.02; 0.95, p=0.04) (135).

Finally, clinically relevant changes from baseline to the 12-months follow-up were found in the CIT group for insomnia (medium improvement, p=0.001) and in the total cohort for global health status (small improvement, p=0.03) and nausea and vomiting (small improvement, p=0.03) (135).

CHAPTER 6. DISCUSSION

The overall aim of this PhD thesis was to examine the potential of PROs in patients with hematological cancer throughout the disease trajectory and to determine if PROs could help facilitate PCC and contribute to increased quality of care in these patients. Three studies were conducted to address the overall aim. The key results, findings, and methodological considerations are discussed below.

6.1. DISCUSSION OF RESULTS AND FINDINGS

In line with the multiple-method research design (Fig. 2), results from all three studies will be discussed in the context of the overall aim, each other, and existing research. The potential value of PROs in patients with hematological cancer will be discussed as well as strengths, limitations and challenges identified during the three studies to be considered when applying PROs in clinical practice.

6.1.1. PATIENT ACCEPTABILITY OF COMPLETING PROS

Overall, the results of Study I and Study II demonstrated that the initiative seemed feasible and that patient experience was mainly positive (133,134). The results of the patient acceptability survey in Study I demonstrated that most patients found it easy to understand the questions and found that it made sense to complete the PRO measures. These results are supported by the findings in Study II, in which most patients had positive experiences with completing the PRO measures. However, results of both studies also suggest that some patients found the PRO measures to be irrelevant to their situation, and in some cases, completing the PRO measures caused frustration because patients found it difficult to get their message across (133,134). This outcome indicates a need for careful consideration of the characteristics of the patient population when selecting or developing PRO measures to ensure that they are relevant and understandable to the selected patients. In fact, patients do have preferences about the content of PRO measures (114). In a randomized controlled trial comparing three PRO measures, researchers found that redundant questions and questions for which responses were unlikely to change over a short period of time were a nuisance to the patients. Furthermore, the patients emphasized that clear response options were important (114). These results are supported by the findings of Snyder et al. (2007) who investigated the importance of the content in selected PRO measures as rated by patients and clinicians (165). These authors found that patients pointed out questions related to

information about treatment and care coordination as important issues they need addressed. Interestingly, the clinicians considered questions related to pain and symptoms to be most important to patients, hence indicating divergent views on the most essential concerns to be addressed in the clinical practice (165). Also, Noonan et al. (2017) reported on factors that are important to consider when implementing PRO in clinical practice and pointed out that patient factors in terms of socioeconomic characteristics and perceived meaningfulness of PRO are essential elements to consider (166) supporting the fact that varying relevance of questions has been established as a barrier to the use of PROs in clinical practice (167). These findings support the argument that the patient perspective should be considered when developing PRO-based interventions. Thus, given the results from studies I and II and supported by existing research, patient interviews should be considered as a part of the process when choosing existing PRO measures for PRO interventions. Such interviews may guide the selection of PRO measures because an *a priori* qualitative inquiry into patient preferences and needs may assist in determining the topics and questions that the specific patient population finds important (166).

6.1.2. PROS AS A TOOL FOR SELF-REFLECTION ON HEALTH

PROs used in clinical practice can be valuable in terms of tracking changes in health status over time as well as generating increased self-focus on health status (117). Greenhalgh et al. (2018) found that as a result of completing PROs in clinical practice, patients would reflect on their health situation (117). These results are consistent with those of Study I, in which most patients reported that completing the PRO measures made it easier for them to recall symptoms and adverse events (133). Furthermore, their accounts in Study II indicate that patients used the PRO measures to track changes over time as well as using them as a screening tool for reflecting on their current health situation (134).

The patients' narratives in Study II suggested a shift in focus from disease-related to a more comprehensive approach to follow-up, highlighting that they would bring up concerns during nurse-led telephone consultations that they would not necessarily have raised during a physician consultation (134). These findings are in line with those of Greenhalgh et al., who reported that patients would raise emotional and HRQoL issues with their physicians but that the physicians viewed such factors as outside of their scope (117). Moreover, Pennery et al. (2000) found that many survivors of breast cancer felt uneasy raising questions especially of an emotional nature during consultations and that the majority of the patients would prefer breast cancer nurses to provide cancer survivorship care (168). Combined, these findings

are suggestive of the need for a multi-disciplinary approach to care for the whole patient in terms of addressing each patient's individual needs for support.

To date, studies have found that using PROs in clinical practice as a basis for consultations positively affects the care process in terms of patient satisfaction and as a tool for dialogue (90,117,169); however, little evidence exists on the impact of PROS on patient outcomes (170). In a systematic review of the evidence, researchers found PROs to be valuable as a screening and management tool but found little evidence that PROs improved patient outcomes (170). In the current work, results of studies I and II indicate that PROs seem to support the immediate care process in terms of better communication and detection of health problems (133,134). Further high-quality research on how PROs affect patient outcomes is still warranted.

6.1.3. PROS AS A TOOL OF IDENTIFYING HEALTH PROBLEMS

Study III was an investigation into HRQoL patterns in patients with relapsed or progressive hematological disease with the aim to identify those who experienced deterioration in HRQoL domains over time (135). Study III demonstrated that the patients reported moderate and severe symptoms and functional problems at baseline and that some patients experienced deterioration at 12 months of follow-up. The fact that these patients experience deterioration in HRQoL domains in the course of relapse treatment is a clear indication of a need for intervention. Research has shown that PROs are valuable in terms of monitoring HRQoL and adverse events during cancer treatment (121). Basch et al. (2016) found that regular monitoring of symptoms in a cohort of patients with advanced solid tumors receiving chemotherapy improved HRQoL compared to the non-intervention group (121). Furthermore, the intervention group was less likely to be admitted to the hospital and tolerated treatment longer than patients not completing PRO measures. Finally, the authors found that regular symptom monitoring was associated with an increase in overall survival compared to the non-intervention group (121,171). This study was conducted in a group of patients with metastatic cancer, which suggests that symptom monitoring during relapse treatment in patients with relapsed or progressive hematological cancer may well be assumed to yield similar positive outcomes. Although based on a small number of patients, Study III highlights the complexity of relapse, as we could not identify obvious factors that might indicate patients who would experience a deterioration in HRQoL during relapse treatment (135). However, by introducing PRO, we established that some patients did experience a deterioration in HRQoL during the year after relapse diagnosis. This

result suggests that routine PRO assessments during relapse treatment may play a role in decision making in terms of initiating earlier symptom management and supportive care interventions.

Routine collection of PROs has proven successful in improving communication between health professionals and patients (117,172), a benefit that Study I also established (133). The findings of Study II add to the evidence, with patient accounts suggesting that the informality of the nurse consultations motivated them to raise health concerns that they might not necessarily have brought up during a consultation with a physician (134), thus indicating improved communication. Efficient communication between health professionals and patients is an essential component of shared decision making and using PROs may allow patients to engage in decision making based on their account of HRQoL and symptoms, hence facilitating targeted and individualized patient care (166,173).

6.1.4. DOES "ONE-SIZE-FIT-ALL"?

Based on the results from all three studies, it is clear that using PROs in hematological cancer survivorship offers potential in terms of increased self-reflection on health, patient involvement, and identifying health problems (133–135). However, looking at the divergent positions among the patients in Study I and Study II in terms of perceived value and relevance of completing PROs, it is clear that a "one-size-fits-all" approach, understood as a fixed cancer survivorship care model applied to all patients, may not support every individual patient's needs. Personal resources, preferences, and stage on the hematological disease trajectory should be considered when assigning patients to follow-up (166). One way of addressing this issue could be to introduce routine assessment of individual needs and preferences before the patient enters survivorship care. A thorough assessment of patient preferences in terms of mode of follow-up and needs in terms of assistance would build a solid basis for patient-centered survivorship care (174).

Study I demonstrated the feasibility of a shared care follow-up initiative based on nurse-led telephone consultations and completion of PROs, which suggests that PRO-based follow-up may have potential for patients with hematological disease (133). PRO-based follow-up was introduced in Denmark by Ambuflex, which developed online platforms for several chronic diseases as well as breast, lung, and prostate cancers (132). The aim of Ambuflex is to use PRO for *"clinical decision support to improve quality of care, promote patient-centered care, optimize the use*

of resources in the healthcare system and use data for research purpose" (132). The Ambuflex solution uses algorithm-based decision making in terms of assessing a patient's need for hospital contact, and low HRQoL scores indicate no need for hospital contact. The implementation of the solution has led to a decrease in scheduled visits in busy outpatient clinics (132), a tendency that the results of Study I also suggested (133). Moreover, the findings from Study II indicate that fewer visits to the outpatient clinic contributed to various positive elements, such as convenience and fewer encounters with other patients with cancer (134). Acknowledging the value of fewer or even no visits have for most patients and for the healthcare system, it is, however, important to consider if this type of follow-up would benefit all patients.

The findings from Study II suggest that although the patients appreciated the convenience of fewer visits, some of them seemed to need physical visits and examination despite having no symptoms or other health-related problems (134). It is well-established that survivors of hematological cancer report unmet needs in terms of fear of recurrence and finding the transition into survivorship difficult (21,22). These needs raise the question of whether they would be addressed if cancer survivorship care was based solely on PROs without consultation with a health professional.

This PhD thesis indicates that PROs may have potential in survivors of hematological cancer in terms of creating self-focus on their health situation and detecting health problems. However, it also indicates that PROs may not work on their own in all cases but need support from health professionals and, in this situation, nurses. Brandenberg et al. (2017) explored cancer survivors needs for support during survivorship and found that they had a deep need for screening, possibly as a result of fear of recurrence (175). Furthermore, the authors found that the patients needed emotional support, in keeping with Marbach et al. (2011), who also found emotional support to be essential to cancer survivors (176). Thus, cancer survivors report supportive care needs that may not be addressed by substituting consultations with PRO assessments and that health professionals should address.

6.1.5. PATIENT-REPORTED OUTCOMES AND PATIENT-CENTERED CARE

Research has established that applying PROs in clinical practice may assist in providing PCC as a result of patient involvement and enhanced communication (117,166). Based on the findings of all three studies (133–135), PROs may have

potential in terms of improving the process of care in patients with hematological cancer, assisting in facilitating PCC within this patient group. PCC is defined as: *"a partnership among practitioners, patients, and their families (when appropriate) to ensure that decisions respect patient's wants, needs, and preferences and that patients have the education and support they need to make decisions and participate in their own care"* (125,128). Based on the findings of Jayadevappa and Chhatre (2011) and Hobbs (2009), this definition implies that delivery of high-quality care is based on the development of a relationship between the health professional / nurse and the patient, as well as on information pratices to ensure that each patient is cared for based on their specific needs and preferences (127,177). Thus, a central element in the provision of PCC is to ensure that healthcare is based on a patient's individual needs.

In recent years, nurse researchers, clinicians, leaders, and educators have developed the Fundamentals of Care framework (FoC) with the aim of addressing challenges within the nursing profession in the pursuit of person-centered and situation-oriented nursing care (178). Kitson et al. (2013) proposed that the nursing profession has lost sight of the fundamental needs of the patients as focus has shifted to a more task-driven provision of nursing care (179). Hence, FoC focuses on directing healthcare and nursing in particular toward patient needs and *"how nursing can put the fundamentals of care at the center of its activity"* (178), emphasizing the demand for PCC. The core element of FoC is the relationship between the patient and the nurse – a relationship that enables both to *"confidently and competently assess, plan, implement and evaluate care around the fundamental care needs"* (178). This relationship should be based on respect, trust, and mutual goals for the patient's care (178). FoC accentuates that the nurse should take a holistic approach to patient care, focusing on the patient as a whole and not solely on the disease or treatment. By viewing the results and findings from Study I and Study II within the framework of FoC, it can be argued that introducing nurse consultations based on PROs gets to the core of FoC because the relationship between the patient and the consulting nurse was described as creating a personal space for dialogue where sensitive issues could be discussed (133,134). Moreover, some patients also stated that they talked not about the disease but about the patient as a person, suggesting a trusting relationship, which according to FoC is essential to providing PCC (134,178,179).

FoC also encompasses action plans for further integration and implementation of FoC and PCC. One of these actions is application or development of assessment tools that tap into physical, psycho-social, and relational needs of the patients (178). This

demand is in line with the purpose and possibilities that lie within the concept of collecting PROs in clinical practice (180).

Study I and Study II indicate that when patients complete PROs prior to consultations, emerging health problems and needs for interventions are identified and addressed (133,134). Moreover, most patients found value in completing PROs, as they themselves became more observant of potential changes in their health situation. Based on these results and findings, FoC may be applied to the care of patients with hematological cancer by implementing PROs in clinical practice, thus eliciting information on physical and psycho-social needs to be addressed in the patient encounter.

Another action needed according to the FoC working group is the development of tools to measure patient experience and quality of care. This emphasis supports the previously noted need to involve patients in the development and implementation of PRO interventions in clinical practice with the aim of facilitating PCC.

6.2. METHODOLOGICAL CONSIDERATIONS

Below, the multi-method research design is discussed, followed by a discussion of the methodological considerations related to studies I, II, and III, including their strengths and limitations.

6.2.1. MULTI-METHOD RESEARCH DESIGN

This PhD thesis was designed as a multi-method study encompassing both quantitative and qualitative research methods (136). This method has allowed for a quantitative understanding of the feasibility of the intervention as well as a deeper understanding of how patients experienced the shared care follow-up and the impact it had on their lives.
Study I and Study II were designed to complement each other in terms of collecting data on the value of the intervention and PRO (133,134). Data from the two studies were collected and analyzed individually and then merged into a joint discussion, enabling a deeper understanding of the potential of the intervention. The multi-method research design has proven successful in this context because the results from Study I were informed and strengthened by the patient narratives in Study II, which confirmed the results of Study I. Also, Study II added the patient perspective on nurse-led telephone consultations and PROs in hematology to the literature, which to date has been limited. Although, a multi-method research approach allows

for a broader and deeper understanding of a subject it may also be assumed that breadth of knowledge about a topic may take precedence over depth as applying both methods may be extra time consuming (137). Thus, if the research design had been solely quantitative, it may have been possible to assess the feasibility of Study I based on stronger and additional estimates. However, a drawback of this argument is that such an approach would have eliminated the possibility of adding the patient perspective, which is vital to provision of PCC.

Study III was not a completely integrated part of the multi-method research design because the included patient population diverged from that in Study I and Study II. The patient population in Study III was pre-specified because it was a sub-study of an ongoing project (ProGen/ProSeq) within the Department of Hematology. This difference has made it more challenging to provide a joint discussion with Study I and Study II. However, the results of Study III offer an answer to the overall aim, and the three studies converged on similar results and findings. Thus, despite the different patient populations, the three studies have all provided answers to the question of the potential role for PROs in the provision of PCC during the hematological disease trajectory.

6.2.2. STUDY I

Study I was designed with the aim of testing the feasibility of the shared care follow-up initiative (133). This study did not include a control group, which limited any conclusions about whether the shared care follow-up initiative increased quality of care compared to standard follow-up. However, this study adds to the existing literature by demonstrating the feasibility of nurse-led telephone consultations in a hematological setting in terms of a high level of patient adherence and low rate of exclusions and extra in-hospital contacts.

During the study period, we included 80/83 patients based on the physician assessment at a scheduled visit. At present, we cannot provide further information regarding the recruitment process in terms of characteristics of patients who were offered participation but declined. In hindsight, the recruitment process could have been conducted more systematically, resulting in a more transparent process. Data in terms of clinical, socioeconomics characteristics and reasons for declining invitation to participate would have been useful for determining any specific and systematic characteristics in patients declining participation (181,182). This information is important for assessing potential selection bias, which may have influenced the interpretation of the results. A biased population would in this

context mean a more favorable outcome, overestimating the feasibility of the intervention. However, only three patients declined participation indicating that this issue may not have contributed considerably to potential overestimation of the feasibility of the intervention.

This feasibility study was designed using international validated and disease-specific PRO measures. EORTC-QLQ-30 and HADS have been used extensively within the PRO literature and as the basis for PRO-based follow-up developed by Ambuflex (132,139,141). In a study investigating the feasibility of Ambuflex, the authors found the interventions to be feasible in terms of high response rates and high satisfaction (132), underlining the value of these PRO measures as part of PRO-based follow-up in clinical practice. However, the results and findings from Study I and Study II also suggest that some patients found the PRO measures to be irrelevant and burdensome (133,134). A patient inquiry into the relevance of the PRO measures is vital for further development of the shared care follow-up initiative and prior to implementation.

6.2.3. STUDY II

In study II, 12 patients were interviewed, all of whom met the selected inclusion criteria in terms of variation in age, sex, diagnoses, and time since primary treatment (134). Although this study presents accounts based on variation within the patient population, it can be argued that because of this small number of patients, the findings offer only a limited narrative within the research context. However, generalizability in qualitative research is often not the goal as researchers generally seek to generate a deep and context-specific understanding of a given situation (137). Schofield (1993) argues that: *"The goal* [of qualitative research] *is not to produce a standardized set of results that any other careful researcher in the same situation or studying the same issues would have produced. Rather it is to produce a coherent and illuminating description of and perspective on a situation that is based on or consistent with detailed study of that situation"* (183). Thus, the findings of this study is based on narratives of patients with hematological cancer who had experience from the shared care follow-up initiative offering a deep exploration of the given situation and as such is assumed to provide a credible answer to the proposed study aim.

Data saturation is an ongoing debate within qualitative research because researchers often claim that saturation has been achieved without being able to prove it (184).

In Study II, the decision about saturated data was made at the timepoint at which no new information was elicited from the patient narratives. However, this rationale for data saturation has been criticized because it offers little information about the underlying assessment on which the decision is based (185). To forestall such unjustified decisions, Malterud et al. (2016) have proposed *"information power"* as a concept to guide choices about sample size in qualitative studies (185): *"Information power indicates that the more information the sample holds, relevant for the study, the lower amount of participants is needed"* (185). This concept holds that the narrower the research question and the denser the sample specificity, the smaller the sample size that will be needed. The aim of Study II was to elicit the experiences of patients with hematological cancer participating in a shared care follow-up initiative, resulting in a group of patients who had highly specific knowledge about this subject. This argument supports the need for a relatively small sample size in Study II, justifying the timepoint chosen for data saturation.

6.2.4. STUDY III

In Study III, 104 patients with relapsed or progressive hematological disease were included, of whom 90 responded to the baseline PRO measures (135). During the study period, 40 patients dropped out, for a dropout rate of 44%. Non-response to PRO measures during longitudinal studies is known to lead to unintended bias as well as loss of study power (186), and the dropout rate has undoubtedly reduced statistical power and decreased the rigor of the study results. However, despite low rigor, this study adds important information to a limited knowledge base about HRQoL in patients with relapsed or progressive hematological disease.

The timepoints for collection of PRO data were set to baseline and 3, 6, 9, and 12 months. It could be argued that the intervals were too widespread for a cohort of patients with advanced disease. The intervals were chosen because the goal was to investigate an overall HRQoL pattern over time. However, by shortening the intervals between PRO assessments, it is likely that we could have presented more robust results in terms of, e.g., a lower dropout rate because of death.

The study population consisted of patients with a wide variety of hematological cancer diagnoses, resulting in a heterogeneous sample. This heterogeneity posed a challenge for grouping the patients for analysis purposes. We chose to group the patients based on treatment strategy – CIT and non-CIT. We opted for this decision because we initially intended to investigate the level of depression and anxiety based on a clinical assumption that patients receiving palliative care would be more

depressed and anxious than patients receiving CIT. However, the results showed that neither group reported any symptoms of either depression or anxiety. In hindsight, to address the current aim of the study, we could have grouped the patients based on estimated survival over/under 2 years after relapse diagnosis because it could be argued that prognosis in terms of survival rather than treatment strategy affects HRQoL, making the former a better indicator of a patient's current situation.

CHAPTER 7. CONCLUSION

This PhD thesis provides new knowledge about the use of PROs as they relate to the trajectory of hematological cancer in the context of PCC and quality of care.

The use of PROs as part of a shared care follow-up initiative in a cohort of patients with B-cell disease in remission and low risk of relapse is feasible, as demonstrated by high patient adherence and a high level of acceptability of completing PROs as part of the follow-up.

A qualitative exploration of patient experiences suggests that completing PROs as part of follow-up is valuable to most patients in terms of tracking changes in their health situation and generating increased self-reflection about their health. Moreover, the patients experienced a shift from a disease-related to a more holistic focus, which seemed to improve communication in terms of engaging in discussions not normally had with the physicians.

Longitudinal HRQoL assessments in a cohort of hematological patients with relapse or progressive disease show that this patient population report moderate and severe symptoms and functional problems at baseline and that some patients experience deterioration of HRQoL during the first year after relapse diagnosis. Hence, routine symptom monitoring may be valuable to detect and manage symptoms and supportive care needs during treatment for relapsed or progressive disease.

Overall, this multi-method PhD thesis demonstrates that PROs are valuable during the trajectory of hematological cancer in terms of increased patient involvement, identifying health problems, and improving patient–provider communication and as a supporting role in shared decision making. Although divergent patient experiences suggest that a one-size-fits-all approach is undesirable, PROs seem to provide health professionals with a valid tool in the pursuit of providing PCC.

CHAPTER 8. IMPLICATIONS FOR CLINICAL PRACTICE AND FUTURE RESEARCH

Based on the results, discussion, and conclusion of this PhD thesis, the following section briefly elaborates on the possible implications of this research for clinical practice and provides a direction for future research.

8.1. IMPLICATIONS FOR CLINICAL PRACTICE

Cancer survivorship care of patients with hematological disease in remission, based on nurse-led telephone consultations and pre-collected PROs, may have the potential to target and individualize consultations that address each individual patient's needs. Implementing PROs in hematological cancer survivorship care may provide positive benefits in terms of increased patient involvement, identification of health problems, and better provider–patient communication and support shared decision making. Moreover, a multi-disciplinary approach to cancer survivorship may allow for a more holistic approach to a patient's supportive care needs and for patients to raise different concerns with the health professionals with whom they are most comfortable in a given situation. Finally, it may be desirable to implement needs assessments prior to entering survivorship care to assess a patient's preferences and need for support.

Patients with hematological cancer with relapsed or progressive disease report moderate and severe symptoms and functional problems. In addition, some patients experience a deterioration in HRQoL during the first year of relapse treatment. These findings suggest the need to focus on symptom assessment and monitoring during treatment to manage individual patient symptom relief and address functional problems to further stabilize or improve HRQoL. Implementation of PROs in hematological clinical practice offers the opportunity to address symptoms earlier and support patients in maintaining usual activities. This support could be provided by multidisciplinary initiatives aimed at facilitating maintenance and, better yet, improvement of HRQoL.

Finally, the routine use of PROs may contribute to provision of PCC within the FoC framework by focusing nursing care on each patient's individual needs.

8.2. FUTURE RESEARCH

The patient perspective and assessment of patient needs and preferences are essential when developing and implementing PRO-based interventions aimed at providing PCC. Therefore, development and implementation of future PRO-based interventions should be preceded by qualitative research studies exploring patient needs and preferences for the intervention in question, ensuring a solid foundation for future PRO-based interventions.

This research established a variable patient experience of the relevance of the applied PRO measures, which caused frustration for some. This finding points to the need to target chosen PRO measures even more; PRO measures for PRO-based interventions should be validated with the patient population in question by qualitative interview prior to study start or implementation.

Solid research on HRQoL in patients with hematological cancer with relapsed or progressive disease is limited. The research presented in this thesis provides some answers but is limited because of small numbers of patients and the disease heterogeneity in this population. Future HRQoL research within this patient population is needed. Of note, to collect solid data and provide robust results, future HRQoL research within this patient population should be designed with the consideration of a relatively large dropout rate because of death.

The results of this research indicated a large symptom burden as well as deterioration in HRQoL among these patients. To address symptoms and supportive care needs during treatment for relapsed or progressive disease, further research should encompass symptom monitoring based on PROs during treatment of these patients to identify potential positive patient outcomes.

This PhD thesis demonstrates that PROs may offer positive potential during the hematological disease trajectory in terms of increased patient involvement and provider–patient communication. However, the literature offers little evidence of positive patient outcomes as a result of applying PROs in clinical practice. Future research should direct attention towards this area to allow assessment of the full potential of PROs in clinical practice

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APPENDICES

Appendix A: European Organization for Research and Treatment of Cancer EORTC-QLQ-C30

Appendix B: Hospital Anxiety and Depression Scale (HADS)

Appendix C: Myeloproliferative Neoplasm – Symptom Assessment Form (MPN-SAF)

Appendix D: Patient Feedback Form – Danish Translation

Appendix E: Interview guide for Study 1b

Appendix A.

European Organization for Research and Treatment of Cancer EORTC-QLQ-C30 (139).

DANISH

EORTC QLQ-C30 (version 3.0)

Vi er interesserede i at vide noget om dig og dit helbred. Vær venlig at besvare alle spørgsmålene selv ved at sætte en ring omkring det svar (tal), som passer bedst på dig. Der er ingen "rigtige" eller "forkerte" svar. De oplysninger, som du giver os, vil forblive strengt fortrolige.

Skriv venligst dine forbogstaver her: ⌊ ⌋⌊ ⌋⌊ ⌋⌊ ⌋
Din fødselsdato (dag, måned, år): ⌊ ⌋⌊ ⌋⌊ ⌋⌊ ⌋⌊ ⌋⌊ ⌋⌊ ⌋⌊ ⌋
Dato for udfyldelse af dette skema (dag, måned, år): 31 ⌊ ⌋⌊ ⌋⌊ ⌋⌊ ⌋⌊ ⌋⌊ ⌋⌊ ⌋⌊ ⌋

		Slet ikke	Lidt	En del	Meget
1.	Har du nogen vanskeligheder ved at udføre anstrengende aktiviteter, som f.eks. at bære en tung indkøbstaske eller en kuffert?	1	2	3	4
2.	Har du nogen vanskeligheder ved at gå en lang tur?	1	2	3	4
3.	Har du nogen vanskeligheder ved at gå en kort tur udendørs?	1	2	3	4
4.	Er du nødt til at ligge i sengen eller sidde i en stol om dagen?	1	2	3	4
5.	Har du brug for hjælp til at spise, tage tøj på, vaske dig eller gå på toilettet?	1	2	3	4

I den forløbne uge:		Slet ikke	Lidt	En del	Meget
6.	Var du begrænset i udførelsen af enten dit arbejde eller andre daglige aktiviteter?	1	2	3	4
7.	Var du begrænset i at dyrke dine hobbyer eller andre fritidsaktiviteter?	1	2	3	4
8.	Havde du åndenød?	1	2	3	4
9.	Har du haft smerter?	1	2	3	4
10.	Havde du brug for at hvile dig?	1	2	3	4
11.	Har du haft søvnbesvær?	1	2	3	4
12.	Har du følt dig svag?	1	2	3	4
13.	Har du savnet appetit?	1	2	3	4
14.	Har du haft kvalme?	1	2	3	4
15.	Har du kastet op?	1	2	3	4
16.	Har du haft forstoppelse?	1	2	3	4

Vær venlig at fortsætte på næste side

I den forløbne uge:	Slet ikke	Lidt	En del	Meget
17. Har du haft diarré (tynd mave)?	1	2	3	4
18. Var du træt?	1	2	3	4
19. Vanskeliggjorde smerter dine daglige gøremål?	1	2	3	4
20. Har du haft svært ved at koncentrere dig om ting som f.eks. at læse avis eller se fjernsyn?	1	2	3	4
21. Følte du dig anspændt?	1	2	3	4
22. Var du bekymret?	1	2	3	4
23. Følte du dig irritabel?	1	2	3	4
24. Følte du dig deprimeret?	1	2	3	4
25. Har du haft svært ved at huske?	1	2	3	4
26. Har din fysiske tilstand eller medicinske behandling vanskeliggjort dit familieliv?	1	2	3	4
27. Har din fysiske tilstand eller medicinske behandling vanskeliggjort din omgang med andre mennesker?	1	2	3	4
28. Har din fysiske tilstand eller medicinske behandling medført økonomiske vanskeligheder for dig?	1	2	3	4

Ved de næste 2 spørgsmål bedes du sætte en ring omkring det tal mellem 1 og 7, som passer bedst på dig

29. Hvordan vil du vurdere dit samlede helbred i den forløbne uge?

1	2	3	4	5	6	7
Meget dårligt						Særdeles godt

30. Hvordan vil du vurdere din samlede livskvalitet i den forløbne uge?

1	2	3	4	5	6	7
Meget dårlig						Særdeles god

Appendix B.

Hospital Anxiety and Depression Scale (HADS) (141).

1

Hospital Anxiety and Depression Scale (HAD)

Dette spørgeskema er udformet med henblik på at hjælpe læger med at finde ud af, hvordan du har det.

Læs hvert spørgsmål og sæt kryds ved det svar, der bedst beskriver, hvordan du har haft det følelses-mæssigt inden for den sidste uge.

1. Jeg er anspændt eller stresset.

- ❑ Det meste af tiden
- ❑ Meget af tiden
- ❑ Engang imellem
- ❑ Overhovedet ikke

2. Jeg glæder mig stadig over de ting, jeg plejede at glæde mig over.

- ❑ Helt bestemt
- ❑ Ikke helt så meget
- ❑ Kun lidt
- ❑ Næsten ikke

3. Jeg får en slags skræmmende for-nemmelse, som om noget forfærdeligt skal til at ske.

- ❑ Helt bestemt og temmelig slemt
- ❑ Ja, men ikke alt for slemt
- ❑ En smule, men det bekymrer mig ikke
- ❑ Overhovedet ikke

4. Jeg kan le og se tingene fra den morsomme side.

- ❑ Lige så meget som jeg altid har kunnet
- ❑ Ikke helt så meget nu
- ❑ Bestemt ikke så meget nu
- ❑ Overhovedet ikke

5. Bekymrende tanker strejfer mig.

- ❑ En meget stor del af tiden
- ❑ Meget af tiden
- ❑ Engang imellem, men ikke så tit
- ❑ Kun engang imellem

6. Jeg er i godt humør.

- ❑ Overhovedet ikke
- ❑ Ikke ofte
- ❑ Nogle gange
- ❑ Det meste af tiden

7. Jeg kan sidde roligt og føle mig af-slappet.

- ❑ Helt bestemt
- ❑ For det meste
- ❑ Ikke ofte
- ❑ Overhovedet ikke

8. Jeg føler det som om, jeg virker sløv.

- ❑ Næsten hele tiden
- ❑ Meget ofte
- ❑ Somme tider
- ❑ Overhovedet ikke

PB
v 03-1994

9. Jeg får en slags bange fornemmelse, lige som "sommerfugle" i maven.

- ❑ Overhovedet ikke
- ❑ Ikke ofte
- ❑ Ret ofte
- ❑ Meget ofte

10. Jeg har mistet interessen for mit udseende.

- ❑ Helt bestemt
- ❑ Jeg er ikke helt så omhyggelig, som jeg burde være
- ❑ Måske interesserer det mig knap så meget som før
- ❑ Jeg er lige så omhyggelig som før

11. Jeg føler mig rastløs, som om jeg hele tiden skal være i gang.

- ❑ I udtalt grad
- ❑ En hel del
- ❑ Ikke så ofte
- ❑ Overhovedet ikke

12. Jeg ser med glæde frem til tingene.

- ❑ Lige så meget, som jeg altid har gjort
- ❑ En del mindre, end jeg plejer
- ❑ Bestemt mindre, end jeg plejer
- ❑ Næsten ikke

13. Jeg får pludselige fornemmelser af panik.

- ❑ Absolut meget ofte
- ❑ Temmelig ofte
- ❑ Ikke ret tit
- ❑ Overhovedet ikke

14. Jeg kan nyde en god bog, et radio- eller TV-program

- ❑ Ofte
- ❑ Nogle gange
- ❑ Ikke ofte
- ❑ Meget sjældent

PB
v 03-1994

Appendix C.

Myeloproliferative Neoplasm – Symptom Assessment Form (MPN-SAF) (140).

Instruktioner: Besvar venligst alle spørgsmål så godt som muligt. Symptomerne gælder den **seneste uge**, hvis intet andet er nævnt.

Symptom	**Graduer fra 1 til 10, hvor 1 er mindste symptom og 10 er værste tænkelige. (0 er ingen symptomer overhovedet)**
Sæt ring om det tal, der bedst beskriver din træthed **netop nu**	0 (ingen træthed) 1 2 3 4 5 6 7 8 9 10 (værst tænkelige)
Sæt ring om det tal, der bedst beskriver din gennemsnitlige træthed **det seneste døgn**	0 (ingen træthed) 1 2 3 4 5 6 7 8 9 10 (værst tænkelige
Sæt ring om det tal, der bedst beskriver den **værste** træthed du har følt **det seneste døgn**	0 (ingen træthed) 1 2 3 4 5 6 7 8 9 10 (værst tænkelige

Sæt ring om det tal, der bedst beskriver hvordan træthed (udmattelse) igennem **det seneste døgn** har indvirket på:	
Dine daglige aktiviteter	0 (slet ikke) 1 2 3 4 5 6 7 8 9 10 (fuldstændigt)
Dit humør	0 (slet ikke) 1 2 3 4 5 6 7 8 9 10 (fuldstændigt)
Din bevægelsesfrihed/evne til at bevæge dig omkring	0 (slet ikke) 2 3 4 5 6 7 8 9 10 (fuldstændigt)
Dit arbejde såvel som dine daglige gøremål	0 (slet ikke) 1 2 3 4 5 6 7 8 9 10 (fuldstændigt)
Din omgang med andre mennesker	0 (slet ikke) 1 2 3 4 5 6 7 8 9 10 (fuldstændigt)
Din livsglæde	0 (slet ikke) 1 2 3 4 5 6 7 8 9 10 (fuldstændigt)

Sæt ring om det tal, der bedst beskriver i hvor høj grad du igennem **den sidste uge** har været generet af:

Tidligt forekommende mæthedsfølelse ved måltider	0 (ingen) 1 2 3 4 5 6 7 8 9 10 (værst tænkelige)
Smerter i maven / bughulen	0 (ingen) 1 2 3 4 5 6 7 8 9 10 (værst tænkelige)
Ubehag i maven / bughulen	0 (ingen) 1 2 3 4 5 6 7 8 9 10 (værst tænkelige)
Inaktivitet	0 (ingen) 1 2 3 4 5 6 7 8 9 10 (værst tænkelige)
Problemer med hovedpine	0 (ingen) 1 2 3 4 5 6 7 8 9 10 (værst tænkelige)
Problemer med koncentrationen – sammenlignet med før min sygdom	0 (ingen) 1 2 3 4 5 6 7 8 9 10 (værst tænkelige)
Svimmelhed	0 (ingen) 1 2 3 4 5 6 7 8 9 10 (værst tænkelige)
Prikken/stikken/følelsesløshed/ i hænder og fødder	0 (ingen) 1 2 3 4 5 6 7 8 9 10 (værst tænkelige)
Søvnproblemer	0 (ingen) 1 2 3 4 5 6 7 8 9 10 (værst tænkelige)
Nedtrykthed eller været ked af det	0 (ingen) 1 2 3 4 5 6 7 8 9 10 (værst tænkelige)
Seksuelle problemer (nedsat lyst eller dysfunktion)	0 (ingen) 1 2 3 4 5 6 7 8 9 10 (værst tænkelige)
Hoste	0 (ingen) 1 2 3 4 5 6 7 8 9 10 (værst tænkelige)
Nattesved	0 (ingen) 1 2 3 4 5 6 7 8 9 10 (værst tænkelige)
Kløe	0 (ingen) 1 2 3 4 5 6 7 8 9 10 (værst tænkelige)
Knoglesmerter (diffus smerte, ikke ledsmerter)	0 (ingen) 1 2 3 4 5 6 7 8 9 10 (værst tænkelige)
Feber (over 37.8)	0 (aldrig) 1 2 3 4 5 6 7 8 9 10 (dagligt)
Utilsigtet vægttab de seneste 6 mdr. (dvs. ikke vægttab som resultat af træning eller slankekur)	0 (intet) 1 2 3 4 5 6 7 8 9 10 (værst tænkelige)
Hvad vejer du i dag? (Kg)	
Hvordan vurderer du din livskvalitet	0 (Bedst tænkelige) 1 2 3 4 5 6 7 8 9 10 (værst tænkelige)

Appendix D.

Patient Feedback Form – Danish Translation (143).

PATIENTTILBAGEMELDING

Patientnr.: _____
Dato: _____

Vi er interesseret i din mening om de spørgeskemaer, som du har besvaret. Vi beder dig besvare alle spørgsmålene selv ved at sætte en ring om det tal, som passer bedst. Der er ingen "rigtige" eller "forkerte" svar på spørgsmålene. Dine svar vil blive behandlet fuldt fortroligt.

		For kort	Passende	For lang
1.	Længden på spørgeskemaet var	1	2	3
		For få	**Passende**	**For mange**
2.	Det antal gange, jeg blev bedt om at besvare spørgeskemaet var	1	2	3

		Meget enig	Enig	Uenig	Meget uenig
3.	Det var nemt at besvare spørgeskemaet	1	2	3	4
4.	Det gav mening at besvare spørgeskemaet	1	2	3	4
5.	Det var nemt at forstå spørgsmålene	1	2	3	4
6.	At besvare spørgeskemaet gjorde det nemmere for mig at huske mine symptomer og bivirkninger, når jeg talte med personalet	1	2	3	4
7.	At besvare spørgeskemaet forbedrede samtalen med personalet	1	2	3	4
8.	Personalet anvendte oplysninger fra spørgeskemaet i forbindelse med min behandling	1	2	3	4
9.	Jeg oplever, at kvaliteten af min behandling blev forbedret, fordi jeg havde besvaret spørgeskemaet	1	2	3	4
10.	Jeg oplever, at kommunikationen med personalet blev forbedret, fordi jeg havde besvaret spørgeskemaet	1	2	3	4
11.	At besvare spørgeskemaet fik mig til at føle, at jeg blev inddraget i min behandling	1	2	3	4
12.	Jeg vil anbefale andre patienter at besvare spørgeskemaet	1	2	3	4
13.	Jeg vil gerne fortsætte med at besvare spørgeskemaet fremover	1	2	3	4

For anvendelse af spørgeskemaet se: Danish translation, cultural adaption and initial psychometric evaluation of the patient feedback form. Lærke K. Tolstrup, Helle Pappot, Graziella Zangger, Lars Bastholt, Ann-Dorthe Zwisler and Karin B. Dieperink *Health and Quality of Life Outcomes* 2018 https://doi.org/10.1186/s12955-018-0900-4

Appendix E.

Interview guide developed for Study II (134).

Tema	**Spørgsmål**	**Supplerende spørgsmål**
Dine oplevelser	• Prøv at fortælle, med dine egne ord, hvordan du overordnet oplevede at deltage i projektet. • Hvordan oplevede du at udfylde spørgeskemaerne? • Oplevede du at du kunne bruge spørgeskemaerne til noget forud for samtale?	• Var der noget, du oplevede som særligt godt? • Var der noget, du oplevede som knap så godt? • Var der noget du undrede dig over? • Hvordan passede antallet af spørgsmål? Var der for mange / for få? • Var spørgsmålene relevante? • Var der noget du savnede? • Hvordan var det at sætte tal på symptomer? • Gav de anledning til forberedelse? • Hvilken betydning havde det for dig? • Hvordan oplevede du, at dine svar blev brugt i opfølgningen?
Ændret praksis	• Hvordan var overgangen mellem at blive fulgt udelukkende af en læge i ambulatoriet til at skulle følges hver anden gang af en sygeplejerske over telefonen? • Hvilken betydning har det haft, at det var en sygeplejerske, du talte med?	• Var der noget, du manglede ved telefonkonsultationen? • Følte du behov for at se en læge efter sygeplejerskekonsultationen? • Hvilken betydning har det haft for dig, at samtalen med sygeplejersken foregik over telefonen? • Kan du fortælle lidt omkring forskellene mellem at tale med en læge og en sygeplejerske, hvis der var nogen? • Hvis ja, hvordan kom det til udtryk? • Hvis ja, hvilken betydning har det ændrede fokus haft for dig?
Behov for støtte til patientens aktuelle tilstand	• Hvad har især fyldt for dig i dit forløb? Er der noget der har været specielt svært for dig?	• Hvordan oplevede du at lægen/sygeplejersken gik op i, hvad der var vigtigt for dig? • Hvordan oplevede du at læge/sygeplejersken støttede

	• I forhold til hvad der har fyldt for dig, hvordan oplevede du at få den støtte, du havde brug for?	dig i, hvad der var vigtigt for dig? • Var der problemstillinger, der var nemmere at tale om / få støtte til? I så fald hvilke? • Er der forskel på, om du fik den støtte, du havde behov for afhængig af om, det var læge eller sygeplejersken du talte med? • Er der problemstillinger, der var nemmere / svære at drøfte igennem en telefon?
Indvirkning på dagligdagen	• Kan du sætte nogle ord på, hvad deltagelsen har betydet for din hverdag? • Hvilken betydning har det haft for dig, at du ikke skulle møde op fysisk i ambulatoriet?	• Har det haft en praktisk betydning? • Har det haft en arbejdsmæssig betydning? • Har det haft en følelsesmæssig betydning? • Andet?

PAPERS

Paper I: Shared care follow-up of patients with B-cell neoplasms based on nurse-led telephone consultations and PRO-data: A feasibility study from the North Denmark Region

Paper II Hematological cancer survivors' experiences of participating in a shared care follow-up – an exploratory interview study

Paper III: The use of patient-reported outcomes in precision medicine and hematological patients with relapse or progressive disease: A longitudinal observational study.

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