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Implementation of the Symptom Navi Program for cancer patients in ambulatory services: A cluster randomised pilot study (Symptom Navi Pilot Study)

Bana Marika

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Implementation of the Symptom Navi Program for cancer patients in ambulatory services: A cluster randomised pilot study (Symptom Navi Pilot Study)

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par

Marika BANA

Master of Science in Nursing UAS Zurich, Zürcher Hochschule für Angewandte Wissenschaften ZHAW, Switzerland

Jury

Prof. Susanne Look, Présidente, experte
Prof. Dr. rer. medic. Manuela Eicher, Directrice de thèse (UNIL)
Prof. Dr. med. Solange Peters, Co-directrice de thèse (CHUV)
Dr. Patrick Jahn, expert
Dr. Antje Koller, experte externe
Prof. Anne-Sylvie Ramelet, rapporteur

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Co-directrice de thèse	Madame la Prof. Solange Peters
Expert.e.s	Monsieur le Dr Patrick Jahn
	Madame la Dre Antje Koller
Rapporteur	Madame la Prof. Anne-Sylvie Ramelet

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Madame Marika Bana
Master of Science in Nursing UAS Zurich, Zürcher Hochschule für Angewandte Wissenschaften ZHAW, Switzerland

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Implementation of the Symptom Navi Program for cancer patients in ambulatory services: A cluster randomised pilot study (Symptom Navi Pilot Study)

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Pour le Doyen
De la Faculté de Biologie et de Médecine

Directeur académique de l'IUFRS

Vice-Directeur de l'Ecole Doctorale

Dissertation Abstract

Introduction The Symptom Navi Program (SNP) is a nurse-led intervention supporting patient symptom self-management. It consists of written patient information leaflets (Symptom Navi Flyers, SN-Flyers), semi-structured consultations, and a training manual. Previous qualitative studies with patients and professionals showed good acceptability and usability of SN-Flyers and patient satisfaction with nurse-led consultations. This dissertation is embedded in the Symptom Navi Pilot Study. The objectives of the dissertation were to evaluate the feasibility of implementing the SNP. Outcomes of interest were a) patient accrual and retention rates, b) training content and nurses' fidelity to the training, c) preliminary safety and impact on patient-reported outcomes.

Methods A cluster-randomised two parallel arm design was employed by randomising the outpatient cancer centres (=clusters) to the intervention group (implementation of the SNP) or the control group (usual care). Adult German-speaking patients starting first-line systemic treatment (for any cancer type) were included. Nurses in the intervention group participated in two training courses and evaluated training content on a study specific questionnaire. Following SNP training, nurses used SN-Flyers to provide at least two semi-structured consultations per patient. Nurses Work-related Sense of Coherence (Work-SoC scale) was used to examine the relationship between nurses' confidence in implementing the SNP and perceptions of their current work situation. To explore nurses' fidelity to the training, study specific questionnaires assessing self-reported adherence to six core-elements of the semi-structured consultations were utilised. In addition to nurses' self-reports, two semi-structured consultations were observed at each intervention centre. To investigate SNP safety, nurses and oncologists reported any adverse events potentially related to the program. Validated questionnaires were used to assess patient-reported symptom interference with daily functions, symptom severity/burden, self-efficacy, and perceived nursing support for symptom management. Patients completed questionnaires at baseline (BL), after 1 – 3 weeks (t1), after 4 – 6 weeks (t2), and 16 weeks post BL.

Analysis Qualitative thematic analysis was used to explore the observations of semi-structured consultations. Statistics included descriptive analyses, the Kendall Tau test, and linear or logistic mixed-effect models. To explore the preliminary impact on patient-reported outcomes change in means between the two groups for each time point (t1, t2, t3) were compared. BL scores, treatment group, time point (i.e. t1, t2, or t3), and interaction of group and time were included as fixed covariates while cluster and patient were considered as nested random effects.

Results Four centres (49 patients) were randomised to the SNP group and 5 centres (85 patients) to the control group. One SNP centre withdrew from the study without recruiting any patients. The SNP group included more women (p = .030), younger patients (p = .001), and more patients living with family members needing care (p = .019). The accrual rate was significantly lower for the SNP group compared to controls (71% versus 90%, risk difference -19%, 95% CI -32% to -7%, p = .003). Overall, 43 patients (88%) received the intervention as intended (= retention rate, range 75% to 100%). Nurses accepted the training format and content. Perceived confidence in implementing the SNP into clinical practice was positively correlated with overall Work-SoC scores (r_{π} =.47, p = .04). Overall, nurse self-reported compliance with the core-elements of the semi-structured consultations was 92% (95% CI: 87% to 97%). However, the analysis of the observations suggest that nurses rarely used self-management education elements to actively facilitate patients' symptom self-management. No adverse events were reported for the SNP group. Symptom interference with daily functions was unchanged by the SNP (mean difference at 16 weeks: -0.50; 95% CI: -1.38 to 0.38; p = 0.25) – as were all other patient-reported outcomes.

Conclusions Overall, accrual/retention rates, nurses' acceptance of the training and their high adherence rates to the training indicate that SNP implementation was well received by participating centres. No adverse events have been observed. Nevertheless, findings reveal that the program had no impact on patient-reported outcomes. Improving the SNP by strengthening symptom self-management education elements and nurses' coaching role should be applied before planning further investigations.

Résumé de la thèse

Introduction Le Programme Symptom Navi (« Symptom Navi Programme » ou SNP) est une intervention menée par le personnel infirmier en vue de soutenir les patient·e·s dans l'autogestion de leurs symptômes. Il comporte une information écrite (dépliants Symptom Navi ou dépliants SN, destinés aux patient·e·s), des consultations semi-structurées et un manuel de formation. Des études qualitatives antérieures auprès de patient·e·s et de professionnel·le·s ont montré une acceptabilité et une utilisabilité élevées des dépliants SN et la satisfaction des patient·e·s à l'égard des consultations dirigées par des infirmières et des infirmiers. La présente thèse s'insère dans l'étude pilote Symptom Navi. Elle avait pour objectif d'évaluer la faisabilité d'une mise en œuvre du SNP. Les résultats visés incluaient a) les taux de recrutement et de rétention des patient·e·s, b) le contenu de la formation et la fidélité du personnel infirmier à cette dernière ainsi que c) la sécurité préliminaire du programme et son impact sur les effets rapportés par les patient·e·s.

Méthodes Une conception à deux bras parallèles randomisée par grappes a été employée pour attribuer les centres d'oncologie ambulatoire (= grappes) au groupe d'intervention (mise en œuvre du SNP) ou au groupe témoin (soins usuels). Ont été inclus·e·s dans l'étude des patient·e·s adultes germanophones commençant un traitement systémique de première ligne pour cancers de tout type. Les infirmières et les infirmiers du groupe d'intervention ont participé à deux cours de formation et évalué le contenu de celle-ci dans un questionnaire spécifique à l'étude. Après la formation relative au SNP, elles et ils se sont servi des dépliants SN pour fournir au moins deux consultations semi-structurées par patient·e. Le sentiment de cohérence au travail du personnel infirmier a été utilisé pour examiner la relation entre sa confiance à appliquer le SNP et sa perception de la situation au travail sur le moment (échelle du sentiment de cohérence au travail [Work-related Sense of Coherence scale ou Work-SoC]. Pour investiguer la fidélité du personnel infirmier à la formation reçue, il a été recouru d'une part à des questionnaires spécifiques à l'étude évaluant son adhésion auto-déclarée à six éléments fondamentaux des consultations semi-structurées. Deux consultations semi-structurées ont d'autre part été observées dans chaque centre d'intervention. Afin de vérifier la sécurité du SNP, les infirmières, les infirmiers et les oncologues ont signalé tout événement indésirable potentiellement lié au programme. Des questionnaires validés ont été utilisés pour évaluer l'interférence des symptômes avec les fonctions de la vie quotidienne rapportée par les patient·e·s ainsi que la gravité/la pression des symptômes, l'auto-efficacité et la façon dont était perçu le soutien infirmier dans la gestion des symptômes. Les patient·e·s ont rempli les questionnaires au début de l'étude (stade baseline ou BL), après 1 à 3 semaines (t1), après 4 à 6 semaines (t2) et 16 semaines après le début (BL).

Analyse Les observations des consultations semi-structurées ont été étudiées à l'aide d'une analyse thématique qualitative. Des analyses descriptives, le test Tau de Kendall et des modèles linéaires ou logistiques à effets mixtes ont servi à analyser les données. Afin d'explorer l'impact préliminaire sur les résultats déclarés par les patient·e·s, les changements de moyenne entre les deux groupes ont été comparés pour chaque point temporel (t1, t2, t3). Les scores de référence (scores BL), le groupe de traitement, le point temporel (t1, t2, ou t3 p. ex.) et l'interaction entre groupe et temps ont été inclus en tant que covariables fixes alors que la grappe et la/le patient·e étaient considérés en tant qu'effets aléatoires imbriqués.

Résultats Quatre centres (49 patient·e·s) ont été attribués aléatoirement au groupe SNP et cinq autres (85 patient·e·s) servaient de contrôles. Un centre SNP s'est retiré de l'étude sans avoir recruté de patient·e·s. Le groupe SNP incluait davantage de femmes (p = .030), de patient·e·s plus jeunes (p = .001) et de personnes vivant avec des membres de leur famille nécessitant des soins. Le taux de recrutement s'est avéré notablement plus bas pour le groupe SNP que pour les contrôles (71% contre 90%, différence de risque -19%, 95% IC - 32% à - 7%, p = .003). Au total, 43 patient·e·s (88%) ont bénéficié de l'intervention telle que prévue (= taux de recrutement variant de 75% à 100%). Le personnel infirmier a accepté la forme et le contenu de la formation. La perception de sa confiance dans l'implémentation du SNP dans la pratique clinique a été corrélée positivement avec les scores globaux de l'échelle Work-SoC (r_{π} =.47, p = .04). Dans l'ensemble, le personnel a fait preuve d'une

adhésion élevée à la formation. Selon ses déclarations, sa fidélité aux éléments centraux des consultations semi-structurées s'est élevée à 92% (95% IC : 87% à 97%). Toutefois, l'analyse des observations faites suggère qu'il a rarement fait usage des éléments de la formation à l'autogestion pour faciliter activement la gestion autonome des symptômes par les patient·e·s. Aucun événement indésirable n'a été signalé pour le groupe SNP. L'interférence des symptômes avec les fonctions de la vie quotidienne est restée inchangée sous application du SNP (différence moyenne à 16 semaines : -0.50; 95% IC : -1.38 à 0.38; *p* : 0.25) de même que tous les autres résultats relatés par les patient·e·s.

Conclusions Dans l'ensemble, les taux de recrutement et de rétention, l'acceptation de la formation par les infirmières et les infirmiers et leur taux d'adhésion élevé à celle-ci indiquent que les centres participants ont bien accueilli la mise en œuvre du SNP. Aucun effet indésirable n'a été observé. Les résultats obtenus révèlent néanmoins que le programme n'a eu aucun impact sur les effets déclarés par les patients. Il convient d'améliorer le SNP en renforçant les éléments de formation à l'autogestion des symptômes et le rôle de coach du personnel infirmier avant de planifier de nouvelles investigations.

Preface

This thesis is based on a previously developed, nurse-led intervention to support patient symptom self-management during anti-cancer treatments. From 2011-2015, Susanne Kropf-Staub at the Lindenhofspital in Bern developed the initial version of written symptom specific information leaflets (Symptom Navi Flyers, SN-Flyers). SN-Flyers provide evidence-based recommendations for patients on specific steps they can take to ease symptom burden and prevent intensifying symptoms. A steering committee has been formed to oversee the development and evaluation of the Symptom Navi Programme (SNP). A qualitative evaluation including health care professionals and patients revealed patients and their family members considered SN-Flyers helpful for supporting patient self-management behaviour. Further, nurses used SN-Flyers to facilitate symptom management conversations (1, 2). In 2015, several cancer centres expressed interest in using the SN-Flyers. At this time, the feasibility of implementing such a program at different centres had not been explored. In addition, data on safety of the SNP and its impact on patient-reported outcomes were lacking. The steering committee decided to collaborate with interested cancer centres and to conduct a pilot study to address these issues.

This dissertation is part of the Symptom Navi Pilot Study evaluating the implementation of the SNP. We use the Reach Effectiveness – Adoption Implementation Maintenance (RE-AIM) framework to examine the process at the individual and organisational levels (3, 4). Implementation research is complex and requires multiple methods because evaluating effectiveness alone is not sufficient for long-term implementation and maintenance of an intervention (5). Effective SNP implementation requires nursing behaviour change from a more passive approach emphasizing information provision to active coaching of patients to self-manage symptoms. In collaboration with the dissertation committee, the following activities related to the Symptom Navi Pilot Study were defined for the dissertation project: 1) to complement the SNP with a standardised nurse training based on the Capability Opportunity Motivation – Behaviour (COM-B) model (6), 2) to collaborate with the SNP steering committee and the University of Bern Clinical Trial Unit (CTU) to develop a multi-method study protocol including a cluster-randomised design, 3) to train all available nurses at participating centres randomised to the SNP intervention group and evaluate nurse training, and 4) to evaluate patient accrual and retention rates, nurse fidelity to the training manual, and preliminary effectiveness and safety of the SNP. We submitted the study protocol to the ethics committee in Bern and subsequently to all cantonal ethics committees of participating centres (Annexe 1).

In this thesis, three articles are integrated in the chapters *Methods* and *Results*. The first article is the study protocol published in the British Medical Journal (BMJ)-Open in July 2019 (7). It constitutes the *Method* chapter.

The *Results* chapter starts with the second article describing development and implementation strategies of the SNP by summarising the development process (since 2011). This article also includes results on the nurse training evaluation. The article has been accepted for publication (November 27th, 2019) in the European Journal of Oncology Nursing and was published online (January 15th, 2020) (8). (Appendix 2) During the submission of the second article, the SNP steering committee decided to omit the copyright sign ("©"). In this dissertation the program's name is therefore written without the © except for previously published articles and those and submitted by the end of 2019.

The second part of this chapter presents the results on patients' accrual and retention rates (representing the Reach dimension of the RE-AIM framework). The third article reports results on preliminary SNP effectiveness with respect to patient-reported outcomes on symptom interference with daily function, symptom intensity and burden, self-efficacy, and perceived nursing support for symptom management. This article has been submitted to the Journal Cancer Nursing in February 2020 (submission confirmation in Appendix 3). After article three, results regarding the dimensions adoption and implementation are presented including results on nurse fidelity to the training manual (adoption) and the time needed to provide semi-structured consultations (implementation).

An overall discussion including limitations of the thesis and conclusions for future research and clinical practice is summarised the dissertation.

List of integrated articles:

Article 1 (published)

Bana M, Ribi K, Kropf-Staub S, Zurcher-Florin S, Naf E, Manser T, et al. Implementation of the Symptom Navi© Programme for cancer patients in the Swiss outpatient setting: a study protocol for a cluster randomised pilot study (Symptom Navi(c) Pilot Study). BMJ Open. 2019;9(7):e027942.

Article 2 (published)

Bana M, Ribi K, Kropf-Staub S, Näf E, Sailer Schramm M, Zürcher-Florin S, et al. Development and implementation strategies of a nurse-led symptom self-management program in outpatient cancer centres: The Symptom Navi© Programme. European Journal of Oncology Nursing. 2020 10.1016/j.ejon.2019.101714 (online available, 15 January 2020)

Article 3 (submitted)

Bana M, Ribi K, Peters S, Kropf-Staub S, Näf E, Zürcher-Florin S, Stoffel B, Blaeuer C, Borner M, Prof; Malin D, Biber R, Betticher D, Kuhn-Bächler T, Cantoni N, Seeger T, Bütikofer L, Eicher E, Pilot-testing of the preliminary effectiveness of a nurse-led programme to support symptom self-management for patients receiving first-line systemic outpatient anticancer treatment (Symptom Navi Pilot Study). Cancer Nursing. Submitted February 2020.

Content

Tables

In order of appearance in thesis.

Figures

In order of appearance in thesis.

Abbreviations

In order of appearance in thesis.

SN©Flyers / SN-Flyers	Symptom Navi Flyers
SN©P / SNP	Symptom Navi Programme
RE-AIM	Reach Effectiveness – Adoption Implementation Maintenance framework
COM-B	Capability Opportunity Motivation – Behaviour model
CTU	Clinical Trial Unit
BMJ	British Medical Journal
SMS	Self-management support
NICE	National Institute for Clinical Excellence
UK	United Kingdom
ESMO	European Society for Medical Oncology
EONS	European Oncology Nursing Society
TSSM	Theory of Symptom Self-Management
TDF	Theoretical Domains Framework
TOUS	Theory of Unpleasant Symptoms
MRC	Medical Research Council
RCT	Randomised Clinical Trial
I-CVI	Item - Content Validity Index
MDASI	MD Anderson Symptom Inventory
SES6G	Self-Efficacy for Managing Chronic Disease questionnaire (6 items)
Mood LASA scale	Mood Linear Analogue Self-Assessment scale
PR-CISE	Patient-Reported Chemotherapy Indicators of Symptoms and Experience
Work-SoC scale	Work-related Sense of Coherence Scale
BL	baseline
ICH-GCP	International Council for Harmonisation – Good Clinical Practice
SNCTP	Swiss National Clinical Trial Portal
IQR	Inter quartile range
uq	Upper quartile
lq	Lower quartile
CI	Confidence interval
min	minimum
max	maximum
sd	Standard deviation
ICC	Intra-class correlation coefficient
GLM	Generalised linear mixed model
SIDF	Symptom interference with daily functions
SAP	Statistical analysis plan
SAE	Serious adverse event

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Introduction

Cancer prevalence and incidence is increasing in most countries over the last decades (9). For many affected people living in wealthy countries (countries with high Human Development Index), cancer has become a long-term condition due to more effective treatments and increased survivorship. In parallel, overall mortality rates are decreasing for these countries (10). In Switzerland, the incidence rate of cancer between 2011 and 2015 was approximately 40'500 people newly diagnosed with cancer per year (11). In 2015, there were almost 317'000 people living with cancer in Switzerland. Based on prevalence rates, approximately 17% of people living with cancer received active anticancer treatments and roughly 19% have stopped treatment and are monitored with continued, regular follow-up visits. The majority, about 64%, are cancer survivors meaning they are five years post-cancer diagnosis and are no longer undergoing regular monitoring visits. Survivors may experience long-term and late effects of cancer treatments (12). Age standardised mortality rates for cancer decreased in Switzerland over the last 30 years by approximately 27% for women and 37% for men while incidence rates rose slightly over this period – largely due to improved diagnostic and screening programs (11). These trends have resulted in increasing numbers of patients who potentially need support in managing physical and psychosocial consequences of cancer and anticancer treatments (13). Cancer affects mainly older adults (12) who often present with co-morbid conditions resulting in concomitant health problems (14). Therefore, increasing cancer prevalence in combination with an aging population have created a growing population in need of support to manage symptoms and/or cancer related problems.

The period of active anticancer treatments is often burdensome and the multidimensional impact of physical, emotional, social, functional, and financial consequences affect patients' daily lives (15, 16). Physical consequences are mostly due to cancer treatments and include a long list of common side effects (i.e. fatigue, nausea, constipation, diarrhoea, skin reactions and others) that often impact daily activities (e.g. housework, childcare, employment) (17). To facilitate a normal life to the greatest extent possible, patients and their families need supportive care to manage symptoms and psychosocial consequences - especially during ambulatory anticancer treatment (18). Supportive care is an umbrella term that includes all care helping individuals to cope with cancer illness and side-effects of treatments from diagnosis through treatment, continued illness, to end-of-life care (19). Supportive care aims to improve patient quality of life and to facilitate his/her self-management. The term self-management was originally used to define tasks and skills patients use to manage a chronic condition. Self-management includes the ability to manage symptoms, treatments, physical and psychosocial consequences inherent to illness and to make life style changes as needed (20). Over the last two decades, self-management became an integral part of supportive care for patients with cancer (21-23). Self-management support empowers patients to monitor their condition related to the cancer and adequately respond to physical and emotional symptoms/problems to maintain quality of life.

Oncology nurses are at the forefront in supporting patients to self-manage symptoms and psychosocial consequences during active ambulatory treatment. Self-management support (SMS) was first developed for patients affected by chronic conditions (e.g. diabetes, arthritis) with the goal of helping patients achieve greater control of their health and live with a chronic condition (24-26). Supporting self-management in patients affected by cancer is based on the principles developed for chronic conditions and has been adapted for the specific needs of patients with cancer. Patients living with cancer experience intensive treatment phases that are punctuated by periods of remission and stable disease. Therefore, need for support fluctuates and interventions should be flexible and tailored to patient's individual situation (22, 23). To date there is a lack of clarity regarding which self-management support components are effective and the optimal approach to patients affected by cancer (22, 27). A systematic review and meta-analysis on SMS effectiveness and components (28), and a scoping review focusing on implementing SMS interventions in clinical practice (29) are presently underway.

Recent studies in Switzerland reveal that patients on active anticancer treatments have unmet supportive care needs (30-33). Osse and colleagues define the need for care as ‘a wish to receive support with regard to an experienced problem’ (34). The manual for ‘Improving Supportive and Palliative Care for Adults with Cancer’ published by the National Institute for Clinical Excellence (NICE) emphasises that not all patients receive needed care and that effective face-to-face communication is essential for high quality care (19). Unmet supportive care needs were also identified in a recent Canadian survey revealing that more than 80% of cancer survivors (one to three years post-treatment) report physical and emotional concerns and approximately a third of individuals seeking help had difficulty getting timely access to support (35). In Switzerland, no national guidance for cancer supportive care exists and we do not know how many patients and/or survivors lack sufficient support when needed. In the absence of national guidelines, international recommendations may serve as important resources and could be applied to help improve clinical practice in Switzerland.

Chapter 1: Thesis Background

Symptom management during systemic cancer treatments: Patient needs

Cancer treatment is becoming increasingly complex due to new oncological medications (e.g. monoclonal antibodies, tyrosine kinase inhibitors, immunomodulatory agents) complementing systemic anticancer treatments. In consequence, health care providers and patients are challenged by a wide array of side-effects and symptoms requiring recognition, monitoring, and management. A study conducted in the UK (including 51 articles with10'092 total participants) revealed that the most prevalent symptoms and problems caused by systemic anticancer treatments are fatigue (mean 90%, range 11-100%), changes in taste and smell (69%, range 12-76%), and difficulty managing everyday tasks (61%, range not reported) (36). The wide ranges in frequency may be explained by individual factors and varied therapy regimens yet underscore the unique nature of individual experiences – suggesting that evaluation should be comprehensive and interventions have to be tailored.

Typically expected symptoms caused by anticancer treatments are frequently investigated and evidence-based recommendations for symptom management for many have been well summarised (37). Most frequently investigated symptoms (in decreasing order) include nausea, vomiting, fatigue, depression, cognitive problems, pain, oral symptoms, problems related to the throat and swallowing, constipation, appetite, and anxiety. (36). Dizziness, gynaecological and urinary symptoms and financial problems are rarely assessed. Patient may express needs for self-management that go beyond the well-known symptoms. For example, patients 60 years and older report a desire for information about their disease/treatment, nutrition, activities of daily living and how to self-manage side-effects at home during systemic cancer therapy (14). A study using qualitative semi-structured interviews with 30 patients revealed that contact with nurses is key for facilitating self-management, becoming familiar with the cancer treatment and its consequences. Importantly, a therapeutic relationship can facilitate patients feeling they are in safe hands thereby reducing anxiety and improving overall well-being during and after cancer treatment (38).

Usual nursing care for self-management support in Swiss cancer outpatient settings

Patients need basic support including receiving relevant information, emotional support, effective communication and symptom management support (15, 19). Such needs are evident when patients are newly diagnosed with cancer, beginning cancer treatments and throughout their cancer trajectory until end of life care. Nurses in Switzerland often use Swiss Cancer League brochures (available in German, French, and Italian) to provide written information to patients and their families (https://shop.krebsliga.ch/). These brochures are detailed and comprehensive. They include information on specific cancers, health behaviour issues (e.g. healthy nutrition), symptom management (e.g. dealing with fatigue, pain), complementary symptom-specific information (e.g. pain diary), and special offerings for patients and caregivers (e.g. courses, rehabilitation). Because these brochures are usually very extensive, it can be challenging for patients to find information that is most needed and relevant for their individual situation. Consequently, many Swiss hospitals have developed brief information leaflets summarising key points and relevant information for a specific diagnosis, concern or a cancer medication. Maintaining up-to-date, evidence-based leaflets poses considerable burden for individual cancer centres. Moreover, such single centre efforts have generated materials of varied detail and quality and may contribute to disparities for patients across centres.

In Switzerland, graduated nurses provide intravenous systemic anticancer treatments and deliver information to patients about anticipated side-effects and explain what patients can do if symptoms occur. Such therapeutic communication follows the treating oncologist's initial discussion regarding treatment and side effects. The nurse interactions regarding systemic therapy is often provided in an '*ad hoc*' manner meaning nurses integrate therapeutic discussions into their existing clinical

routines and demands. Nurses typically cannot schedule an extra consultation so discussions are relatively unstructured and lack a systematic approach. Before the start of the Symptom Navi Pilot Study, nurses from cancer centres randomised to the intervention group participated in focus group discussions. The aim was to gather information on how they support patient symptom self-management during their usual care or consultations. Results showed that all nurses aimed to: i) provide general and tailored information, ii) facilitate patient-centred care to meet patient's individual needs, and iii) document care and information provided. Each centre used different tools and approaches to attain these aims illustrating a large variability of current SMS standards in Swiss oncology centres (39). These findings from focus group interviews confirmed preliminary discussions with Swiss oncology nurses that SMS approaches differ in cancer outpatient centres.

Based on the use of SMS in Swiss cancer outpatient centres, we identified a need for a feasible and useful tool to facilitate communication with patients on symptom self-management. In 2011, the Lindenhofspital in Bern began developing written information leaflets called Symptom Navi Flyers (SN-Flyers) to improve and standardise nurse-led SMS. SN-Flyers are symptom-specific leaflets providing basic information on a specific symptom accompanied by evidence-based interventions to mitigate symptom intensity. The SN-Flyers are written in lay language and summarise the most important information on a symptom in four (A5) pages (example in German in Appendix 4). SN-Flyers are complementary to Swiss Cancer League Brochures and potentially facilitate patient usability because nurses can provide SN-Flyers based on specific patient symptoms. However, simply providing written information is not sufficient for a comprehensive SMS intervention (40). A more standardised approach would include a structured process for introducing SN-Flyers into nurse-led patient consultations, and ultimately, provide training for nurses to implement SN-Flyers into clinical practice via semi-structured SNP consultations. Development and content of the SNP is integrated in the second article included in chapter 5.

Chapter 2: Literature Review

Self-management support

Self-management refers to the abilities and activities a person initiates and performs to manage symptoms and treatment, physical, psychosocial, and emotional problems inherent to a chronic condition or cancer (21). Therefore, SMS is an educational intervention that is part of an ongoing process to facilitate patient self-management behaviour. Self-management comprises sufficient knowledge, adequate skills, and effective confidence to achieve feasible goals (21-23). Importantly, SMS has gained greater attention, is increasingly investigated and several systematic reviews have been published on several key SMS objectives. A structured search in Embase (search date 18.12.2019) using the keywords in Table 1 identified 1962 articles. Notably, 475 articles have been published in the past two years representing a 24% increase since July 2017 (n= 1487 as of July 2017). Limiting the search to review articles identified 96 published citations. Scanning the titles and abstracts of the reviews indicated, 14 were performed on SMS interventions for cancer patients (2010 - 2019). Herein the results of the reviews specific to cancer are synthesised.

Table 1: Keywords used for the data base literature search

Database	Keywords
Embase	('neoplasm'/exp OR (Cancer* OR neoplas* OR oncolog* OR carcino* OR sarcom* OR tumor* OR tumour*):ab,ti) AND ('self care'/de OR 'self medication'/de OR (Self NEAR/3 (manag* OR care OR monitor*)):ab,ti) AND ('nursing intervention'/de OR 'program evaluation'/exp OR 'education program'/de OR 'health program'/exp OR 'patient education'/de OR (program* OR (nurs* NEAR/4 intervention*) OR (nurs* NEAR/3 led)):ab,ti)

Keywords were developed in collaboration with a librarian of the 'bibliothèque universitaire de médecine' (Lausanne, Switzerland)

Overall, the SMS literature is heterogeneous in relation to included cancer diagnose, trajectory/treatment phases, investigated outcomes, terms used to categorise outcomes, and different targeted behaviours for testing effectiveness. The majority of reviews included patients diagnosed with breast cancer (41-44), whereas lung cancer (45, 46), colorectal cancer (44, 47), and prostate cancer (44, 48) were less often represented. In order to frequency of investigation, cancer trajectory phases included survivorship (41, 42, 45, 46, 49, 50), active treatment combined with post-treatment phases (43, 44, 51-53), and during active treatments (22, 47, 54, 55). Very few systematic reviews investigated SMS interventions for patients across different cancer diagnoses who were undergoing active outpatient cancer treatments (55).

The range of investigated outcomes and variety of terms used to categorise results pose challenges to interpreting study results. Regularly investigated outcomes included fatigue (22, 41-43, 45, 49, 56), depression (22, 41, 42, 45), distress (22, 49, 51), anxiety (22, 42), dyspnoea (45), pain (22), insomnia (42), and lymphedema (50). Health related quality of life (HRQOL) was frequently used to report physical, psychological and social outcomes (22, 41, 51, 53, 54). Additional, psychosocial outcomes include emotional functioning (53), emotional problems (48), and self-efficacy (41, 49). Physical functioning (42, 49), functional status (54), and/or functional problems (48) were reported as complementary outcomes in evaluating patient health status. Outcome measures also focused on skills relating to self-management (47), self-care (51), and behaviour change (46). Despite the variety of measured outcomes, the majority of systematic reviews did in fact perform meta-analysis (41-44, 50-53, 56, 57), while others argued that heterogeneity of study interventions/outcomes measured precluded meta-analysis.

Reported effects on measured outcomes were inconsistent, likely due to the diverse intervention content and duration, varied delivery modes (e.g. individual face-to-face coaching or telephone-based interventions), as well as methodological limitations of study design introducing potential bias. SMS interventions achieved better outcomes when they involved multiple components supporting self-management behaviours (41) and when content development was guided by a theoretical framework (51). It remains unclear whether a longer intervention duration or more follow-up SMS

interventions (i.e. dosing) achieve enhanced outcomes (44, 50). Mitigating symptoms (43, 53, 54), the adherence to the recommended behaviour (e.g. practice exercises) (44, 48), patients' behaviour change (44, 46, 48), or HRQOL in general (22, 41, 51, 53, 54) were frequently used to measure intervention effect. Evidence suggests tailored SMS interventions focusing on a specific physical symptom are effective in reducing fatigue (41-43, 45, 56, 57), dyspnoea and depression (45), lymphedema (50), and general physical functioning (48, 49). Further, positive effects have been reported for anxiety (42), distress (51), and emotional problems (48). However, interventions supporting SMS in general cancer outpatient settings to support patients diagnosed with different cancer diagnoses require a broader focus than single symptoms (e.g. physical functioning).

Reported self-management outcomes used different terms to categorise intervention approaches, components, contents, and health care professionals delivering interventions. Categories related to behaviour change techniques (44, 46), psychosocial interventions (49, 56), and multidimensional programmes (consisting of educational, physical, and psychosocial components) (42) were used. Terms frequently used to describe patient self-management behaviour included self-management skills, self-care, and coping ability (47, 51, 57). Generally, intervention characteristics defined desired improvement (outcomes), intervention duration/intensity, and mode for delivering the intervention (22, 41, 42, 44, 47, 52, 53). SMS interventions may be provided face-to-face individual single patient encounters or group format (22, 49), via telephone (51), and increasingly, via web-based applications/platforms (41). Two systematic reviews identified nurses as delivering the intervention (53, 54), whereas most SMS studies employed other health care professional to deliver interventions. Thus, individual nurse-led face-to-face interventions delivered in general cancer outpatient settings were seldom noted in published systematic reviews. The most common comparator for the SMS intervention was usual care. Few studies compared a SMS intervention with a lower intensity/different intervention, or with an attention control group (42).

In summarising systematic reviews to date reveal a lack of SMS guidelines and little clarity on what components work for improving outcomes. Best practices are obscured by varied terminology describing intervention approach and heterogeneity of outcomes. Therefore, in spite of a growing body of research, it is difficult to draw firm conclusions regarding best practices guiding SMS components and approaches to delivering interventions. Further, there is scant data on SMS including patients with different cancer diagnoses being treated in the general outpatient setting. However, evidence suggests that theoretical frameworks are crucial for developing interventions and justifying outcomes for evaluation.

Self-management support is a complex intervention

Supporting self-management requires nurses to change their behaviour from an approach based on providing generic information to a more active, patient-centred approach based on self-management education. Howell and colleagues (22) have developed a self-management education framework comprising eight core elements (Table 2). These core elements encompass characteristics of health care providers as coaches for patients and necessitate tailoring interventions to support and facilitate individual patient skills. The framework explicitly requires trained health care professionals to provide self-management education (Table 2).

Table 2: Self-management education: core elements and educator actions, based on Howell et al (22)

Core elements of self-management education	Educator Actions
Tailored to individual illness and treatment burden, risk	Information provision
Coaching in behaviours by a specially trained instructor*	Coaching: behaviour change, self-monitoring, daily decision making, congnitive refraiming of beliefs
Facilitate patient's confidence (self-efficacy) to manage illness and care	Facilitating: management of stress/emotions, problem solving skills, self-efficacy; goals/action plans
Facilitate patient self-monitoring of tempo/trends of illness for tailoring of behaviours	Facilitating: management of stress/emotions, problem solving skills, self-efficacy
Support patient to develop skills for effective communication with health team	Positive feedback; motivational interviewing
Support development of problem-solving skills and daily decision making	Coaching: behaviour change, self-monitoring, daily decision making, cognitive refraiming of beliefs
Facilitate knowledge and uptake of health behaviours through goal setting and action plans	Information provision; Goals/action plans
Collaborative partnership with health care team use of support	Motivational interviewing

* This framework requires that SMS providing health care professionals to be trained in providing interventions.

Tailoring self-management education to meet patients' individual needs is critical for intervention feasibility yet can be challenging nurses and another health care professionals. Specific self-management support needs depend on the anti-cancer treatment regimen, individual characteristics, co-morbidities (concurrent chronic conditions), and his/her social environment (21, 25, 58, 59). Tailoring demands the clinician collaboration with the patient to identify the relevant information and support the patient in developing expertise to manage their symptoms given the individual context (19, 21-23). Such interactions represent a dynamic, complex process requiring advanced communication and coaching skills. Moreover, contextual factors, such as the outpatient cancer centre environment also plays an important role in facilitating or hindering interventions supporting self-management (60).

Chapter 3: Theoretical frameworks

Frameworks are models to systematically develop, manage, and evaluate interventions. In contrast, theories support the understanding of inter-related concepts to explain relationships between variables. Frameworks and theories can also be called models - especially when they are visualised in graphic or picture format (61).

The Medical Research Council (MRC) framework for complex interventions (62) defines four phases for development, feasibility/piloting, evaluation and dissemination of complex interventions. We decided to use different theoretical frameworks for completing the development phase, structuring the feasibility/piloting and the evaluation phases. The three frameworks used for the Symptom Navi Pilot Study were: the COM-B (Capability Opportunity Motivation – Behaviour) model (6), the Reach Effectiveness – Adoption Implementation Maintenance (RE-AIM) framework (3), and the Theory of Symptom Self-Management (TSSM) (63, 64).

We identified the need for a model to structure the nurse training to ensure consistent SNP application at each participating centre and supporting behaviour change of nurses and fidelity with the SMS training manual. The COM-B model was employed to standardise and evaluate the nurse training to complete the development of the SNP. Therefore, the COM-B model was applied to facilitate first behaviour change on nursing level to empower nurses in supporting patient behaviour change to self-manage symptoms. The RE-AIM framework was employed to evaluate the SNP implementation process including feasibility and piloting as well as exploring the impact of the programme on patient reported outcomes. The strength of this framework is to consider outcomes on individual and organisational level for a comprehensive evaluation of multiple factors potentially impacting the implementation process. The SNP is based on advanced nursing skills to tailor SMS interventions (e.g. semi-structured nurse-led consultations) to patient's needs. The aim of the SNP is to support symptom self-management by using appropriate information leaflets (SN-Flyers) in at least two semi-structured consultations to facilitate patient's perceived self-efficacy for self-management (8). To operationalise patient-reported outcomes related to symptom experience, perceived self-efficacy, and patient self-management behaviour, the RE-AIM framework was complemented with the TSSM. All applied frameworks are summarised in the following paragraphs.

Capability Opportunity Motivation – Behaviour (COM-B) Model

The COM-B model identifies four correlated dimensions (capability, opportunity, motivation, and behaviour) that are crucial for behaviour change (6). The model posits that motivation is influenced by individual capabilities and opportunities that are defined by social and group norms (67). Therefore, motivation is a moderator for individual behaviour. Capabilities and opportunities influence behaviour achievement directly as well as indirectly (via motivation) (see Figure 5, second article, page 36). Capabilities, opportunities, and motivation are targets for changing behaviour. An individual's psychological and physical capacity to perform an activity comprise the capability dimension, whereas opportunities (i.e. social and physical factors) may support or hinder behaviour respectively. Motivation is a moderator and is influenced by individual capacity and contextual opportunities. Motivation incorporates reflective and automatic processes inherent in analytical decision-making as well as emotional responses (6). The COM-B model consider successful behaviour change depends on involved individuals and environmental factors that support/hinder a specific behaviour. The Theoretical Domains Framework (TDF) complements the COM-B model to facilitate intervention development and reporting (68).

We used COM-B components and TDF constructs to guide the structure of the nurse training procedures and content. The synthesis aims to support nurses in adopting the SNP (i.e. six key elements of semi-structured consultations) and to consider potential adaptations needed to meet workflows at participating centres (Table 4).

Table 3: Mapping the COM-B model to training content

COM-B components		TDF domains	Training content
Capability	Psychological	Knowledge Skills Memory, attention, and decision process Behavioural regulation	Initial training: Introduce the SNP: SN-Flyers content, techniques on SMS, patient education, procedures for semi-structured consultations Follow-up training: clarify questions
	Physical	Skills	Not applicable
Opportunity	Social	Social influences	Acknowledge local competencies
	Physical	Environmental context and resources	Place where consultations will be employed, collaboration in nursing team
Motivation	Reflective	Social / professional role & identity Beliefs about capabilities Optimism Beliefs about consequences Intentions Goals	Collaboration with oncologists Documentation of the intervention Expected benefit for patients Facilitating conversations with patients
	Automatic	Social / professional role & identity Optimism Reinforcement Emotion	Follow-up training based on nurses' questions / concerns on feasibility and acceptability of the SNP

Abbreviations: COM-B, capability, opportunity, motivation, behaviour; SN-Flyers, Symptom Navi Flyers; SNP, Symptom Navi Programme; TDF, Theoretical Domains Framework

The COM-B model is applicable for structuring the necessary procedures (i.e. nurse SNP training) to implement a new intervention at different cancer outpatient centres. However, to define and operationalise the outcomes for every RE-AIM dimension requires a third framework – the Theory of Symptom Self-Management.

Reach Effectiveness – Adoption Implementation Maintenance (RE-AIM) framework

Implementing a complex intervention in different clinical settings demands iterative procedures - starting with an accurate description of the intervention and identified components which may need to be adapted in different settings (62, 65). It is also important to evaluate the implementation process to recognise how components work in real life and what adaptations nurses make apply when delivering the intervention. Successful implementation depends on serval factors. Health care providers must find the intervention acceptable and be willing to deliver it as intended. Additionally, effective implementation also depends on a benevolent and supportive environment.

The RE-AIM framework includes five dimensions for a comprehensive evaluation of the implementation process and has been used widely for nearly 20 years (66). Reach and effectiveness dimensions operate at the individual level meaning the people who potentially benefit from the intervention. The other dimensions (adoption, implementation, and maintenance) focus on staff and setting of the intervention (66). Table 3 provides definitions of the five RE-AIM dimensions in relation to the SNP. An overview of the outcomes based on the RE-AIM framework is included in the study protocol (7).

Table 4: Definition of RE-AIM dimensions related to the SNP

Dimension	Focus at level	Definition
Reach	Individual	The absolute number, proportion, and representativeness of patients willing to use the SNP
Effectiveness	Individual	The impact of the SNP on patient-reported outcomes and potential negative effects.
Adoption	Organisational	The absolute number, proportion, and representativeness of cancer centres and nurses willing to employ the SNP.
Implementation	Organisational	The fidelity to the key-elements of the semi-structured consultations defined in the training manual; the consistency of delivery as intended, adaptations made, time used for consultations.
Maintenance (not included in pilot study)	Individual and organisational	At the individual level: The long-term effects of the SNP on outcomes after 6 or more months after the most recent semi-structured consultation. At the organisational level: The extent to which the SNP becomes institutionalised or part of the routine practices.

In the Symptom Navi Pilot Study, the maintenance dimension of the RE-AIM framework was not included as it relates to long-term evaluation of the program what is not feasible within the context of a pilot study.

Theory of Symptom Self-Management (TSSM)

The effectiveness dimension of the RE-AIM framework aims to evaluate the impact of SNP at the patient individual level. The TSSM was chosen to operationalise patient reported outcomes because it integrates a nursing symptom management theory (Theory of Unpleasant Symptoms TOUS) and Bandura's self-efficacy theory (58, 69) to measure perceived self-efficacy for self-managing fatigue. The TOUS emphasises that symptoms are multidimensional, influenced by individual characteristics, and affect patient functional status (70). Bandura proposes that individuals who believe they can self-manage their symptoms (termed self-efficacy) achieve better functional outcomes. The mediating function of self-efficacy is central to the TSSM which suggests that SMS interventions should facilitate self-efficacy for a target behaviour. This position is consistent with the self-management education framework published by Howell and colleagues (22).

The TSSM assumes that patient self-management behaviour will be affected by his/her symptom severity and burden as well as perceived self-efficacy for self-management behaviour. Consequently, patient physical status will be affected by co-morbidities, cancer treatment and self-management behaviour (58, 64). An initial evaluation of the TSSM investigated correlations between patient characteristics, cancer related fatigue (and other concomitant symptoms) and perceived self-efficacy for fatigue self-management. Analysis revealed that more comorbidities ($t = -7.47$), increased cancer-related fatigue severity ($t = -5.30$) and more symptoms ($t = -2.71$) predicted lower physical functional status (63).The observed relationship was re-tested confirming that perceived self-efficacy for fatigue self-management partially mediated the relationship between fatigue severity and physical functional status in patients affected by cancer (71). Several studies have used the TSSM to examine self-management behaviours including patients after surgery for lung cancer (64, 71-74).

The SNP was developed for patients with any cancer diagnosis, and therefore, evaluating its effectiveness cannot focus on a single symptom (i.e. fatigue). However, we assumed that a circular relationship exists between symptom severity, perceived self-efficacy, and self-management behaviour and these aspects will be important for any symptom self-management caused by cancer/treatment. Based on this assumption, we posit the SNP could affect the proposed circular relationship and ultimately improve patient physical functional status during active anticancer treatments (Figure 1).

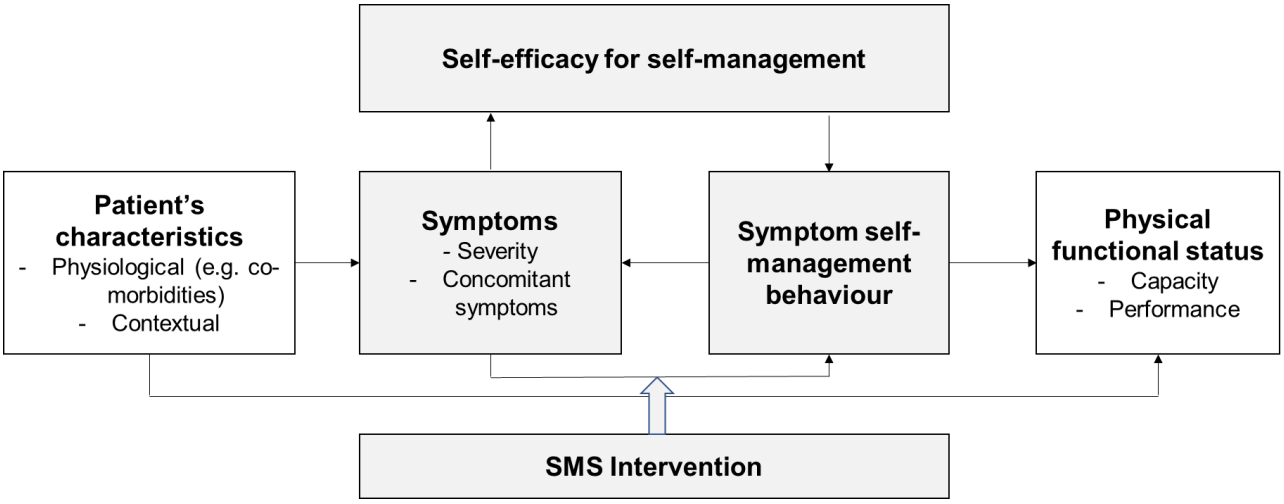

Figure 1: **Model for operationalising the outcomes of the Symptom Navi Pilot Study based on the TSSM**

Based on the RE-AIM framework, symptom self-management behaviour, and ultimately, patient physical functional status will depend on delivering the intervention as intended and therefore outcomes on individual and organisational level should be assessed and evaluated. The Methods chapter describes how the selected frameworks were applied in the pilot study.

Objectives of the doctoral thesis

By the end of 2015, several cancer outpatient centres expressed interest in implementing the SNP program at their centres. Initial evaluations showed the SNP was highly accepted and deemed helpful by patients and health care professionals in standardising SMS (1, 2, 75). Implementing the SNP is challenging for nurses as it demands behaviour change to tailor every intervention. Nurses are expected to shape interventions based on patient needs and the prescribed anticancer regimen while concurrently setting collaborative priorities and considering a variety of outcomes. According to the Medical Research Council (MRC), the SNP is considered a complex intervention because it integrates multiple interacting components, requires challenging behaviours, includes a variety of outcomes, and demands intervention tailoring. Accordingly, effectiveness and safety should be tested prior to disseminating a complex intervention into widespread practice (62).

Evidence suggests that implementing a new program into clinical practice requires stakeholders' involvement and a systemic approach (76). Therefore, we designed a multi-method pilot study (Symptom Navi Pilot Study) to comprehensively evaluate the implementation process. This doctoral thesis focuses on four objectives decided at the intermediate thesis exam in March 2017:

1) Evaluate feasibility regarding patients' accrual and retention rates,
2) Evaluate nurses training,
3) Test preliminary effectiveness of the SN©P,
4) Explore nurses' fidelity to training manual.

Therefore, this doctoral thesis work informed a "go versus no go" decision for proceeding with a subsequent large, multinational study to formally test SNP effectiveness (77).

Chapter 4: Methods

Guided by the RE-AIM framework, this thesis evaluates preliminary SNP effectiveness and aspects relating to dimensions of reach, adoption, and implementation embedded in the Symptom Navi Pilot Study. The thesis includes the RE-AIM dimensions: reach (accrual and retention rates), effectiveness (exploring expected impact on patient-reported outcomes), adoption (evaluating nurses training), and partly implementation (evaluating nurses' fidelity to the training). We published the study protocol in the British Medical Journal-Open (BMJ-open) and include it to describe the Methods chapter. However, the methodology addressing the dimension of reach (i.e. accrual and retention rates) is only briefly described in the published study protocol. Therefore, an overview on the evaluation of reach has been added before including the study protocol of the Symptom Navi Pilot Study in this chapter. The application of theoretical frameworks (RE-AIM and TSSM) for the Symptom Navi Pilot study completes the introduction of this chapter.

It is challenging to include every RE-AIM dimension to evaluate the implementation process of a new intervention. As such, studies rarely apply all RE-AIM dimensions. A pragmatic approach is recommended for feasibility studies (78). Best practices recommend pilot-testing newly developed complex interventions to evaluate feasibility of intervention procedures, estimating recruitment and retention, and determining sample size for an appropriately powered study (62). A structured pilot study evaluating SNP effectiveness is important for identifying potential problems with study design/procedures, intervention components in measuring outcomes and drawing valid conclusions on findings. For example, an important question may be whether or not acceptance of the training content is crucial for effective SNP implementation at different centres. Additionally, do patient reported outcomes depended on how nurses applied the SNP in a real-life context? We considered a variety of potentially confounding factors by merging the RE-AIM and TSSM to operationalise targeted outcomes (Figure 2). Detailed description of outcome assessments and instruments utilized for the evaluation are reported in the published study protocol.

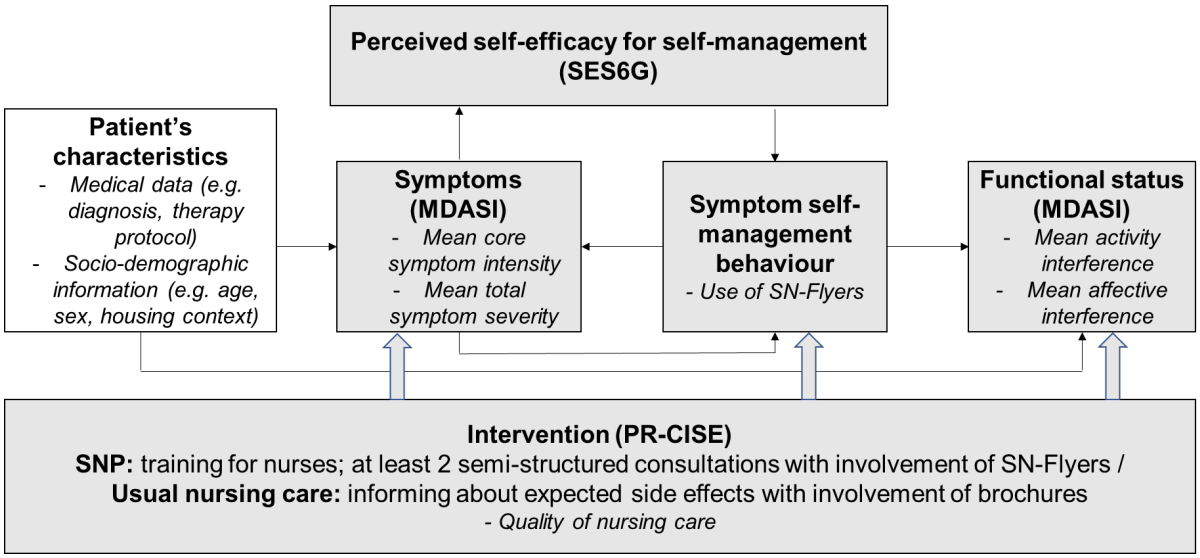

Figure 2: Investigated outcomes operationalised based on the RE-AIM framework and merged with the TSSM

Abbreviations: MDASI, MD Anderson Symptom Inventory; PR-CISE, Patient-reported Chemotherapy Indicators for Symptoms and Experience; SES6G, Self-efficacy for Chronic Disease 6 item Scale; SN-Flyers, Symptom Navi Flyers; SNP, Symptom Navi Programme.

The reach dimension of the RE-AIM framework was assessed by examining patient accrual and retention rates. The accrual rate was defined by the proportion of eligible patients who were included in the Symptom Navi Pilot Study (both groups). The retention rate was defined as the proportion of included patients in the intervention group who received the intervention as intended (7). The accrual rate is an indicator of feasibility for patient recruitment in a future, planned full-powered clinical trial.

To deliver the intervention as intended, each included patient received an initial semi-structured consultation at the onset of his/her first-line systemic treatment, and at least one follow-up consultation during his/her cancer treatment at the participating centre. The first consultation had to take place between one week before the first treatment was provided and the initial day of the treatment at the centre. We selected a one-week period because we knew that at some participating centres, dedicated nurse-led appointments were scheduled to inform patients about procedures and expected side-effects of the planned treatment. We considered that nurses at participating centres could integrate the first semi-structured SNP consultation within their routine procedures at these designated appointments. The SNP intervention is described in detail in the second published article integrated in the chapter Results.

Study Protocol for Symptom Navi Pilot Study (first article)

Implementation of the Symptom Navi© Program for cancer patients in the Swiss outpatient setting: A study protocol for a cluster randomised pilot study (Symptom Navi© Pilot Study)

Marika Bana[1,2], Karin Ribi[2,3], Susanne Kropf-Staub[4], Sabin Zürcher-Florin[4], Ernst Näf[5], Tanja Manser[6], Lukas Bütikofer[7], Felix Rintelen[7], Solange Peters[8], Manuela Eicher[2,8] On behalf of the Symptom Navi© Pilot Study Group

Affiliations:

[1] HedS-FR, School of Health Sciences, Fribourg, Switzerland; [2] Université de Lausanne, Faculté de biologie et médecine, Institut de formation et de recherché en soins IUFRS, Lausanne, Switzerland; [3] International Breast Cancer Study Group (IBCSG), Bern, Switzerland; [4] Lindenhofgruppe, Bern, Switzerland; [5] Solothurner Spitäler AG, Department of Practice Development in Nursing, Olten und Solothurn, Switzerland; [6] Fachhochschule Nordwestschweiz, Hochschule für Angewandte Psychologie, Olten, Switzerland; [7] Universität Bern, CTU, Bern, Switzerland; [8] CHUV, Department of Oncology, Lausanne, Switzerland

Corresponding author:

Manuela Eicher: manuela.eicher@chuv.ch

IUFRS, SV-A Secteur Vennes, Route de la Corniche 10, 1010 Lausanne, Switzerland

Tel: +41 21 314 87 60

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Abstract

Introduction Self-management interventions show promising results on symptom outcomes and self-management behaviours. The Symptom Navi© Program (SN©P) is a nurse-led intervention supporting patients' symptom self-management during anti-cancer treatment. It consists of written patient information (Symptom Navi© Flyers), semi-structured consultations, and a training manual for nurses.

Methods and Analysis This pilot study will evaluate the implementation of the SN©P based on the RE-AIM (Reach Effectiveness – Adoption Implementation Maintenance) framework at Swiss outpatient cancer centres. We will use a cluster-randomised design and randomise the nine participating centres to the intervention or usual care group. We expect to include 140 adult cancer patients receiving first-line systemic anti-cancer treatment. Trained nurses at the intervention clusters will provide at least two semi-structured consultations with the involvement of Symptom

Navi© Flyers. Outcomes include patients' accrual and retention rates, patient-reported interference of symptoms with daily functions, symptom burden, perceived self-efficacy, quality of nursing care, nurse-reported facilitators and barriers of adopting the program, nurses' fidelity of providing the intervention as intended, and patients' safety (patients timely reporting of severe symptoms). We will use validated questionnaires for patient-reported outcomes, focus group interviews with nurses and individual interviews with oncologists. Linear mixed models will be used to analyse patient-reported outcomes. Focus group and individual interviews will be analysed by thematic analysis.

Ethics and Dissemination The Symptom Navi© Pilot Study has been reviewed and approved by Swiss Ethic Committee Bern (KEK-BE: 2017-00020). Results of the study will be disseminated in peer-reviewed journal and at scientific conferences.

Trial Registration numbers NCT03649984 and SNCTP000002381

Résumé:

Introduction Les interventions d'autogestion présentent des résultats prometteurs tant au niveau des effets sur les symptômes que des comportements en matière d'autogestion. Le Programme Symptom Navi© (« Symptom Navi© Programme » ou SN©P) est une intervention conduite par le personnel infirmier pour aider les patient·e·s suivant un traitement anticancéreux à gérer leurs symptômes. Ce programme comporte des informations écrites (dépliants Symptom Navi©), des consultations semi-structurées et un manuel de formation destiné audit personnel.

Méthodes et analyses La présente étude pilote vise à évaluer l'implémentation du SN©P sur la base du cadre RE-AIM (Reach Effectiveness – Adoption Implementation Maintenance, c'est-à-dire portée, efficacité, adoption, mise en œuvre et maintien) dans des centres d'oncologie ambulatoire en Suisse. Nous utiliserons une conception randomisée en grappes et répartirons aléatoirement les neuf centres impliqués en les attribuant au groupe d'intervention ou au groupe recevant les soins usuels. Nous prévoyons d'inclure dans l'étude140 patient·e·s adultes subissant un traitement anticancéreux systémique de première ligne. Des infirmières et infirmiers diplômés réaliseront auprès des grappes d'intervention au moins deux consultations semi-structurées en utilisant les dépliants Symptom Navi©. Les résultats comprendront les taux de recrutement et de rétention des patient·e·s, leur compte rendu de l'interférence des symptômes avec les fonctions de la vie quotidienne, le poids de leurs symptômes, leur perception de leur propre efficacité, la qualité des soins infirmiers, les facteurs favorisant et entravant l'adoption du programme du point de vue du personnel infirmier, la réalisation fidèle par ce dernier de l'intervention telle que prévue ainsi que la sécurité des patient·e·s (signalement des symptômes graves en temps utile). Nous recourrons à des questionnaires validés pour répertorier les résultats rapportés par les patient·e·s, à des entrevues avec les infirmières et infirmiers dans le cadre de groupes de parole de même qu'à des entretiens individuels avec les oncologues. Des modèles linéaires mixtes serviront à analyser les résultats consignés par les patient·e·s. Les entrevues communes et individuelles feront l'objet d'une analyse thématique.

Ethique et diffusion L'étude pilote consacrée au programme Symptom Navi© a été examinée et approuvée par la Commission cantonale bernoise d'éthique de la recherche (CCER BE: 2017-00020). Les résultats seront diffusés dans des publications revues par les pairs et lors de conférences scientifiques.

Strengths and limitations of this study

- One strength of the study protocol is its integration in a larger research and development program: After several steps of development and content validation of the SN©P, we now conduct a pilot implementation study including the evaluation of preliminary effectiveness of the SN©P.
- This pilot study explores the implementation of the Symptom Navi© Program (SN©P) based on the RE-AIM (Reach Effectiveness – Adoption Implementation Maintenance) framework.

- We apply a cluster-randomised design with nine Swiss outpatient cancer centres allocated to the implementation of the SN©P or usual care complemented with qualitative methods.
- We assess patient-reported outcomes over 16 weeks to explore effect sizes for calculating the sample size for a full powered cluster RCT.
- Long-term impact and maintenance of the SN©P are not included in this pilot study and will need further investigation.

Keywords

Nurses/nursing / self-efficacy / RE-AIM framework / symptom self-management / implementation research /

Introduction

Anti-cancer treatments are increasingly provided in the outpatient setting (12, 79). Cancer outpatients report substantial symptom burden related to disease and side effects of anti-cancer treatments (80, 81). Symptom intensity usually increases between treatment applications (82), when patients are at home and health care providers are not immediately available. Cancer patients report unmet supportive care needs to learn how to self-manage their symptoms (83).

Symptom self-management is a dynamic process of integrating adequate behaviours and strategies to prevent, relieve or decrease symptoms (58). This process includes symptom and treatment management, dealing with the emotional and physical consequences of disease and treatment, and adapting life roles (20, 84). Self-management behaviours are based on several core competencies including problem solving, decision making, communication with health care professionals, tailoring recommendations to the individual situation, and taking action (21, 85, 86). There are two core elements of self-management interventions that are most frequently applied: 1) tailoring the content of the intervention to patient's needs, and 2) facilitating patient's self-efficacy by using goal setting and action planning (22).

Self-efficacy is a subjective belief that a person can achieve a planned task or action, even if it becomes challenging (69). Fostering patient self-efficacy is a pivotal core element because of its impact on patient self-management behaviours (22, 23). Self-efficacy is a mediator for a persons' ability to acquire self-management behaviours (69, 85) and to manage symptoms (21, 84). Therefore, supporting self-efficacy might play a key role for self-management interventions and successful self-management behaviours.

It is still unclear what combination of core-elements makes a self-management intervention effective (22) because the format, content and outcomes of the investigated interventions are very heterogeneous (22, 41, 46, 53, 87). The heterogeneity of intervention and outcomes preclude meta-analyses in systematic reviews and this has led to mainly narrative syntheses (22, 47, 49, 53, 87). Frequently reported effects of self-management interventions were decreased symptom intensity or burden (e.g. fatigue, depression, anxiety, distress) (22, 41, 42, 48, 49, 53, 54), increased quality of life (22, 41, 42, 54), better physical functioning (87) or performance (53), and improved self-efficacy (41, 47, 49, 53). However, two systematic reviews reported ambiguous effects on quality of life (47, 48) and self-efficacy (48). Further research should clarify whether the intervention's content was ineffective, or whether contextual factors (e.g. nurses' workload) prevented the intended effects.

Important aspects of interventions supporting self-management remain scarcely investigated. A majority of recently published systematic reviews focused on self-management interventions during survivorship or the rehabilitation phase of cancer patients (41, 42, 46, 48, 49, 87), and a minority on interventions during active treatment phase (47, 54, 88). Studies rarely included a description of how to support patients in communicating their symptoms and asking for support when needed (89), or at what moment they have to make contact the care team if a symptom becomes severe (90). Trained health care professionals who work collaboratively within a multidisciplinary team should provide support and guidance about care seeking (22, 23). In most studies, health care professionals other than nurses provided the interventions for supporting self-management (47, 48, 54).

Nurses are in close contact with cancer patients and should play a key role in supporting symptom self-management (83, 91, 92). In a randomised controlled trial, a nurse-led intervention for cancer patients during chemotherapy was associated with decreased patient-reported problems (92), and showed reduced symptom intensity/burden, improved self-efficacy and enhanced self-management behaviours (93). However, nurse-led interventions supporting symptom self-management are challenging and complex because they require a structured but flexible behaviour of nurses in tailoring the intervention to individual situations (23, 55, 62). Implementation of such complex interventions should include a thorough analysis of contextual factors (e.g. organisational readiness for change, workload) and take into account the resources needed to apply the intervention (94, 95).

In 2011, nurses from a Swiss hospital initiated the Symptom Navi© Program (SN©P) for patients during anti-cancer treatments to address the need of cancer patients asking for more information about symptom management (30, 31). The SN©P has received attention from other Swiss cancer centres who are interested to implement this program.

Aim and objectives

The overall aim of this study is to evaluate the implementation of the SN©P at Swiss outpatient cancer centres and to explore its preliminary effectiveness compared to usual care. Implementation of newly developed interventions depend on organisational structures and the collaboration of involved stakeholders (96). Therefore, we based the evaluation of the implementation process on the RE-AIM (Reach Effectiveness – Adoption Implementation Maintenance) framework (3, 4, 97). This five-dimension framework considers outcomes on individual and organisational level. The *Maintenance* dimension cannot be addressed in a pilot study.

Patients' perceived self-efficacy is associated with self-management behaviour, symptom outcomes, and daily functioning (98). The primary objective is to explore the impact of the SN©P on patients' symptom interference with their daily functions (affective and activity) compared to usual care.

Secondary objectives are to:

1. Assess accrual and retention rates of patients (Reach);
2. Investigate the impact of the SN©P on patient symptom severity and burden, and their self-efficacy (Effectiveness);
3. Explore barriers and facilitators (e.g. work-related factors, available resources) of adopting the SN©P in the outpatient cancer centres (Adoption);
4. Explore nurses' fidelity to the SN©P training manual within daily routines, and estimate needed resources to implement the SN©P (Implementation);
5. Explore patients' evaluation on nurses' support for symptom management (Implementation).

Methods and analysis

Design

We will apply a cluster randomised design with two parallel arms complemented with qualitative methods. The unit of randomisation is the participating outpatient cancer centre with each centre representing a cluster. A cluster-randomised design was chosen to avoid contamination between the intervention and control groups (99). Cluster-randomised trials need thorough sample and cluster size estimations (100), which are based on assumptions about the relevant effect size, recruitment potential and intra-cluster correlation; because reliable information on these parameters is not available, we decided to conduct a pilot study based on a sufficient but feasible sample size. We will use this pilot study to estimate effect sizes and sample size needed for future studies, and to monitor patient safety (101). For the evaluation of the RE-AIM dimensions *Reach* and *Effectiveness,* we will mainly apply quantitative methods; for the dimensions *Adoption* and *Implementation,* we will use qualitative methods.

Setting and eligibility criteria

The study will take place at nine outpatient cancer centres in the German-speaking parts of Switzerland. Cancer centres providing systemic outpatient anti-cancer treatments (chemo-, targeted-

, immune-, and hormonal therapies) will be eligible. We will exclude outpatient cancer centres where a former version of the SN©P is already implemented. Eligibility criteria for patients are listed in Table 5.

Table 5: Eligibility criteria for patients

Inclusion criteria	Exclusion criteria
• 18 years and older • Newly diagnosed with any early or advanced/metastatic cancer disease within 15 weeks of providing informed consent • Scheduled for a first-line anti-cancer treatment	• Insufficiently literate in German • Diagnosed with a recurrence of cancer disease • Solely treated by surgical and radiation therapy • Receiving complementary care by a professional palliative care team • Already participating in another psychosocial study

Registered and regularly employed nurses who have worked for at least one year in cancer care will provide the SN ©P. Physicians with at least one-year experience in oncology will be involved to assess the acceptance of the SN©P at an institutional level.

Intervention: Symptom Navi© Program

The SN©P is a nurse-led intervention to facilitate cancer patients' symptom self-management including semi-structured consultations with the involvement of symptom-specific information leaflets (Symptom Navi© Flyers). We outlined in the nurse-training manual the delivery of the consultation and the use of flyers. The development of the SN©P was guided by patient education principles considered effective in patients with chronic health conditions; such as building partnership with patients, focusing on patients' needs (86, 102) and self-management strategies (21, 84, 85). The development, content, and evaluation of the SN©P is detailed in a separate manuscript (Bana et al, in preparation).

Symptom Navi© Flyers

Symptom Navi© Flyers (SN©Flyers) are written leaflets about sixteen commonly occurring symptoms that patients may experience with anti-cancer treatments (Table 6). Each SN©Flyer describes one symptom, guides patients to rate the severity of the symptom (mild, moderate, severe), and provides easy understandable evidence-based recommendations for symptom relief and management. If a patient perceives a symptom to be severe, they are asked to immediately contact the treating outpatient centre. During the development phase of the SN©Flyers, the contents were evaluated by 48 health care professionals and patients using the Item Content Validity Index (I-CVI) (103) achieving an excellent I-CVI of 0.9 (75). In addition, ten cancer patients who used the SN©Flyers, confirmed the utility of the recommendations for self-management and the benefit of semi-structured nurse-led consultations, assessed with semi-structured interviews (1).

Semi-structured nurse-led consultations

Nurses will provide two semi-structured consultations with all patients starting a first-line systemic anti-cancer treatment, tailored to the patient's treatment protocol and expected side effects. These consultations are structured along six key-elements: 1) preparing the semi-structured consultation and choosing relevant SN©Flyers, 2) evaluating patient's willingness and motivation for a consultation, 3) providing information on common side effects with the SN©Flyers, 4) introducing symptom self-management, 5) facilitating symptom self-management, and 6) documenting the consultation.(2) Patient's willingness will be assessed by asking his consent for the consultation. The interpretation of patient's motivation will be based on the active participation and being attentive during the conversation. Nurses will have to structure the key-elements according to patient's needs, often leading to circular and iterative conversation-sequences (21, 86). While the first semi-structured consultation will focus on explaining expected side effects and how to use the SN©Flyers at home, all following consultations will explicitly focus on a patient's individual situation and needs. Nurses may provide additional written information as available at their centres and will decide on whether or not further consultations are needed. The SN©P is an intervention that aims to stimulate

patient's self-management of symptoms and complements usual care, which mainly focuses on information provision. Differences between centres regarding information provision might be a bias. To reduce this bias, we will record all additional information material delivered at each centre and report them descriptively (brochures, leaflets). Motivational interviewing techniques (resisting the 'righting reflex', understanding patient's motivation, listening with empathy, and empowering the patient) will be used to enable patient's active participation during the conversation, to support patient's self-efficacy and to facilitate behavioural changes, if needed (104). Patients will be invited to ask for additional SN©Flyers if they desire more information.

Table 6 Available SN©Flyers and timing of semi-structured nurse-led consultations

Available SN©Flyers	**Timing of semi-structured nurse-led consultations**
Leaflets for symptom self-management: - Alopecia - Anxiety -Breathlessness - Diarrhoea - Emesis and nausea - Fatigue - Increased susceptibility: infections and bleeding - Irradiated skin - Loss of appetite - Inflamed oral mucosa - Obstipation - Pain - Peripheral neuropathy - Sexuality - Skin alteration: feet and hand - Skin alterations related to target therapies	**First semi-structured consultation:** All patients will be provided with the complementary leaflets marked with * and approximately three symptom-specific SN©Flyers based on most expected side effects in line with planned treatment protocol; this consultation takes place during the first treatment application at the outpatient cancer centre. **Second semi-structured consultation:** Patients will be provided with complementary SN©Flyers based on their experienced symptoms and needs. This consultation takes place during the second treatment application at the outpatient cancer centre.
Complementary leaflets: - Complementary interventions to reduce pain - General information on SN©Flyers* - Information on Oxaliplatin - List of all available SN©Flyers* - Pain relieve by medication - Support at home (useful addresses)	

Legend: SN©Flyers: Symptom Navi© Flyers

Training for nurses

The two trainers are members of the research team that developed the training courses, hold a master's degree in nursing science, and are senior lecturers. Nurses will be trained with two standardised training courses (in total 6 hours of training) based on a training manual that has been validated by a steering committee including two clinical experts for oncology nursing, a nursing manager, and two researchers. Details about the content of the trainings are described in Table 7. Between the initial and the follow-up training, nurses will practise semi-structured consultations using the SN©Flyers according to the initial training and the training manual. Additionally, nurses will receive a handbook and pocket cards to facilitate the implementation of semi-structured consultations within their daily routines. Pocket cards provide nurses with concrete examples how to guide the communication during the consultations based on motivational interviewing techniques. Nurses will use the pocket cards during consultations. The follow-up training will address nurses' experience with the SN©P, as well as questions and potential challenges that might have occurred during the semi-structured consultations.

Control: Usual nursing care supporting self-management of symptoms

Nurses at the control centres will provide symptom management support according to their usual practice. This generally includes providing oral information about expected side effects of treatments, handing out written information as available at the centre (e.g. pharmaceutical and Swiss Cancer League brochures), and getting in touch with patients by phone calls, if needed.

Table 7 Objectives and content of SN©P training courses

Training and duration	**Objective**	**Content**
Initial training: about 4 hours	Introduce SN©P	Self-efficacy Symptom self-management Nurse-patient communication Strategies for selecting appropriate SN©Flyers How to conduct semi-structured consultations according to the six key-elements* Motivational interviewing techniques
Follow-up training: about 2 hours	Reinforce acquired knowledge / skills	Answering nurses' questions regarding their experience with providing the semi-structured consultations embedded in discussions and role plays

Legend: SN©Flyers: Symptom Navi© Flyers (written information leaflets for patients); *six key elements: 1) preparing the semi-structured consultation and choosing relevant SN©Flyers, 2) evaluating patient's willingness and motivation for a consultation, 3) providing information on common side effects with the SN©Flyers, 4) introducing symptom self-management, 5) facilitating symptom self-management, and 6) documenting the consultation

Outcomes

Outcomes will be based on the RE-AIM framework and represent individual and organisational levels. We will assess patient accrual and retention rates (*Reach*); evaluate the impact of the SN©P on patient reported outcomes (*Effectiveness*); explore barriers and facilitators at participating centres to deliver the intervention (*Adoption*); evaluate nurses' fidelity to the training manual in routine clinical practice and patients' evaluation on nurses' support for symptom management (*Implementation*).(3) Outcomes addressing effectiveness will be based on the Theory of Symptom Self-Management (TSSM) (58, 64). The TSSM addresses five patient-related dimensions: 1) perceived self-efficacy, 2) current symptoms, 3) symptom self-management behaviours, 4) demographic and psychosocial characteristics, and 5) functional status (performance outcomes). This framework considers self-efficacy as a mediator between symptom intensity and patients' functional status. An overview of used instruments to assess patient reported outcomes are provided in Table 8, and an overview of all study outcomes, data collection methods and assessment schedule are provided in Table 9.

Reach

Patients' characteristic data will include medical (age, gender, diagnosis, co-morbidities, pharmaceutical information of treatment, and Karnovsky index) and socio-demographic information (mother tongue, housing context, highest education degree). Accrual and retention rates of patients' participation in the study will be obtained by recruitment logs completed at each site.

Effectiveness

The main outcome of interest will be the mean change in symptom interference with daily functions from baseline (i.e. before treatment starts) to 16 weeks after baseline. The rationale for the primary outcome is based on a previous study using the TSSM reporting that patients' functional performance increased after nurse-led interventions on symptom self-management support (64). Number and type of experienced symptoms depend on cancer type and treatment (105). We therefore chose a period of 16 weeks assuming that most patients are still under treatment. We also assume that the SN©P might affect patient's estimation on symptom interference over this period, because patient's positive attitude for self-management has been shown to be associated with increased physical, emotional, and functional well-being over six months (106). Other outcomes will

include mean changes in symptom intensity, perceived self-efficacy and quality of nursing care assessed four times over a period of 16 weeks. The following outcomes to assess effectiveness will be used:

- Symptoms severity, their interference with daily functioning and symptom burden will be assessed by the validated German version of the *MD Anderson Symptom Inventory* (MDASI) (107). The MDASI contains two dimensions: 1) the severity of thirteen common symptoms, and 2) the interference of these symptoms with daily function on an activity and an affective sub-dimension. The dimensions symptom severity and symptom interference summarise an overall symptom burden score.
- Perceived self-efficacy will be assessed with the validated German version of the *Self-Efficacy for Managing Chronic Disease questionnaire* (SES6G) (108). We added an item asking, 'How confident do you feel that you can manage your symptoms to be able to do things you would like to do?' This general question on perceived self-efficacy complements the more specific items of the SES6G (e.g. self-efficacy for managing fatigue or pain).

Depressive moods might affect a person's belief to accomplish a desired behaviour or to achieve a target outcome (self-efficacy) (109). To control for the emotional state of the patients, we added a one-item Visual Analogue Scale on mood asking 'how do you rate your mood during the last two weeks?' (110).

Table 8 Instruments used to assess patient-reported outcomes

Instruments (RE-AIM dimension)	**Outcomes**	**Scale**	**Validity / reliability**
MDASI (effectiveness)	13 items on symptoms, and 6 items on symptom interference with daily functions	11-point Likert-scale, 0 = not present and 10 = as bad as you can imagine	Developed for cancer setting German version: Cronbach alpha 0.82 (symptom intensity) and 0.84 (interference)(107)
SES6G (effectiveness)	6 items on patient's perceived self-efficacy	10-point Likert-scale, 1 = not at all confident and 10 = totally confident	Developed for chronic conditions, applied in cancer settings German version: Construct validity r=0.578, p<0.001; internal consistency: Crohnbach alpha 0.93(108)
LASA Mood Scale (effectiveness)	1-item: emotional well-being	Visual analogue scale (100mm), 0 = happy 100 = miserable	Concurrent validity between LASA Mood scale and a comprehensive 28 item adjective checklist (Bf-S) was acceptable (median r=0.6, p<0.001) with breast cancer patients, and has proven to be valid for emotional distress screening(111)
PR-CISE (implementation)	5 items on patient's experience of nurse-led supportive care	Yes; somewhat; no	Developed for chemotherapy setting;(91) translation of items into German for study: validation has to be confirmed.

Legend: MDASI: MD Anderson Symptom Inventory; SES6G: Self-efficacy for managing chronic disease; LASA: linear analogue self-assessment; PR-CISE: Patient-reported chemotherapy Indicators of Symptoms and Experiences

Adoption

We will assess the characteristics of participating outpatient cancer centres and nurses (i.e. specialised cancer centre, nurses' formation, number of employed nurses and oncologists at each intervention centre, average number of delivered anti-cancer treatments per day, number of treated patients at the centre per year, information leaflets usually delivered to patients).

We will conduct a first focus group interview with nurses before they will be trained for the SN©P to learn about the current symptom self-management support and handling of written information at

each intervention centre. A second focus group interview (after last patient is out of study at the centre) will be conducted with those nurses who provided the intervention to assess perceived barriers and facilitators (e.g. work-related factors, available resources) for adopting the SN©P within daily routines (figure 3).

Interview guidelines for semi-structured focus groups will be based on Morgan (112).

Implementation

To evaluate the success of the implementation we will assess:

1) Acceptance and appropriateness of the nurse-training course by using a 5-item paper and pencil questionnaire based on the training manual. We developed five questions regarding content and acceptability using 7-point Likert scales rated from 1 (not at all) to 7 (greatest possible). Two open-ended questions for narrative feedback on both training courses complement the Likert scales. To assess potentially influencing work-related factors for implementing the SN©P into practice, we added the Work-related sense of coherence (Work-SoC) scale (113). The Work-SoC scale is a 9-item validated screening instrument for assessing employees' perceived quality of work situation on three subscales: comprehensibility, manageability and meaningfulness (113).
2) Acceptance and feasibility of the SN©P within daily routines will be explored using focus group interviews with nurses and a telephone interview with one oncologist from each of the intervention centres. Interviews with oncologists were included to represent the institutions voice regarding acceptance and feasibility of the SN©P within daily routines. Focus group and telephone interviews will be directed by semi-structured interview guidelines (112, 114). Topics addressed in both interviews will focus on symptom self-management support based on the frameworks of Howell (22) and Schofield (23).
3) Nurses report on fidelity to the training manual by using electronic questionnaires. These questionnaires were developed based on the six key-elements of semi-structured consultations. Sixteen questions are in dichotomous format (yes-no); three text fields are added for reporting patients' complaints, their goals regarding symptom self-management behaviours, and observed 'unsafe' behaviour of patients. We consider as unsafe behaviour for example a delayed reaction of a patient despite severe symptoms such as fever with neutropenia or exacerbated diarrhoea. In addition, a study team member will observe two semi-structured consultations at each centre by using the above-mentioned questionnaire in printed format to record observed behaviour of nurses.
4) Patients' safety will be also explored with focus group interviews with nurses and telephone interviews with oncologists. Serious adverse events will be assessed electronically according to authority guidelines (115, 116).
5) Resources needed to implement the SN©P at the centres will be assessed based on training duration and number of participating nurses documented on training logs. Nurses will assess electronically time needed for semi-structured consultations including preparation and documentation of consultations.
6) Quality of nursing care evaluated by patients will assess five concerns: do nurses ask patients about symptoms, provide useful information, and / or practical advice to manage symptoms, are they aware of patient's symptom severity, and whether patients feel confident to manage symptoms. The *Patient-Reported Chemotherapy Indicators of Symptoms and Experiences* (PR-CISE) (91) is a quality measure for outpatient chemotherapy settings. We translated five items of the original PR-CISE questionnaire following a forward and backward translation process based on a translation and cultural adaptation guideline (117). The translation was reviewed by two nursing experts and pilot-tested with 10 cancer patients from an outpatient cancer centre that will not participate in this study.

Table 9 Overview of assessed outcomes based on RE-AIM framework

RE-AIM dimensions (Level of evaluation)	**Outcomes**	**Data collection methods**	**Assessment schedule**
Reach (Individual)	Patients' characteristics, accrual & retention rates	Medical records, recruitment logs at each centre	Study start: patients' recruitment and enrolment
Effectiveness (Individual)	Symptom interference with daily function (activity & affective sub-dimensions), symptom severity, overall symptom burden, self-efficacy, mood	Paper and pencil questionnaires: MDASI, SES6G, LASA Mood Scale	4 measurements over 16 weeks: from BL to t3
Adoption (Organisational)	Characteristics of participating centre & staff, usual support for SSM, facilitators & barriers for SN©P adoption	Focus group interviews (1), electronic questionnaires	Study start: before patient recruitment starts
Implementation (Organisational)	1) Acceptance & appropriateness of nurses' trainings: training content, nurses' confidence to integrate SN©P into practice, work-related factors with implementing SN©P	Paper and pencil questionnaire, Work-SoC scale	After first & second training
	2) Nurses' and physicians' acceptance of SN©P	Focus group interviews (2) and telephone interviews	After patients completed all questionnaires (last patient out of study)
	3) Nurses' fidelity to training manual: key-elements applied, patients' complaints & goals, number & topic of delivered SN©Fyers, additionally delivered information leaflets	Electronic questionnaires Observations	After every semi-structured consultations
	4) Patients' safety	Electronic questionnaires Focus group interviews (2)	After semi-structured consultations
	5) Resources: time needed for trainings, preparing and providing nurse-led consultations, documentation	Training logs Electronic questionnaires	After training courses and after semi-structured consultations
	6) Quality of nursing care estimated by patients	PR-CISE (paper and pencil questionnaires)	3 measurements: t1 – t3
Maintenance	Not applied	Not applied	Not applied

Legend: SSM: Symptom Self-Management; SN©P: Symptom Navi© Program; SN©Flyers: Symptom Navi© Flyers (written information leaflets for patients); MDASI: MD Anderson Symptom Inventory; SES6G: Self-Efficacy for Managing Chronic Disease Questionnaire; PR-CISE: Patient-Reported Chemotherapy Indicators of Symptoms and Experiences; Work-SoC: Work-related Sense of Coherence scale; BL: baseline; Focus group interviews (1): takes place before patient recruitment starts at the centre; Focus group interviews (2): takes place after last patient is out of study.

Sample size and randomisation

We aim to include a total of 140 patients in 9 clusters—with approximately 70 patients to be included in both the intervention and the control group, and about 10 to 20 patients in each cluster (at each centre).

Due to the lack of data on the expected magnitude of effect of SN©P on outcomes, we did not formally calculate a sample size (101), but rather estimated the power for the expected sample size. Assuming an intra-class correlation of 0.05, a type I error rate of 5%, and an equal distribution of the patients among the clusters, a total sample size of 135 patients (i.e. 9 clusters with 15 patients) would allow a detection of an effect size of 0.5, 0.75 and 1 with powers of about 60%, 91% and 99%, respectively, based on a two-sample comparison of means in a cluster-randomised design.

The Clinical Trial Unit of the University of Bern (CTU Bern) will execute the randomisation at the level of cancer outpatient centres. Randomisation will be stratified by the expected recruitment potential (fast versus slow recruiters) and will be based on randomly permuted blocks with a block size of two to minimize potential imbalances within the small number of included clusters. We assume that nurses are more familiar with treatment protocols at faster recruiting centres, and therefore might also be more experienced with supporting patients during anti-cancer treatments. Stratification will also help with balancing the number of patients between treatment groups since cluster size depends on the recruitment potential. We will not implement allocation concealment or blinding procedures.

Data collection and management

A data capturing system (secuTrial) will be set up for data entry at CTU Bern for all quantitative data. Nurses and physicians involved with the study procedures will have a personal login to secuTrial for data recording. A dedicated nurse and a principal investigator (an oncologist who has worked for at least one year at the centre) at each centre will be responsible for identifying eligible patients for study inclusion and informing patients orally and in written format about the study.

The study procedure is summarised in a participants' flow-chart (see Figure 3). The baseline assessment (BL) will take place before patients start their first treatment application at the outpatient cancer centre. Two further assessments will take place between subsequent treatment applications (t1 between second and third, t2 between third and fourth treatment application) when the patient is at home. This takes into account the variety of treatment protocols with different administration schedules. The last assessment (t3) will again be completed by the patient at home, 16 weeks (± one week) after the BL assessment.

Nurses will hand over questionnaires and pre-stamped addressed envelopes to patients and inform them when they should fill in the questionnaire at home. Returned questionnaires will be entered centrally into secuTrial by a study team member. After every semi-structured consultation with a patient, nurses will complete an electronic questionnaire assessing their fidelity to the training manual, and patient's complaints and goals for symptom self-management as discussed during the consultation.

All focus group interviews will be audio-recorded and transcribed. After patient recruitment is completed at an intervention centre, a telephone interview with one oncologist will be conducted. Data management of qualitative data will be based on excel sheets and logbooks, if applicable.

Patient recruitment started in November 2017. We expect the last patient to complete the study by the end of April 2019 and to complete the qualitative data assessment by the end of June 2019.

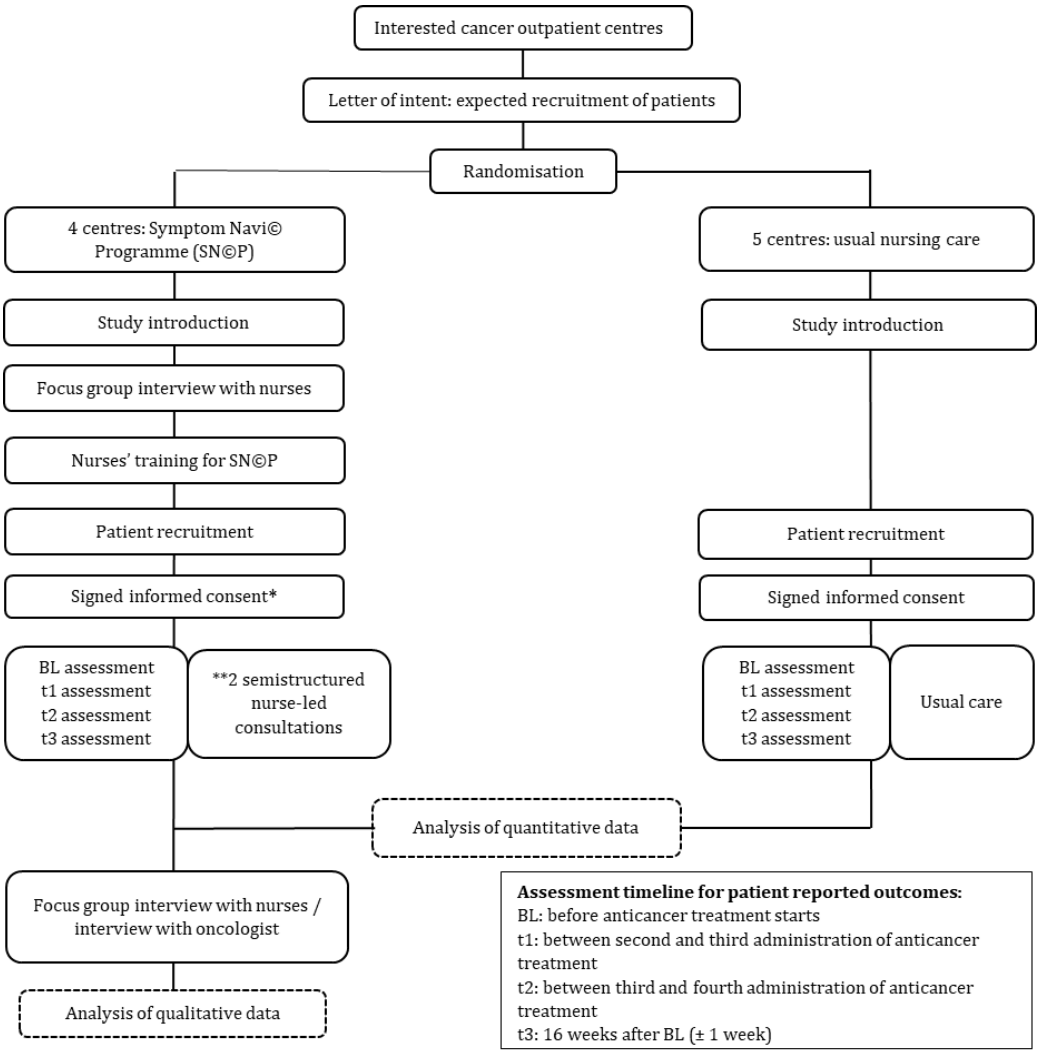

Figure 3: Study flowchart for the Symptom Navi© Pilot Study with included patient timeline

*Every patient enrolled for the pilot study will start with SN©P and will be followed by two semistructured nurse-led consultations. **Semistructured nurse-led consultations take place during first and second scheduled treatment application at the outpatient centres of the intervention arm. BL, baseline.

Analysis

The null hypothesis, that there is no difference in the changes of symptom interference score of the MDASI between intervention and control group, will be tested against a two-sided alternative. We will perform a primary analysis on the intention-to-treat population (i.e. analysing all patients according to the intervention they were assigned to at randomisation) and a secondary analysis on the per-protocol population (i.e. excluding patients that were not treated according to protocol). All effectiveness outcomes will be analysed using linear or generalised linear mixed-effects models. Baseline measurement, treatment group, time point (i.e. t1, t2, or t3) and the interaction of group and time point will be included as fixed covariates, cluster and patient as nested random effects. We will present all results using an effect measure with a two-sided 95% confidence interval and a p-value. In a sensitivity analysis, we will adjust the model for potential confounders, i.e. patient, nurse, or cluster characteristics that show imbalances at baseline.

All other outcomes will be analysed descriptively. A statistical analysis plan with a detailed description of data preparation and analysis will be written in collaboration with a statistician before completion of recruitment. Quantitative analysis will be performed in collaboration with the CTU in Bern using an appropriate statistical software (e.g. R or STATA).

Transcripts of focus group and individual interviews, as well as narrative information from the questionnaires on fidelity including patients' goals for symptom self-management will be analysed by thematic analysis (118). Thematic analysis is a six-phase approach to identify patterns (themes): 1) familiarising with data, 2) generating initial codes, 3) searching for themes, 4) reviewing themes, 5) defining and naming themes, and 6) producing the report (118). Transcripts will be coded independently by two members of the research team. A third member will be involved to discuss discordances between the two coders until consensus is reached.

Patient and Public Involvement

We did not involve patients or public for developing this pilot study. Results of the study will be presented at each participating cancer outpatient centre. An assessment of patients' burden of the intervention was not included in the pilot study based on previous evaluation of the intervention from patients' perspective confirming that the SN©P did not cause burden for patients.

Ethics and Dissemination

This pilot study has been reviewed by four Swiss Ethics Committees and approved by the Swiss Ethic Committee in Bern (KEK-BE: 2017-00020), and will be conducted in accordance to the Declaration of Helsinki (119) and the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use / Good Clinical Practice (ICH-GCP) guidelines (120). Any modification of the protocol will be submitted to and approved by the leading Ethic Committee in Bern. Patients will sign a written informed consent form (supplementary file 1) before being included in the study. Signed informed consent forms and patient enrolment logs will be stored at the outpatient cancer centres. All data will be anonymised when presented at scientific meetings or published. Serious adverse events will be assessed by local principal investigators and evaluated according standard serious adverse reporting procedures (121). We registered this pilot study at ClinicalTrials.gov (NCT03649984) and at the Swiss National Clinical Trials Portal (SNCTP): SNCTP000002381.

Results of this study will be disseminated at national and international conferences and published in peer-reviewed journals with a preference of open access journals. Nurses at the control group centres will be trained on the SN©P to implement it at their centre after pilot study completion and confirmation that the SN©P can be considered to be safe. If the safety of the SN©P will be confirmed with this study, we plan to collaborate with the Swiss Cancer League for broader dissemination of the SN©P in Switzerland. Supporting self-management strategies of cancer patients is an explicit aim of the Swiss National Strategy against Cancer (122, 123).

Discussion

The Symptom Navi© Pilot Study aims to evaluate the implementation of the SN©P within daily routines. We will evaluate preliminary effectiveness and safety of the intervention on patient-reported interference of symptoms with daily functions, symptom intensity and burden, perceived self-efficacy and quality of nursing care. The results may contribute to greater insight into the mediating role of self-efficacy for self-management of symptoms (64). We expect the SN©P to enhance nurse-led support for cancer patients in the outpatient setting. Estimated effect sizes will serve for effect and sample size calculations for a fully powered cluster randomised controlled clinical trial.

Successful implementation of complex interventions depends on providing the intervention as intended, but also on contextual factors (62, 97). To meet these challenges we have designed a

study based on the RE-AIM framework using a cluster-randomised design complemented with qualitative methods (124). The SN©P has been thoroughly developed (2) and patients confirmed that they could improve their self-management behaviours by using SN©Flyers (125). Therefore, the SN©P is a promising nurse-led intervention to support patients' symptom self-management and enrich current usual care practices in the outpatient cancer setting, but its implementation and effectiveness need to be investigated.

Authors' contributions

MB: SN©P development, study design and conduct, manuscript writing. **KR:** study conduct, manuscript writing. **SKS + EN**: SN©P development, study design and conduct, manuscript review. **SZF**: SN©P development, study design, manuscript review. **TM + SP**: study design, manuscript review. **LB + FR**: study design and statistical support, manuscript review. **ME**: SN©P development, study design and conduct, obtained funding, manuscript writing.

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Competing interest statement

Solange Peters has received education grants, provided consultation, attended advisory boards, and/or provided lectures for: Abbvie, Amgen, AstraZeneca, Bayer, Biocartis, Boehringer-Ingelheim, Bristol-Myers Squibb, Clovis, Daiichi Sankyo, Debiopharm, Eli Lilly, F. Hoffmann-La Roche, Foundation Medicine, Illumina, Janssen, Merck Sharp and Dohme, Merck Serono, Merrimack, Novartis, Pharma Mar, Pfizer, Regeneron, Sanofi, Seattle Genetics and Takeda , from whom she has received honoraria. Manuela Eicher received education grants, provided consultation, attended advisory boards, and/or provided lectures for: Vifor, Roche, and Bristol-Myers Squibb. All other authors have no competing interests to declare.

Data sharing statement

All data within secuTrial are at the CTU Bern and are available to the principal investigator (ME). No data agreement is in place and therefore data sharing is not applicable.

Chapter 5: Results

Two articles are included in this chapter. The first article is the second published article resulting from this thesis and introduces this chapter by summarising the development process and the evaluation of nurse training. This article provides a detailed description of the evaluation of nurse training. The second article included in this chapter reports on effectiveness of the RE-AIM framework. Therefore, results regarding the reach dimension, effectiveness (third article), adoption (nurse adherence to training) and implementation (nurses' fidelity to SNP training and patient safety), will follow. Used questionnaires to evaluate nurse training and patient reported outcomes are attached to Appendix 5 and Appendix 6 respectively.

Development and implementation strategies of a nurse-led symptom self-management program in outpatient cancer centres: The Symptom Navi© Programme (second article)

Marika BANA, RN, MScN[a,b]. Karin RIBI, PhD[b,c], Susanne KROPF-STAUB, RN, MScN[d], Ernst NÄF, RN, MScN[e], Monique SAILER SCHRAMM, RN, MScN[a,1], Sabin ZÜRCHER-FLORIN, RN, MScN[d], Solange PETERS, MD, PhD[f], Manuela EICHER, RN, Dr. rer. medic.[b,f],

[a] University of Applied Sciences and Arts Western Switzerland, School of Health Sciences, Route des Arsenaux 16a, CH-1700 Fribourg, Switzerland; marika.bana@hefr.ch , monique.sailer@medizentrum.ch

[b] Institute of Higher Education and Research in Health Care IUFRS, University of Lausanne and Lausanne University Hospital, Faculty of Biology and Medicine, SV-A Secteur Vennes, Route de la Corniche 10, CH-1010 Lausanne, Switzerland; marika.bana@unil.ch , karin.ribi@unil.ch , manuela.eicher@unil.ch

[c] International Breast Cancer Study Group (IBCSG), Effingerstrasse 40, CH-3008 Bern, Switzerland; karin.ribi@ibcsg.org

[d] Hospital Group Lindenhof, Lindenhof, Bremgartenstrasse 117, Postfach, CH-3001 Bern, Switzerland; susanne.kropf@lindenhofgruppe.ch , sabin.zuercher@lindenhofgruppe.ch

[e] Department of Practice Development in Nursing, Solothurner Spitäler, Kantonsspital Olten, Baslerstrasse 150, CH-4601 Olten, Switzerland; ernst.naef@spital.so.ch

[f] Department of Oncology, Centre Hospitalier Universitaire Vaudois (CHUV), Rue du Bugnon 21, CH-1011 Lausanne, Switzerland; solange.peters@chuv.ch ; manuela.eicher@chuv.ch

Corresponding author:

Manuela Eicher: manuela.eicher@chuv.ch

IUFRS, SV-A Secteur Vennes, Route de la Corniche 10, 1010 Lausanne, Switzerland

Tel: +41 21 314 87 60

[1] Present adress : MediZentrum Täuffelen AG, Breitenfeldstrasse 4, CH-2575 Täuffelen, Switzerland

Authorship:
All authors contributed to: 1) conception and design of the study, or acquisition of data, or analysis and interpretation of data; 2) drafting the article or revising it critically for important content; 3) final approval of the version to be submitted.

Abstract

Purpose: The Symptom Navi© Programme (SN©P) is a structured nurse-led intervention supporting symptom self-management in cancer patients. We describe the development and evaluation of the intervention, implementation strategy, and the evaluation of nurse training for the Symptom Navi© Pilot Study.

Methods: The intervention was developed using multiple methods (e.g. literature synthesis, focus groups) to produce SN©P information leaflets (SN©Flyers in French and German) and standardised training for nurses to deliver semi-structured consultations. We evaluated the SN©P using online surveys, focus groups, interviews, and the Item-Content Validity Index (I-CVI). Nurse training was evaluated in relation to content, acceptability, and confidence in implementing the SN©P. We examined the association between scored on the Work-related Sense of Coherence (Work-SoC) scale and nurses' confidence in implementing the SN©P. Thematic analysis was used to analyse qualitative data. Quantitative data was descriptively analysed and the Kendall Tau test was employed for correlations.

Results: Patients and health care professionals confirmed that SN©Flyers and semi-structured consultations facilitated symptom self-management. Nurses considered training content/format acceptable and appropriate and felt confident in implementing the SN©P. Overall Work-SoC scores were correlated with nurses' confidence in implementing the SN©P (r_π = .47, p=.04).

Conclusions: Health care professionals and cancer patients perceived the SN©P as a useful support. Successful implementation of the SN©P depends on centre-specific factors including time, resources and workflow.

Keywords: Behaviour change; complex intervention; implementation research; neoplasm; self-management; symptom management

Clinical trial registry: NCT03649984 and SNCTP000002381

Résumé

Objectif: le Programme Symptom Navi© (« Symptom Navi© Programme »ou SN©P) est une intervention structurée menée par le personnel infirmier en vue de soutenir les patient·e·s atteint·e·s d'un cancer dans l'autogestion de leurs symptômes. Nous décrivons le développement et l'évaluation de l'intervention, la stratégie de son implémentation et l'évaluation de la formation des infirmières et infirmiers effectuée pour l'étude pilote Symptom Navi©.

Méthodes: l'intervention a été développée au moyen de multiples méthodes (synthèse de littérature, groupes de parole, p. ex.), afin d'élaborer des dépliants d'information SN©P en français et en allemand ainsi qu'une formation standardisée destinée au personnel infirmier portant sur la conduite de consultations semi-structurées. Nous avons évalué le SN©P par le biais de sondages en ligne, de groupes de parole, d'entretiens et de l'indice de validité du contenu (Item-Content Validity [Index I-CVI]). La formation a été évaluée quant à son contenu, à son acceptation et à la confiance montrée par le personnel infirmier dans l'implémentation du SN©P. Nous avons examiné l'association entre cette confiance et les scores de l'échelle du sentiment de cohérence au travail (Work-related Sense of Coherence [Work-SoC]). Les données qualitatives ont été soumises à une analyse thématique,

les données quantitatives à une analyse descriptive. Le test Tau de Kendall a servi à vérifier les corrélations.

Résultats: Les patient·e·s et les professionnel·le·s de la santé ont confirmé que les dépliants Symptom Navi© et les consultations semi-structurées facilitaient l'autogestion des symptômes. Les infirmières et les infirmiers ont estimé le contenu et la forme de la formation acceptables et appropriés et se sentaient confiant·e·s dans la mise en œuvre du SN©P. Les scores globaux de l'échelle Work-SoC ont été corrélés avec la confiance du personnel infirmier dans l'implémentation du SN©P (r_{τ} = .47, p = .04).

Conclusions: les professionnel·le·s de la santé et les patient·e·s atteint·e·s d'un cancer ont perçu le SN©P comme un soutien utile. Le succès de l'application du programme dépend de facteurs spécifiques aux différents sites tels que le temps, les ressources et les flux de travail.

Introduction

Evidence suggests that health care providers offer supportive care to meet physical, emotional, psychosocial, informational, and practical needs of patients diagnosed with cancer (15). Oncology nurses are well situated to assist patients in communicating needs, values and preferences during chemotherapy (91, 126) and to support ambulatory cancer patients with symptom self-management (92, 93, 127). A growing number of patients undergo outpatient cancer treatment and are at risk for multiple potential adverse events that require self-management (82, 128). Ambulatory cancer patients report on average eight co-occurring symptoms (92). Consequently, patients need to know how to recognise, evaluate, interpret, monitor, and manage their symptoms (83, 129). However, providing information alone is not sufficient to support patient symptom self-management (21, 40). Symptom self-management is a dynamic process that involves integrating adequate behaviours and strategies to prevent, relieve or decrease symptoms (58). The process includes managing symptoms and supportive treatments, dealing with emotional and physical consequences of the disease, and adaptive behaviours (21, 84). Therefore, it is recommended that symptom self-management be addressed at the start of anticancer treatment (15). Additionally, evidence-based psycho-educational interventions guided by principles of behaviour change should be offered (23). Core elements for self-management educational interventions include facilitating problem solving and adequate decision-making skills, fostering patient self-efficacy for effectively communicating with health care professionals, tailoring recommendations to the individual's situation, and defining goals with action plans (22).

Best practices include standardising self-management support to maintain effectiveness and sustainability (23) and providing detailed descriptions of interventions to facilitate behaviour change (130). Moreover, it is important to employ well-developed training techniques to facilitate effective implementation (131). Evidence supports the importance of providing symptom self-management interventions within the context of a multi-professional health care team (22).

The Capability Opportunity Motivation - Behaviour (COM-B) model (6) identifies three essential conditions for behaviour change: capabilities, opportunities, and motivation. To facilitate behaviour change in practice, nine intervention functions should be considered (educating, persuading, incentivising, coercing, training, enabling, modelling, environmental restructuring, and restricting). In addition, seven policy aspects (guidelines, environmental / social planning, communication / marketing, legislation, service provision, regulation, and fiscal measures) should be taken into account (6).

Successful implementation of complex interventions/new tasks into a service may depend on contextual and work-related factors (e.g. usual workload, available resources for providing services, access to private rooms for patient conversations) (60). Work resources and demands are correlated with an individual's perceived work-related sense of coherence. Work-related sense of coherence

includes perceived comprehensibility, manageability and meaningfulness of the work situation and is a mediator between job resources and employee work engagement (113).

Despite a growing body of evidence of the importance of symptom self-management support for cancer patients, nurse-led interventions for are rarely implemented into routine clinical practice (127). In Switzerland, patients report needing more information and support to self-manage their symptoms during cancer treatment (30, 31). To address this need, Swiss oncology nurses initiated the development of the Symptom Navi© Programme (SN©P) in 2011. The SN©P consists of 16 evidence-based written information leaflets (Symptom Navi© Flyers, SN©Flyers), and a training manual for nurses to deliver semi-structured nurse-led consultations. SN©Flyers provide patients with structured information on self-management options to relieve common physical and psychosocial symptoms. Semi-structured nurse-led consultations using SN©Flyers begin at the onset of a treatment. Nurses tailor consultations to the prescribed therapy in order to support patient's individual symptom self-management. Each patient should receive at least two consultations. If symptom intensity and/or patient needs persist, semi-structured consultations are intended to continue until patients successfully achieves alleviation of symptoms via self-management. Nurse training is standardised to facilitate the semi-structured approach of the intervention.

Aims and objectives

We describe the development of the SN©P, its implementation and evaluation of the SN©P nurse training. Our objectives are to:

i. Summarise the development of the SN©P and evaluation of SN©Flyers by patients and health care professionals;
ii. Describe the development and content of the SN©P training for nurses;
iii. Investigate oncology nurses' evaluation of the content of the SN©P training, its acceptability, and to describe nurses' confidence in implementing the SN©P into practice;
iv. Describe the association between nurses' confidence in implementing the SN©P within their clinical daily routines and their current work situation (contextual/work-related factors).

Methods

The SN©P (SN©Flyers, semi-structured nurse-led consultations, and training) has been developed over several years in a sequential process (Figure 4). Development and evaluation phases employed an iterative process. We used multiple methods to develop the SN©P including literature synthesis, consensus panels, online surveys, focus group discussions, and interviews with cancer patients and health care professionals. A description of the development process of SN©Flyers and semi-structured consultations has been previously published in German (1, 2). Herein, we provide a comprehensive overview of the development of the Symptom Navi© Pilot Study (NCT03649984) and evaluation of the nurse training program. An ongoing two-arm cluster-randomised study (complemented with qualitative methods) is underway to assess feasibility and determine preliminary effectiveness of the SN©P (approved by cantonal Swiss ethic committee, KEK-BE: 2017-00020) (7).

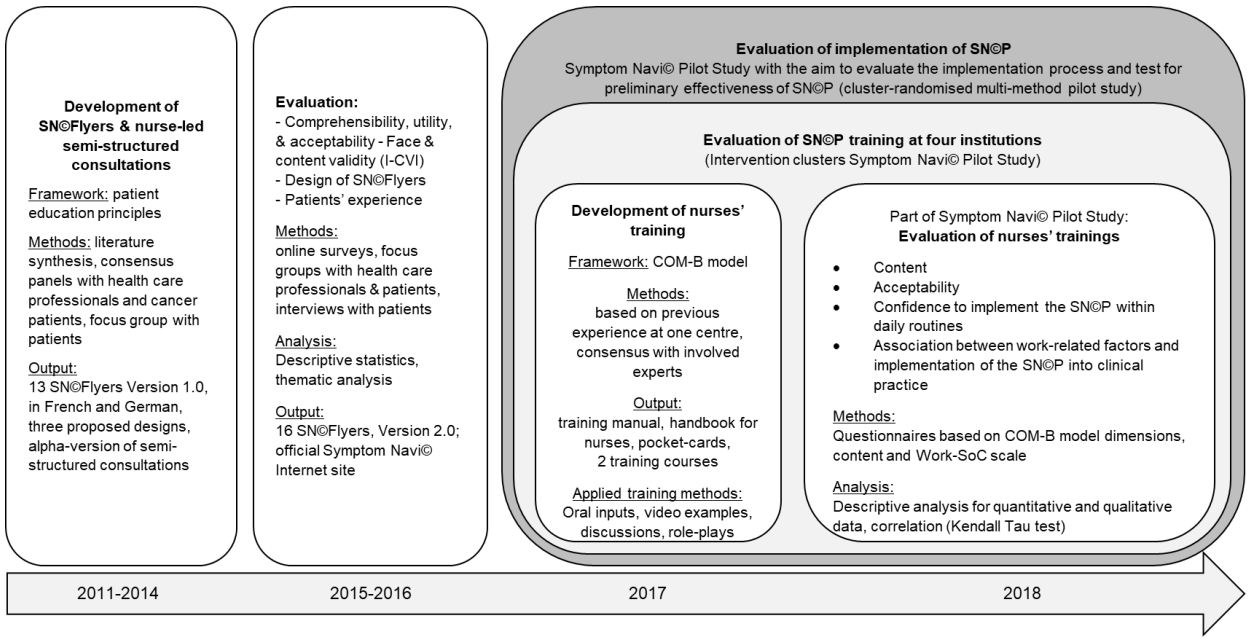

Figure 4: Development and Evaluation of the Symptom Navi© Programme 2011 to 2018

Legend: SN©P: Symptom Navi© Programme; SN©Flyers: Symptom Navi© Flyers; I-CVI: Item-Content Validity Index; COM-B model: Capability Opportunity Motivation – Behaviour model; Work-SoC: Work-related Sense of Coherence

Development of SN©Flyers and nurse-led semi-structured consultations (2011-2014)

SN©Flyers were developed for symptoms frequently experienced during anticancer treatments (17). The SN©Flyers synthesize international evidence-based recommendations/guidelines (132) and recent literature reviews were incorporated into (21, 48, 54, 133, 134). SN©Flyer recommendations aim to support patient self-management and identify steps patients can take to relieve specific symptoms.

To design the SN©Flyers, we assessed Swiss cancer patients' needs and preferences in a series of patient focus group discussions in collaboration with members of the Swiss Oncology Nursing Society and the University of Applied Science and Arts Western Switzerland. This process led to three alternate designs for SN©Flyers. All versions included: a) symptom intensity levels (mild, moderate and severe), b) descriptions of physical changes patients may observe related to respective intensity level, and c) evidence-based symptom self-management recommendations across intensity levels. The three versions used different colour-codes to visually identify symptom intensity levels and different symbols (emoticons) relating to patients' subjective rating of symptom intensity. SN©Flyers are available in both German and French.

SN©Flyers were provided to patients during individual, face-to-face, semi-structured nurse-led consultations guided by principles of therapeutic patient education (21-23, 25). The self-management education intervention was intended to be delivered by graduate-level nurses to complement standard nursing care in daily clinical practice at the cancer centre. Broadly, semi-structured consultations focused on patient's needs and building a therapeutic partnership with the patient. Importantly, the semi-structured consultations were based on six key-elements (table 1). Two key-elements specifically focused on supporting self-management strategies: *addressing symptom self-management* and *facilitating self-management* (Table 1, key elements 4, 5). Key element 5 (*facilitating self-management)* included assessing patient self-efficacy for self-

management. Nurses provided at least two semi-structured consultations with each patient at the beginning of systemic treatment. Ideally, the intervention took place in a separate, private room.

The first consultation included key elements 1-3 and 6 (Table 10). Initial goals were to inform the patient about expected symptoms and how to recognise, evaluate and interpret symptoms. Nurses tailored the initial semi-structured consultations according to the patient's individual treatment protocol. Patients also received additional written information (e.g. Swiss Cancer League brochures) as part of the cancer centre's standard care practices. The first consultation was planned to occur within the first two or three systemic treatments (i.e. three to four weeks). From the second consultation on, nurses included all six key elements and focused on symptom self-management behaviours.

If symptoms persisted, nurses continued providing semi-structured consultations based on patient needs until symptom self-management was achieved. Nurses' fidelity to the intervention (as delineated in the training manual) was assessed as part of the Symptom Navi© Pilot Study and will be published elsewhere.

Table 10 Symptom Navi© Program six key-elements of nurse-led semi-structured consultations

Key-element	Content	Target
1) **Preparing** the semi-structured consultation	Patient medical history, treatment protocol and expected common side-effects	Nurses tailor the consultation and select relevant Symptom Navi© Flyers for anticipated side effects of therapy
2) **Evaluating** patient's willingness & motivation	Patient capability to be attentive and his/her motivation to actively participate in the consultation	Patient agrees to the consultation, evaluation of his/her attention during the conversation
3) **Providing** information	Information about expected side effects of therapy, introduction of Symptom Navi© Flyers	Patient understands how to use Symptom Navi© Flyers at home and what he/she can do to relieve symptoms experienced at home; and know when he she should contact the care team/oncologist
4) **Addressing** symptom self-management	Discussion of symptoms experienced and symptom-relieving activities used at home	Patient communicates his/her side effects, receives tailored information recommendations for his/her situation; individual support for patient's perceived self-efficacy for self-managing symptoms
5) **Facilitating** symptom self-management	Assessment of barriers/facilitators of individual symptom self-management	Patient learns about alternatives for self-managing symptoms in challenging situations; referrals to complementary health professionals (as needed); individual support for patient's perceived self-efficacy
6) **Documenting** the consultation	Recording Symptom Navi© Flyers used, assessments implemented, patient goals	Additional consultations scheduled based on progress towards previously established goals, recognize/validate goals achieved by the patient, continued support and encouragement for self-management

Six key-elements are tailored to individual patient needs in an iterative fashion rather than a linear consultation structure. Each patient receives at least two face-to-face semi-structured consultations at outpatient cancer centre during chemotherapy.

Evaluation of SN-Flyers (2015-2016)

SN©Flyers were evaluated using anonymised online surveys and focus groups conducted in French and German by one of the authors (ME) and a scientific collaborator not familiar with the study. Health care professionals, patients and family members evaluated 1) understandability, utility and acceptability of SN©Flyers; 2) preferred design among the three versions; and 3) face validity of evidence-based recommendations. Understandability, utility, acceptability and preferred design version of SN©Flyers were evaluated in three patient focus groups and an online survey of both patients and health care professionals. Focus groups were conducted using an interview guide and qualitative data were analysed using thematic analysis (118). Three groups of health care professionals and cancer patients (n = 7 – 9 per group) rated five to six SN©Flyers in an online survey. Invited participants were purposefully sampled to represent a variety of health care professions, language regions and different cancer diagnoses. Participants rated each SN©Flyers recommendation (item) as 'not relevant', 'somewhat relevant', 'quite relevant', or 'highly relevant' per the Item-Content Validity Index (I-CVI) (103). To analyse I-CVI overall score for each SN©Flyer, we transformed answers into a 'dummy' variable ('not relevant' and 'somewhat relevant' = 0, 'quite relevant' and 'highly relevant' = 1). Participants were also invited to provide open-ended comments on each item. A committee of four academic oncology nursing experts led the SN©Flyer evaluation.

The online survey including 48 patients and health professionals revealing excellent face validity with overall I-CVI of 0.95 and 0.9 for French and German versions, respectively (range (French): 0.43 – 1.0,(German): 0.33 – 1.0, 1.0 = maximum validity). Patient focus group discussions (n=3) included 14 patients and one family member (two in German, one in French). Two health care professional focus groups were conducted involving 16 professionals (Table 11). Participants thought SN©Flyers were easy to understand, provided important information and facilitated rating of symptom intensity. The design using smiley-emoticons and colour coding (green=mild, yellow=moderate, red=severe) was the preferred design by patients and health care professionals alike. Subsequently, SN©Flyers were refined (Version 2.0) based the online survey results and focus group discussion. The final SN©Flyers version included 16 symptom-specific flyers (three flyers were added to the first version) (7).

Table 11 Focus group participants

	n		n
Health care professionals (n = 16)		**Patients and family members (n = 15)**	
German-speaking	13	German-speaking	9
French-speaking	3	French-speaking	6
Nurses in clinical practice	3	Cancer diagnosis:	
Nurses in education and research	8	Gynaecological	4
Oncologists	3	Colo-rectal	4
Graphic design specialists	2	Lung	2
		Other*	5
		Family members	1

* Cancer diagnoses: testicular, pancreatic, hepatic, chronic lymphatic leukaemia

Patients experience with semi-structured consultations

Semi-structured interviews (in German) were conducted (author: SKS) to explore patients' experiences with SN©Flyers and semi-structured consultations. Patients were asked how they used the SN©Flyers and about their experiences with nurse-led consultations and perceived symptom self-management support. An interview guide included five open-ended questions: 'How did you

perceive the conversation on SN©Flyers? Which information were important for you? How was your experience with the SN©Flyers? Are there any kind of questions that could not be answered? Is there an issue you would like to add?'. Interviews were audio-recorded, transcribed verbatim, and analysed using thematic analysis (118).

In total, 10/15 eligible patients (i.e. received the SN©P at a regional Swiss hospital) were interviewed. Participated semi-structured interviews: Seven women and three men (35-77 years old) with different cancer diagnoses were interviewed. Thematic analysis revealed five main themes: being emotionally challenged, meaning of social support for self-management, self-management support based on needs, orientation by SN©Flyers, and achieve manageability of symptoms. Themes and sub-themes are presented in Table 12.

Table 12 Main themes and subthemes from semi-structured interviews with cancer patients

Main themes	Subthemes
Being emotionally challenged	Having to decide alone
	Desire to survive
	Uncertainty and anxiety for therapy
	Insecurity in everyday life
Meaning of social support for self-management	Motivated by family members
	Becoming strong to reduce anxiety
	Self-management experiences from peers
Self-management support based on needs	Patient-centeredness is crucial for care
	Talking to different health care professionals is complementary
	Enhance competencies by conversations and daily tips
Orientation by SN©Flyers	Relief by proactive information
	Alleviation by need-oriented and serious source
	Gain overview
	Evaluate intensity
	Develop capacity to act
Achieve manageability of symptoms	Recognise urgency / priority
	Avoid too much information (hyper information)
	Apply appropriate everyday recommendations
	Become active

Developing SN©P nurse training program (2017)

The training program for nurses aimed to standardise the procedure, ensure that the implementation of the SN©P could be replicated at different sites and effectively integrated into daily clinical routines. The nurse training module was based on clinical experience and drew on the COM-B model as a guiding theoretical model (6). The COM-B model posits that capability (i.e. knowledge and skills) and opportunities (i.e. external work-related resources needed for the target behaviour) influence motivation (intrapersonal conditions such as individual habits, analytical and emotional processes) to perform a target behaviour. The three dimensions (capability, opportunities, motivation) are inter-related (Figure 5).

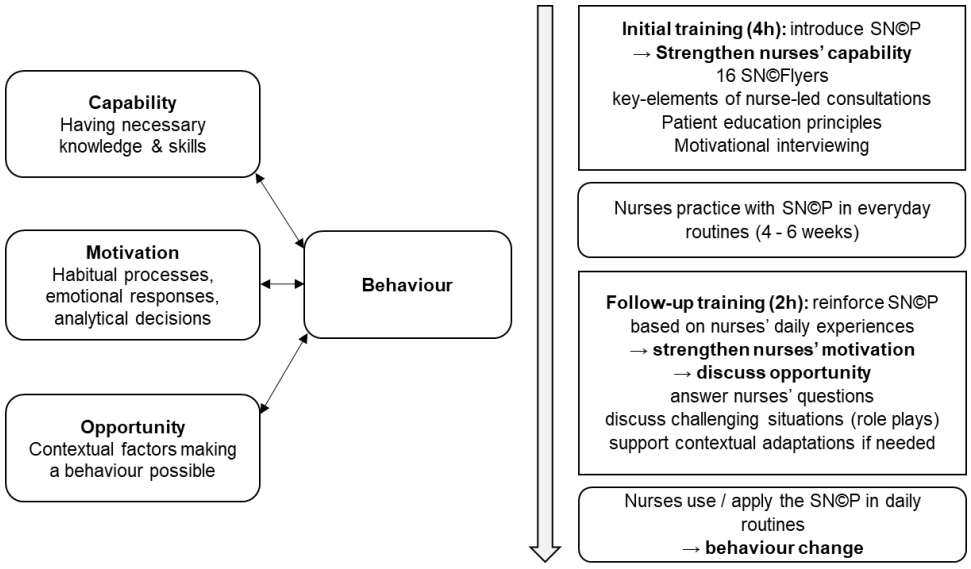

Figure 5: Nurse training content and procedure, based on COM-B model (Michie, van Stralen, & West, 2011)
Legend: SN©P: Symptom Navi© Programme; SN©Flyers: Symptom Navi© Flyers

We designed two consecutive, complementary training courses. The initial training (approximately 4 hours) was followed by a subsequent, separate 2-hour training (Figure 5). Both courses aimed to support nurse behaviour change from current practice (i.e. providing information) to perform interventions supporting patient symptom self-management. Teaching methods included didactic oral presentations, video examples of nurse-led consultations and interactive group exercises. The initial training introduced the SN©Flyers, reviewed the six-key elements for semi-structured consultations (Table 10), summarized principles of therapeutic patient education, and outlined basic motivational interviewing techniques. Following the initial training, nurses applied the SN©P at their centre over the next four to six weeks.

The follow-up training had two goals: 1) to support nurses' motivation for implementing the SN©P at their centres, and 2) to identify potential barriers to implementing the SN©P within daily routines and discuss opportunities to overcome identified roadblocks. Discussion focused on nurses' initial experiences with implementing the SN©P into their daily routine. Between the courses, the nurses were asked to prepare for the follow-up training by recording their experiences and reflections to inform the follow-up training and support an interactive and participative exchange (135).

Training content was based on standardised material. Each centre received a training manual and nurses' handbook. The training manual included details on the theoretical framework, content and procedures of the SN©P. The training manual was developed by four health care experts from Swiss hospitals, European universities, and the SN©P steering committee (the training manual in German is available from the corresponding author upon request). The nurse's handbook was an abbreviated version of the training manual written in everyday (lay) language to facilitate nurses' in delivering semi-structured consultations. Additionally, participating nurses received laminated pocket cards and copies of the materials used in the training sessions. Pocket cards included model questions related to each key-element of the semi-structured consultations. Recommended questions were tailored to support patients' symptom self-management and based on 'motivational interviewing' communication styles (i.e. guiding – following – directing the conversation) (104). The goal of these pocket cards was to provide a quick reference familiarising nurses with the semi-structured consultations and support their motivation to deliver the SN©P. The training program was reviewed and approved by the SN©P steering committee - consisting of two clinical experts in oncology nursing, a nursing manager, and two study researchers. The committee also identified two clinical

oncology-nursing specialists (who were experienced lecturers) to conduct the nurse training programs.

Evaluation of nurses' training (2018)

The training evaluation took place at outpatient cancer centres in the German-speaking part of Switzerland that were randomised to the intervention group in the Symptom Navi© Pilot Study. Registered nurses with at least a bachelor's degree or a diploma of higher education and who were salaried at the centre were eligible to participate in the pilot study. We excluded nurses who had worked less than one year in an oncology care setting. All available eligible graduate nurses at each centre participated in the training courses.

We described centres by type (e.g. breast cancer centre), number of employed nurses (full time equivalent), and mean number of anti-cancer treatments provided over the preceding month at study launch. We also collected characteristics of participating nurses including the total number of participating nurses, their type of oncology nursing education as well as the number of nurses who participated in both training courses and the cumulative duration of training (in hours). Nurses completed 10 questions about the training content and their perceived confidence in implementing the SN©P as described in the training manual. Nurses rated the training manual content using a seven-point Likert-like scale (1= 'not at all' to 7 = 'very much'). Questions were adapted to reflect the content of the two training sessions.

We assessed training acceptability using open-ended questions to capture both positive (i.e. "Particular positive during the initial / follow-up training was ….") and negative feedback (i.e. "Rather inappropriate during the initial / follow-up training was…."). We assessed contextual and work-related factors regarding available resources at the centre i.e. COM-B *opportunity* dimension (6). Nurses completed the Work-related Sense of Coherence (Work-SoC) scale (136). This 9-item instrument uses a 7-point Likert-like scale to assess three-factors (comprehensibility, manageability, meaningfulness) and has good internal consistency (Cronbach α 0.83). Previous work has demonstrated higher Work-SoC scores are related to lower perceived work-related stress (113). For this study, we assumed that lower work-related sense of coherence would represent increased work-related stress. We hypothesized that lower Work-SoC scores could be a barrier to implementing the SN©P at participating cancer centres.

Anonymous questionnaires were completed following training. Given the limited sample size, we calculated median, upper quartile (75% percentile: evaluate whether a majority of nurses benefit from the training), interquartile range (IQR), minimum, and maximum values for each item assessing content and confidence. Narrative (open-ended) comments regarding acceptability were descriptively analysed and organised according to positive and negative keywords respectively. Following the follow-up training, nurses responded to a single question based on the COM-B model ('I feel confident to provide semi-structured consultations based on the SN©P within daily routines'). We employed the Kendall's tau test to analyse the relationship between perceived confidence and overall Work-SoC score. Statistical analyses were performed using STATA 15.0 software.

Results

Two master-prepared nurses from the development team trained 21 graduated nurses at four outpatient cancer centres (two general outpatient cancer centres, 2 gynaecological/breast centres). In total, 11 nurses participated in both training courses. Full time equivalent nursing staff at the participating centres ranged from 2.0 to 7.1. Approximately half (10/21) of the nurses who participated in the training were specialised oncology nurses. On average, centres provided 44 anti-cancer treatments per day, and 2 treatments provided on two days per week. Three centres conducted both training courses while the fourth did not complete the second training due to a significant drop in newly diagnosed cancer patients. The number of participating nurses varied

between three and eight nurses per centre. Initial training lasted between 3.5-4 hours, follow-up training between 1-2 hours.

Nurses' evaluation of training content and acceptance of training

Overall, the nurses considered the training content to be suitable and supportive for implementing the SN©P into clinical practice. Three quarters of the nurses gave the maximum rating of 7/7 (most medians = 6/7, IQRs = 1 or 2). The video examples presented during the initial training received slightly lower ratings (median = 5/7, IQR = 2) with larger variability (minimal rating = 2, maximal rating = 6) (Table 13).

Narrative feedback confirmed that both training courses were supportive and appropriate. Positive aspects included the interactive approach, use of reflections, and participant discussion. Exercises to familiarise nurses to the 16 SN©Flyers and the six key-elements of the semi-structured consultations were considered important. Nurses valued learning about the different approaches for supporting cancer patients' symptom self-management. Individual statements were consistent with feeling prepared to 'apply the SN©P in clinical daily routine'.

Nurses also reported some negative aspects. Several nurses missed the introduction of the Symptom Navi© Pilot Study during the initial training and would have appreciated having a summary (recap) of the initial training at the beginning of the follow-up training. Some respondents considered the training sessions to be 'too long' in duration.

Nurses' confidence to implement the SN©P within daily clinical routines

In general, nurses felt confident to implement the SN©P within their daily clinical routines (Table 13). Three quarters of all nurses gave maximum confidence ratings (7/7) for four of five items. Only one ('I feel confident to practice semi-structured consultations') was lower at the completion of the first training (median = 6/7, IQR = 2). Respondents' ratings for 'feeling confident to practice semi-structured consultations' and 'use motivational interviewing' varied. The minimum and maximum ratings were 4 and 7 for 'practicing semi-structured consultations', and 5 and 7 for 'using motivational interviewing' respectively. After the follow-up training, nurses felt confident to explain the SN©Flyers (median = 6/7, IQR = 1, range = 4 - 7) and to implement semi-structured consultations based on the SN©P (median = 6/7, IQR = 2, range = 4 - 7). No narrative feedback were available to potentially explain the observed disparity.

Table 13: Nurse Training regarding duration, nurses' ratings on training' content and their confidence to apply the SN©P after the training

Initial training (n=18)	**Median**	uq	IQR	Min	Max
Duration in hours	4		0.5	3.5	4
1) Introduction was comprehensible✳	6	7	2	1.5	7
2) Oral presentation was informative and comprehensible✳	6	7	1	3	7
3) I learned from video examples✳	5	5	2	2	6
4) I am confident to practice semi-structured consultations‡	6	6	2	4	7
5) I am confident to apply motivational interviewing‡	6	7	2	5	7
Follow-up training (n=14)	**Median**	uq	IQR	Min	Max
Duration in hours	1.5		0.9	1	2
1) I asked my questions✳	6	7	2	4	7
2) I got satisfying answers✳	6	7	1	4	7
3) I feel empowered to apply SN©P‡	6	7	1	4	7
4) I feel confident to explain SN©Flyers‡	6	7	1	4	7
5) I feel confident to provide semi-structured consultations based on the SN©P within daily routines‡	6	7	2	4	7

Legend: uq: upper quartile (75% percentile); sd: standard deviation; SN©P: Symptom Navi© Program; SN©Flyers: Symptom Navi© Flyers (written information leaflets in brochure format)

✳Items assessing training content; ‡Items assessing confidence to implement the SN©P into practice, Question scales from 1 = not at all, to 7 = very much

Association between Work-SoC score and nurses' confidence to implement the SN©P

Work-SoC scores for both trainings are presented in Table 14. We used the Kendall Tau test to assess the relationship between overall Work-SoC score (post follow-up training) and perceived confidence ('I feel confident to provide semi-structured consultations based on the SN©P within daily routines') (Table 13, question 5 for follow-up training). Work-SoC was positively correlated with perceived confident in delivering the SN©P (r_T = .47, p < .05) (Figure 6).

Table 14: Overall Work-SoC scores for training 1 and 2

	Mean (sd)	**Median (lq, uq)**
Training 1	5,41 (0.78)	5,33 [4.77, 6.11]
Training 2	5,08 (0.80)	4.55 [4.55, 5.66]

Legend: lq = lower quartile (25% percentile), uq = upper quartile (75% percentile)

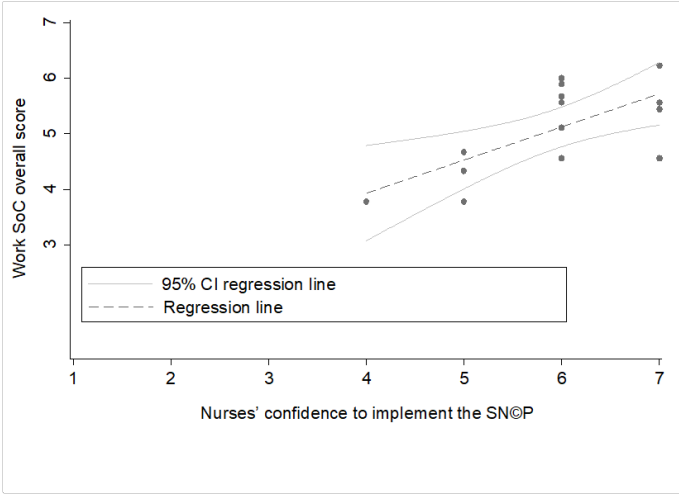

Figure 6 Correlation between overall Work-SoC score and confidence in providing SN©P semi-structured consultations within daily routines (n=14); r_{π} = .47, p = .04

Discussion

Development and evaluation of the SN©P

To our knowledge, the SN©P is one of the first prospectively evaluated, nurse-led standardised programs to support cancer patient symptom self-management during cancer treatments. The development of the SN©P comprised four steps with alternating development and evaluation phases. The SN©Flyers demonstrated excellent face validity and showed promising beneficial results for cancer patients. Involving relevant stakeholders is recommended for successful and sustainable implementation of complex interventions (60, 62), and to facilitate behaviour change of health care professionals (6). Accordingly, we involved patients, nurses, oncologists, and psycho-oncologists in all stages of the development process (1, 2).

Other programs have been developed to support cancer patients' symptom self-management. The SN©P differs from prior programs in several important ways. Patients only received SN©Flyers targeting their current, individual symptoms. This is in contrast to the CHEMO-SUPPORT program, in which patients were provided an all-inclusive booklet covering self-care and cancer (93). Self-management interventions can be efficient if they provide patients with the most relevant information for their individual situation and do not overburden patients with too much or irrelevant information (23). The SN©P is intended for cancer patients irrespective of diagnosis and can be used during any stage of the illness trajectory. Implementing diagnosis-specific nurse-led intervention is not feasible in most ambulatory cancer centres. Programs such as the PROSPECTIV for prostate cancer survivors (137) may be too specific for the needs of patients in the general outpatient cancer setting.

Nurse perspectives on acceptability and content of training

Overall, the content of the SN©P training was well-received. However, minimum and maximum ratings for the video examples and introduction of the SN©P varied considerably. The observed difference may reflect different experiences in supporting cancer patients with symptom self-management as well as different educational preparation for working in oncology nursing. As such, tailoring training content to nurses' education level and individual needs may warrant consideration (138).

Narrative feedback received in open-ended responses was generally positive - further suggesting that the training content and format were acceptable. Nurses provided a few critical remarks regarding trainers' guidance through the courses and this will be a target for improvement in future

training courses. The initial training helped most nurses become familiarised with the SN©Flyers and principles guiding the semi-structured consultations. Importantly, nurses underscored the importance of learning from each other thus supporting the interactive approach to training. We aimed to train all graduate nurses at each centre for a total of six hours. However, only about half of nurses attended both training courses. This observation suggests that it may not be feasible to train all nurses from a centre by offering only two training opportunities and perhaps additional training opportunities should be offered.

Nurses' confidence to implement the SN©P

Overall, nurses felt confident to apply the SN©P within their daily clinical routine. However, some nurses were not fully convinced they could accomplish this type of semi-structured consultation with high fidelity. It is plausible that educational preparation and oncology experience might have influenced perceived confidence for providing such a complex intervention involving relatively high level communication skills (138, 139). Nursing leaders could play an important role in supporting nurses and facilitate behaviour change (i.e. delivering the intervention) (60, 140).

Work-related factors associated with nurses' confidence in implementing the SN©P

Mean Work-SoC scores in this study were similar to those observed in a study testing the instrument's validity (mean ± SD = 5.10 ± 0.89 vs. 5.30 ± 0.93 respectively) (136). It seems that the work situation at participating centres might have influenced nurses' confidence to implement semi-structured SN©P consultations within clinical daily routines. Due to the limited number of nurses attending the follow-up training (n = 14), the significant correlation between overall Work-SoC score and nurses' perceived confidence to integrate educational consultations within daily clinical routines should be interpreted with caution. Nevertheless, this finding is consistent with the COM-B model that posits individual knowledge, motivation and work-related factors influence behaviour change (6). Given the initial findings, we plan to use focus groups in ongoing studies to further explore the role of work environment factors in implementing the SN©P in ongoing work.

Limitations

Best practices call for evaluating novel complex interventions in pilot studies to examine feasibility of introducing a new intervention under real life conditions as well as for exploring effect sizes prior to conducting appropriately-powered clinical trials (62, 141). Due to the limited sample of trained nurses (n = 21), the results should be considered preliminary and interpreted with caution. Results from the current study may guide refinement of training content to enhance acceptability and improve nurses' confidence to implement the SN©P within their daily clinical routine.

In summary, we successfully implemented the SN©P in three outpatient cancer centres randomised to intervention clusters. However, the implementation of the SN©P was driven by nurses who were motivated to enhance self-management support at their centres. Therefore, acceptability of the training at other, potentially less motivated, centres might be different. The three centres with successful implementation were in urban areas yet we were unable to successfully implement the SN©P at the lone rural centre due to a significant decrease in patients receiving anti-cancer treatments at that centre. Accordingly, feasibility of implementing the SN©P at rural centres merits further investigation.

Herein we described the training content and nurses' evaluation of the training. However, we did not specifically report how nurses applied the SN©P at their respective centres. Nurses' fidelity to training manual and their evaluation of the SN©P within their daily clinical practice will be crucial for long-term implementation and sustainability.

Implications for clinical application

The small number of nurses participating in both training courses may point to logistical barriers for planning/conducting training. Such logistical roadblocks could limit broad dissemination and implementation of the SN©P. One potential avenue for mitigating such challenges may involve using an e-learning tool to offer asynchronous training for nurses. However, such individual e-learning experiences may not be acceptable as nurses expressed significant value in discussions and peer-to-peer learning. An e-learning tool introducing the SN©P combined with a face-to-face follow-up training could be a potential mixed approach that would accommodate group-learning.

Conclusion

The SN©P is a nurse-led program to enhance symptom self-management in patients diagnosed with cancer. The training prepared nurses to provide symptom self-management support and is a first step in standardising nurse-led self-management education for patients diagnosed with cancer. Based on our development process and the promising initial results, we believe the SN©P could help drive change in oncology nursing practice. The SN©P may help shift perspectives on self-management support from simply providing generic information to a more tailored approach empowering patients to self-manage symptoms.

Patient accrual and retention rates (reach)

Subsequently to the second article, the reporting of the thesis results follows the RE-AIM framework dimensions starting with patient accrual and retention rates illustrating the reach dimension. These results were not integrated in the third article submitted to the journal “Cancer Nursing” that will follow this chapter. The third article reports on the effectiveness dimension of the RE-AIM framework.

Overall, we included 80% of all eligible patients to the Symptom Navi Pilot Study (71% to SNP intervention, 87% to control group). Recruitment of patients into the two respective groups differed considerably with a smaller proportion of eligible patients being included in the SNP group (risk difference – 19%, 95% CI: -32 to -7%, *p* =0.003) (Table 15).

Table 15: Accrual rates for patients’ inclusion into Symptom Navi Pilot Study for both groups

	Symptom Navi		Control		Risk difference	*P*-value
	N	n (%)	N	n (%)	(95% CI)	
Included patients	69	49 (71%)	94	85 (90%)	-19% (-32 to -7%)	0.003

N refers to the number eligible, n to the number in included patients. This calculation is based on a Mantel-Haenszel risk difference stratified for the recruitment potential.

Patients recruited into the intervention group differed across the three participating centres (67% to 77 %), whereas recruitment in the control group varied between 75% and 100%. In both groups, we included relatively ‘fast’ and ‘slow’ recruiting centres based on *a priori* estimated recruitment potential of the respective centres. The control group included three ‘fast’ and two ‘slow’ recruiting centres because one centre was randomised in a second round resulting in the observed imbalance (Table 16).

Table 16: Recruitment per centre

	Allocation	Recruitment potential	No. screened	No. included (%)
Centre 1	SNP	Fast	30	20 (67%)
Centre 2	SNP	Fast	13	9 (69%)
Centre 3	SNP	Slow	26	20 (77%)
Centre 4	SNP	Slow	0	0
Centre 5	Control	Fast	20	20 (100%)
Centre 6	Control	Slow	16	12 (75%)
Centre 7	Control	Slow	13	12 (92%)
Centre 8	Control	Fast	24	20 (83%)
Centre 9	Control	Fast	25	21 (84%)
Total			167	134 (80%)

Legend: No : number ; SNP Symptom Navi Programme (intervention group) ; Control : control group

A high proportion of patients in the intervention group (n = 48, 98%) received the initial consultation with the SN-Flyers, and 90% (n = 44) received one follow-up consultation as defined for minimal basic support in the training manual. Reasons for not receiving the follow-up consultations included therapy cessation (n = 4, 8%) and death (n = 1, 2%). Additional follow-up consultations were infrequently provided (n = 5, 10%). Reasons for continuing with additional follow-up consultations were not assessed in the pilot study. However, during training nurses were encouraged to continue delivering semi-structured consultations based on observed patient needs. Overall retention rates and intervention per protocol are summarised in Table 17.

Table 17: Retention rates for patients receiving the SNP as intended

	N	n (%)	Proportion (95% CI)*
Included patients			
Centre 1	30	20 (67%)	67% (49 to 81%)
Centre 2	13	9 (69%)	69% (42 to 87%)
Centre 3	26	20 (77%)	77% (58 to 89%)
Overall, naive	69	49 (71%)	71% (59 to 80%)
Overall, cluster-adjusted	69	49 (71%)	71% (54 to 84%)
Overall, cluster-adjusted via GLM	69	49 (71%)	71% (63 to 78%)
Intervention per protocol			
Centre 1	20	15 (75%)	75% (53 to 89%)
Centre 2	9	8 (89%)	89% (57 to 98%)
Centre 3	20	20 (100%)	100% (84 to 100%)
Overall, naive	49	43 (88%)	88% (76 to 94%)
Overall, cluster-adjusted	49	43 (88%)	88% (33 to 99%)
Overall, cluster-adjusted via GLM	49	43 (88%)	88% (59 to 97%)

* Confidence intervals (CI) for the overall proportions were calculated using Wilson score method (naïve), the Wilson score method adjusted for clustering on the level of centre (cluster-adjusted), or logistic regression with cluster robust standard errors (cluster-adjusted via GLM). N refers to the number of eligible, n to the number of included patients.

Pilot Testing of a Nurse-led basic Symptom Self-Management Support for Patients Receiving First-line Systemic Outpatient Anticancer Treatment: A Cluster-randomised Study (Symptom Navi Pilot Study) (third article)

Marika Bana; Karin Ribi; Solange Peters; Susanne Kropf-Staub; Ernst Näf; Sabin Zürcher-Florin; Barbara Stoffel; Cornelia Blaeuer; Markus Borner; Diana Malin; Rebecca Biber; Daniel Betticher; Trudy Kuhn-Bächler; Nathan Cantoni; Thomas Seeger; Lukas Bütikofer; Manuela Eicher On behalf of the Symptom Navi Program Group

Authors affiliations:

School of Health Sciences, University of Applied Sciences and Arts Western Switzerland - Fribourg, Switzerland (Mrs Bana); Institute of Higher Education and Research in Health Care IUFRS, University of Lausanne and Lausanne University Hospital, Faculty of Biology and Medicine, Lausanne, Switzerland (Mrs Bana, Dr Ribi, Prof Eicher); International Breast Cancer Study Group (IBCSG), Switzerland (Dr Ribi); Hospital Group Lindenhof, Bern, Switzerland (Mrs Kropf-Staub, Mrs Zürcher-Florin); Department of Practice Development in Nursing, Solothurner Spitäler, Switzerland (Mr Näf); Departement Onkologie / Hämatologie Kantonsspital Graubünden, Chur, Switzerland (Mrs Stoffel); Gynäkologisches Tumorzentrum, Universitätsspital Basel, Switzerland (Dr Bläuer); Brustzentrum Bern, Oncocare, Switzerland (Prof Borner); rundum Onkologie am Bahnhofplatz, Sargans, Switzerland (Mrs Malin); Tumorzentrum ZeTuP Rapperswil-Jona, Switzerland (Mrs Biber); freiburger spital HFR, Switzerland (Prof Betticher); Onkologie- und Hämatologiezentrum Thun-Berner Oberland, Switzerland (Mrs Kuhn-Bächler); Division Onkologie, Hämatologie und Transfusionsmedizin, Kantonsspital Aarau, Switzerland (Dr Cantoni, Mr Seeger); Universität Bern, CTU, Bern, Switzerland (Dr. Butikofer); Department of Oncology, Centre Hospitalier Universitaire Vaudois (CHUV), Lausanne, Switzerland (Prof Peters, Prof Eicher);

Correspondence:

Prof Dr Manuela Eicher, Institute of Higher Education and Research in Health Care IUFRS, Faculty of Biology and Medicine, University of Lausanne and Lausanne University Hospital, SV-A Secteur Vennes, Route de la Corniche 10, CH-1010 Lausanne, Switzerland (manuela.eicher@chuv.ch)

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Précis:

The Symptom Navi Programme was appreciated by patients and accepted by health professionals, but the pilot-testing did not show any preliminary impact on symptom interference with daily living.

Abstract

Background: The Symptom Navi Programme (SNP) is a nurse-led intervention supporting basic symptom self-management for patients with any cancer diagnosis. It has been accepted well by patients and health care professionals.

Objective: To evaluate preliminary indications of effectiveness of the SNP on patient reported symptom outcomes, nursing support for symptom management, and patient safety.

Interventions / Methods: Using a cluster-randomised design, we randomised centres to the intervention (SNP) or control group (usual care). Adult patients starting a first-line systemic cancer treatment were included. The primary outcome was the change (from the onset of treatment to 16 weeks) in symptom interference with daily functions (SIDF). Secondary outcomes included changes in symptom severity, symptom burden, self-efficacy, and perceived support for symptom management and patient safety. We employed linear or logistic mixed-effect models to pilot-test differences in mean changes between groups. The trial was registered at Clinical Trials Gov (NCT03649984).

Results: Changes in SIDF did not significantly differ (mean difference at 16 weeks: -0.50; 95% CI: -1.38 to 0.38; p-value: 0.25) between SNP (3 centres, 49 patients) and control (5 centres, 85 patients) as for all other outcomes. No adverse events were reported.

Conclusions: Our preliminary findings did not indicate an effect of the SNP on patient-reported symptom outcomes, self-efficacy, and symptom management support. SNP components (e.g. insufficient training, low number of follow-up consultations) may have attributed to this lack of effect, as well as inadequate power.

Implications for practice: The SNP needs reconsideration of the training content and intervention procedures.

Résumé:

Contexte : le Programme Symptom Navi (SNP) est une intervention menée par le personnel infirmier en vue d'offrir un soutien de base dans l'autogestion de leurs symptômes aux patient·e·s atteints·e·s de tout type de cancer. Ce programme a été bien accepté par les patient·e·s et par les professionnel·le·s de la santé.

Objectif : évaluer les indications préliminaires d'efficacité du SNP en ce qui concerne les effets sur les symptômes rapportés par les patient·e·s, l'aide du personnel infirmier à la gestion des symptômes et la sécurité des patient·e·s.

Interventions / Méthodes : utilisant une conception randomisée par grappes, nous avons attribué aléatoirement des centres d'oncologie au groupe d'intervention (SNP) ou au groupe de contrôle (soins usuels). Ont été inclus dans l'étude des patient·e·s adultes commençant un traitement anticancéreux systémique de première ligne. Le résultat principal visé portait sur le changement intervenu dans l'interférence des symptômes avec les fonctions de la vie quotidienne (du début à 16 semaines de traitement). Les résultats secondaires comprenaient les changements de gravité des symptômes, la pression de ceux-ci, l'auto-efficacité, l'aide ressentie dans la gestion des symptômes par les patient·e·s et la sécurité de ces derniers. Nous avons utilisé des modèles linéaires ou logistiques à effets mixtes pour effectuer un test pilote des différences dans les changements moyens entre les groupes. L'essai a été enregistré dans la banque de données Clinical Trials Gov (NCT03649984).

Résultats : les changements intervenus dans l'interférence des symptômes avec les fonctions de la vie quotidienne n'ont pas différé significativement (différence moyenne à 16 semaines: -0.50; 95% IC : -1.38 to 0.38; valeur p : 0.25) entre groupe SNP (3 centres, 49 patient·e·s) et groupe de contrôle (5 centres, 85 patient·e·s). Il en va de même de tous les autres résultats. Aucun événement indésirable n'a été signalé.

Conclusions : nos constatations préliminaires n'indiquent pas que le SNP influence les effets des symptômes rapportés par les patient·e·s ou l'auto-efficacité de ces derniers, ou encore l'aide à la gestion des symptômes. Certaines composantes du SNP (formation insuffisante, nombre peu élevé de consultations de suivi, p. ex.) peuvent avoir contribué à cette absence d'effet, ainsi qu'une puissance statistique inadéquate.

Implications pour la pratique : il convient de réexaminer le contenu de la formation et les procédures d'intervention du SNP.

Key words: Symptom Management, Behaviour change; Implementation Science; Nurse-led interventions; Self-Efficacy; Self-Management Support

Other information:

Registration: ClinicalTrails.gov: NCT03649984; and Swiss National Clinical Trials Portal: SNCTP000002381

Protocol: The study protocol has been published http://dx.doi.org/10.1136/bmjopen-2018-027942

Introduction

All patients diagnosed with cancer need relevant information, emotional support, good communication, and support for symptom management to better cope with the cancer disease, the side effects of treatments and their interference with daily living (15). A shift to outpatient cancer treatments increasingly calls on patients to self-manage their symptoms because symptom severity often increases between treatment administrations (142). As a consequence, patients treated in outpatient settings need at least basic symptom self-management support at the onset of a treatment (83, 143).

Self-management support (SMS) is based on a collaborative partnership between caregivers and patients including a set of techniques and tools to facilitate patient's self-management of daily duties and challenges (144). The concept of SMS has been applied since several decades for chronic conditions like diabetes, arthritis, chronic heart or lung diseases, and human immunodeficiency virus infection. SMS expands traditional patient education approaches with the aim to facilitate behaviour change by using different approaches (e.g. care planning, motivational interviewing, health coaching) (25). Most research on SMS has been in relation to chronic conditions. The research indicates that it should be an integral part of high quality care because SMS has been shown to improve clinical outcomes and potentially reduces costs (24, 25, 40). Patients diagnosed with cancer differ from other chronic conditions. They experience intensive treatment phases with close surveillance by the treatment team, alternating with remission phases during which contact to health care professionals are less likely and challenges to self-manage more likely.

Since SMS was introduced in the cancer setting, a growing body of research indicates that SMS can reduce physical symptoms (e.g. pain, fatigue, nausea) and psychosocial consequences (e.g. not returning to work), and can improve quality of life in general (41). However, systematic reviews have shown that the components of SMS interventions are very heterogeneous with variable magnitudes of effects on outcomes (22, 27). Therefore, it remains unclear which components of SMS interventions are crucial for obtaining optimal patient outcomes in relation to cancer symptom self-management.

Fostering patient self-efficacy has been identified as an essential aim of SMS interventions (64, 142, 145, 146). Self-efficacy is a subjective perception that one can achieve a desired behaviour or task, even if it becomes challenging (69). In several studies, the facilitation of self-efficacy was an integral part of the SMS intervention leading to better outcomes (64, 147, 148). Higher perceived self-efficacy is associated with lower symptom prevalence and distress, better quality of life, and may predict physical well-being (98). Fostering self-efficacy of patients with cancer treatments is challenging because they have to manage a variety of co-occurring symptoms and a cumulating toxicity over the treatment trajectory (92).

Nurses are in close contact with patients and monitor their symptoms earlier and more frequently than other health care professionals (149). Nevertheless, SMS is not integrated in the standard care provided by oncology nurses in many outpatient settings (93) even though they are well suited to play an important role in SMS (91). To date, most research on SMS has focused on symptom outcomes (22, 150). However, the implementation process of self-management interventions into clinical routines has rarely been investigated (29).

To address the lack of standardised approaches to nurse-led SMS in Switzerland, the development of the Symptom Navi Program (SNP) started in 2011 in collaboration with health care professionals and patients diagnosed with cancer (8). The SNP complements usual nursing care and consists of written information leaflets called Symptom Navi Flyers (SN-Flyers), nurse-led semi-structured consultations using the SN-Flyers, and a training manual for standardised implementation of the SNP (7). Best practice suggests to test the feasibility and effectiveness for complex interventions such as the SNP before widespread implementation (62).

This article reports on the preliminary indications of effectiveness of the SNP that is part of a multi-method pilot study (Symptom Navi Pilot Study) evaluating the implementation process (the study protocol has been published elsewhere) (7). The primary objective is to explore the impact of the SNP on patients' symptom interference with their daily functions compared with usual care. Secondary objectives were: to investigate the impact of the SNP on patients' symptom severity/burden and their perceived self-efficacy, to explore patients evaluation on nurses' support for symptom management, and to report patient safety with the SNP. Further evaluated objectives of the Symptom Navi Pilot Study will be published elsewhere.

Methods

We conducted a cluster-randomised pilot study with two parallel arms. Reporting of the study is based on the extended CONSORT guideline for cluster-randomised trials (99). Centres interested in implementing the SNP were considered as clusters to prevent cross contamination between patients in the intervention and the control group (151). The pilot-testing of the SNP was planned to estimate effect sizes and intra-cluster correlation in order to calculate needed sample and cluster sizes for a full powered study (101, 151). The Symptom Navi Pilot Study is registered at Clinical Trials Gov (*NCT03649984)* and no methodological changes of the study protocol have been applied.

The Theory of Symptom Self-Management (TSSM) (64) was the guiding framework for evaluating investigations of the potential impact of the SNP. The TSSM emphasises that patients self-management behaviour will depend on multiple connected dimensions: symptom severity will influence patient's symptom self-management behaviours and perceived self-efficacy for self-management behaviour. Complementary, perceived self-efficacy will influence self-management behaviour. Ultimately, patient's personal and social health context and applied self-management behaviour will affect the individual functional status (Appendix 7, Supplementary figure 1).

Setting and Sample

German-speaking Swiss cancer outpatient centres administrating systemic anti-cancer therapies and interested in implementing the SNP were eligible to participate in the pilot study. We included regularly employed graduated nurses with at least one-year experience in oncology nursing who were administering systemic anticancer treatments at the centres. Eligible participants were adult patients (≥ 18 years) newly diagnosed with any type of cancer within 15 weeks before signing informed consent. We excluded patients who could not read or speak in German, had a cancer recurrence, or were exclusively treated with surgical or radiation therapy. Also excluded were patients being followed by a palliative care team or participating in another psychosocial study.

Study procedures

At every participating centre, a dedicated nurse and/or oncologist were responsible for screening eligible patients and patient recruitment for the study. Nurses approached eligible patients and invited them to participate. After patients provided written informed consent, they were asked to complete the baseline assessment at the centre.

Usual nursing care for supporting symptom management included the provision of oral and written information on expected side effects at the beginning of a new therapy by asking patients ad hoc about their symptom experience during a scheduled treatment at the centre. Standardised and validated assessment tools are rarely a compulsory part of usual care in Swiss cancer outpatient settings. Some centres had implemented extra nurse-led consultations to reduce the amount of information shared at the onset of a cancer treatment. Patients also had access to information brochures from the Swiss Cancer League and/or information leaflets from the treatment centres based on pharmaceutical drug information.

Intervention: Symptom Navi Programme

The SNP consists of: i) the SN-Flyers (16 symptom-specific and 6 complementary flyers), ii) nurse-led semi-structured consultations using the SN-Flyers, and iii) a training manual for standardised implementation of the SNP. All components were based on the TSSM. SN-Flyers includes information on symptom signs at three levels (mild, moderate, and severe) and provide evidence-based recommendations to self-manage the symptom at every level. Colour codes (green = mild, yellow = moderate, and red = severe) and emoticons (smiling, concerned, and sad face) facilitate patient's estimation on symptom level. When symptoms reach the severe (red) level, patients were requested to contact the care team. To meet a patient's individual need, nurses prioritise which information flyers are important and appropriate starting a conversation with the patient. This avoids an overload of information and helps to facilitate patient's collaboration.

Six key elements structured the consultations: 1) preparing the consultation, 2) evaluating patient's willingness and motivation for the consultation, 3) providing information based on patient's need and/or expected treatment side-effects, 4) addressing symptom self-management, 5) facilitating symptom self-management, and 6) documenting the consultation. The nurse-led semi-structured consultations were based on self-management education principles (21, 59) and included Motivational Interviewing (MI) techniques. MI is an evidence-based and client-centred conversation method to strengthen client's motivation to facilitate behaviour change based on individual goals and action plans (104, 152).To achieve a standardised application of semi-structured consultations, we trained all nurses in the intervention sites before patient recruitment started.

The nurse training was based on the Capability Opportunity Motivational – Behaviour (COM-B) model (131) and standardised in the SNP training manual. The COM-B model emphasises that changes in nurses' practice behaviours will depend on their knowledge and skills (capabilities), on analytical decisions (motivation), and centre-specific factors that make the behaviour possible (opportunities). Two research team members (MB and SKS, experts in SMS and familiar with the SNP) provided two training courses with four and two hours respectively. To implement standardised symptom management assessments were not part of the SNP training to prevent overloading nurses' tasks and behaviour change challenges.

Nurses provided a first consultation tailored to the therapy protocol shortly before or during the first anticancer treatment at the centre. To assess patient's context nurses asked for previous experiences with health care providers and the availability of family caregiving support. During a subsequent treatment delivery at the centre, nurses supported patient's individual self-management behaviour at a follow-up consultation. At this moment, nurses asked the patient about individual experience of their symptoms and applied self-management strategies. Further, nurses guided the patient to set attainable goals and name concrete actions to achieve these goals to facilitate his/her self-efficacy. We recommended nurses to use symptom assessment tools to evaluate symptom intensity and to facilitate the conversation about self-management behaviours. Details on the SNP and nurse training have been published elsewhere (8).

Outcomes

Medical records and questionnaires developed for the pilot study were used to assess patient and cluster characteristics. For patient's characteristics, we assessed mother-tongue, housing context, education, and medical data concerning diagnosis, co-morbidities and treatment information. For cluster characteristics, we included centre-specific information (e.g. full time equivalent of employed health professionals) and nurse qualifications.

The outcome of primary interest was the mean change in symptom interference with daily functions (SIDF) over all follow-up time points from baseline to 16 weeks after baseline. Outcomes of secondary interest included symptom severity, symptom burden, self-efficacy and quality of nursing care. All applied outcomes, assessment time points, and assessed patient and cluster characteristics are summarised in table 18.

Symptom severity, symptom burden and SIDF were assessed by the MD Anderson Symptom Inventory (MDASI) German version (107), and self-efficacy by the Self-efficacy for Chronic Disease 6 item Scale German version (SES6G) (108). The MDASI consists of 19 items using 11-point Likert scales, higher ratings indicating increased symptom severity, burden, and interference with daily functions. Symptom burden is the sum of symptom severity scores and SIDF scores (between 0 and 20), higher ratings indicating higher symptom burden (153). The SES6G questionnaire uses 10-point Likert scales with higher ratings indicating higher perceived self-efficacy, i.e. more confidence to achieve symptom self-management. To assess patient estimation on nursing support for symptom management, we translated and culturally adapted five items of the Patient-Reported Chemotherapy Indicators for Symptoms and Experience (PR-CISE) questionnaire to German (91). Details on scoring and psychometric properties of the outcome measures are described in the study protocol (7). As specified in the statistical analysis plan, we dichotomised the PR-CISE outcomes (yes, somewhat = yes, vs no) because very few patients answered these items with no. As a potential confounder, we also assessed mood using the one item Mood Linear Analogue Self-Assessment Scale (Mood LASA Scale) (110). To evaluate safety, we used standardised Serious Adverse Event (SAE) reporting and specific questions for nurses on observed 'critical' behaviour of patients or any signs and problems that might indicate an adverse event. We considered for example, delayed contact with the care team, despite occurrence of a severe symptom as a critical behaviour (e.g. fever with neutropenia, or exacerbated diarrhoea). Nurses answered these safety questions online after every provided semi-structured consultation.

Data Collection

Patients completed the baseline assessment at the treatment centre and all three follow-up assessments (t1= 1-3 weeks, t2= 4-6 weeks, t3= 16 weeks [± one week] after baseline assessment) at home. Nurses at the treatment centres provided patients with the questionnaires and pre-stamped addressed envelopes to return them to a research team member (MB) who was responsible for data entry.

Randomisation

Randomisation occurred at the level of participating cancer outpatient centres (= clusters). Patients were recruited consecutively and assigned to intervention (SNP) or control based on the randomisation result of their treatment centre. We stratified the randomisation based on a priori assessed recruitment potential of centres (fast versus slow recruiting centres: i.e. estimated patients meeting the inclusion criteria at the centre per year ≤ 150 were slow recruiters). For each strata, we generated blocks of two due to the small number of clusters for this pilot study. No stratification procedures have been applied at the individual patient level.

Allocation concealment of the cancer centres to intervention or control group was ensured by a clinical trial unit (CTU) generating the random allocation sequence and assigning them to the respective clusters (SNP vs control). The local principal investigator (responsible oncologist) gave informed consent for the centre before randomisation was performed. Because of the intervention characteristics, no blinding procedures were applicable.

Table 18. Assessed Outcomes and Covariates

Level	Instruments (N items)	Assessed	Outcomes
Cluster / centre	Cluster characteristics (6)	BL	Specialised cancer centre, nurses' formation, number of employed nurses and oncologists at each intervention centre, average number of delivered anti-cancer treatments per day, number of treated patients at the centre per year, information leaflets usually delivered to patients
Individual / patient	Patient's characteristics (9)	BL	Age, gender, diagnosis, co-morbidities, pharmaceutical information of treatment, and Karnofsky index, mother tongue, housing context, highest education degree
Individual / patient	Primary outcome: MDASI (6)	BL, t1, t2, t3	6 items on symptom interference for daily functions (general activity, mood, work, relations with others, walking, enjoyment of life)
Individual / patient	Secondary outcomes: MDASI (13)	BL, t1, t2, t3	Symptom severity: pain, fatigue, nausea, disturbed sleep, distress, shortness of breath, difficulty remembering, poor appetite, drowsiness, dry mouth, sadness, vomiting, numbness or tingling
Individual / patient	PR-CISE (5)	BL, t1, t2, t3	Nurse support for symptom management, patient-reported: - Nurses ask about your symptoms - Nurses are aware of your symptoms' severity - Nurses provide useful information to manage symptoms - Nurses provide practical advice to manage symptoms - Are you confident to manage the symptoms you are experiencing?
Individual / patient	SES6G (6)	BL, t1, t2, t3	Self-efficacy for: - Managing fatigue, - Managing physical discomfort, - Managing emotional distress, - Keeping symptoms from interfering with things they want to do, - Managing health conditions without doctors help, - Generally feeling confident to find alternative approaches than just taking medications to relieve a symptom.
Individual / patient	Further covariate: Mood LASA scale (1)	BL, t1, t2, t3	How do you rate your mood during the last two weeks?
Individual / patient	Safety (2)	At any time occurring and regularly at BL, t1, t2, t3	Reporting on serious adverse events related to SNP Narrative reporting by nurses (online)

Abbreviations: BL, Baseline; LASA, Linear Analogue Self-Assessment; MDASI, MD Anderson Symptom Inventory; N, number; PR-CISE, Patient-Reported Chemotherapy Indicators for Symptoms and Experience; SES6G, Self-efficacy for Chronic Disease 6 item Scale; t1, 1-3 weeks (between second and third treatment application); t2, 4-6 weeks (between third and fourth treatment application); t3, 16 weeks (± one week).

Statistical methods

Our assumption was that the SNP supports patients during active anticancer treatments to reduce their symptom interference with daily functions. We did not perform a formal sample size calculation due to the lack of data about expected effect sizes or correlations, and a limited number of clusters available. Based on preliminary estimates on number of patients meeting the inclusion criteria at the centres, we assumed that recruiting 10 to 20 patients would be feasible for every centre. Therefore, a sample size of approximately 140 patients was planned (approximately 70 patients for each group). Assuming an intra-class correlation of 0.05 and a type I error rate of 5%, 9 clusters with 15 patients (i.e. a sample size of 135 patients) would allow for a detection of effect sizes of 0.5, 0.75, and 1 with powers of about 60%, 91%, and 99%, respectively (7).

Wilcoxon-Mann-Whitney tests and Fisher's exact tests were used to compare continuous and categorical patient baseline characteristics, respectively. We performed primary analysis on the full analysis set according to the intention-to-treat principle (i.e. analysing all patients of the randomized clusters according to the centre), and secondary analyses on the per-protocol set (PPS) and the complete cases (only including patients with complete follow-up of the respective outcome).

Continuous outcomes were analysed by using linear mixed-effects regression models including all measurement time points (i.e. t1 = 1-3 weeks, t2 = 4-6 weeks, or t3 = 16 weeks). We used baseline measurement (BL), treatment group (SNP vs Control), time point, the interaction of treatment group and time point, and the stratification factor (recruitment potential) as fixed covariates. To account for correlations within centre and patients, we added a random intercept for centre and a random intercept and slope for patient (nested within centre). The models were fitted with restricted maximum likelihood (REML) and we used the Satterthwaite approximation for the degrees of freedom. A joint p-value over all time points and treatment effects (as mean difference with 95% CI) at each time point was calculated.

We analysed binary outcomes using logistic mixed-effects regression models (i.e. generalized linear mixed-effects models with binomial distribution and logit link) with treatment group, time point, the interaction of group and time point, and the stratification factor used in randomization as fixed effects, and random intercepts for centre and patient (nested within centre). A joint p-value over all time points and treatment effects (as odds ratio with 95% CI) was calculated at each time point.

Partially missing follow-up data was handled via the mixed-effects models. The proportion of patients with missing baseline or completely missing follow-up data was lower than 10% for all outcomes and they were excluded from the analysis.

We performed three pre-specified sensitivity analyses: adjustment for potential confounders; separate analysis of time point t3; and analysis on averaged data on the cluster level. In order to adjust for potential confounders, we included all baseline outcomes that showed imbalances between treatment groups with $p<0.1$ and mood as covariates in the mixed model. We omitted the therapy scheme, combined chemo-radiotherapy and mental disease because of very few cases in the sample. Further, we merged categories for the Karnofsky Index to either four (merging levels lower than 80) or two categories (normal Karnofsky Index = 100%, yes and no). The separate analysis at time point t3 was done with a simplified linear or logistic mixed model (for continuous and binary outcomes, respectively) with treatment group and stratification factor as fixed covariates and cluster as random intercept. Cluster means were compared between groups using a linear or logistic regression with treatment group and stratification variable as covariates.

Pre-specified subgroup analyses for symptom interference were performed with daily functions at time point t3 by recruitment potential (fast versus slow recruiters), combined chemo-radiotherapy and number of applied anticancer treatments (≤ 25 versus > 25 therapies per day) at the centre. Subgroups were analysed using linear mixed-effects models with the treatment group, the subgroup and their interaction as fixed, and the cluster as random effect. We calculated p-values for interaction based on likelihood ratio tests and treatment effects for the individual subgroups from the interaction

models using contrasts. We also calculated intra-class correlation coefficient (ICC) for all outcomes at every time point or overall using the linear mixed-effect models specified above.

Because we assumed that nurses' education level for oncology nursing (higher education level versus education level at university level) could be a confounding variable, we added a post-hoc analysis based on centre-specific education level of nurses for all patient-reported outcomes. For this analysis, we included centre-specific education level of nurses in the mixed model.

All analysis were performed using STATA version 15.1 and R version 3.5.3 (2019-03-11).

Results

Sixteen centres were assessed for eligibility between May and November 2017, of these five centres refused to participate, one centre already used the SN-Flyers, and one centre did not have enough resources (figure 7). Of the nine participating clusters (i.e. centres), we allocated four clusters to SNP and five clusters to control. One centre of the SNP group withdrew their consent before recruiting any patient. Patient recruitment started in October 2017 and ended in January 2019. Overall, 20% of screened patients (33 patients) were excluded from the study or did not sign the informed consent (20 patients (29%) in the SNP group and 9 patients (13%) in control). In one of the SNP clusters, recruitment was slow and fewer patients were recruited than expected. To reduce imbalance in patient recruitment between the two groups, we stopped recruiting patients at the slow recruiting control clusters. In total, 49 patients were allocated to SNP and 85 patients to control.

Baseline Characteristics

The included outpatient cancer centres represented the Swiss context with a mix of small regional and large urban tertiary cancer centres. Among the centres randomised to the SNP, two were breast cancer centres. All other centres included patients with different cancer diagnosis. Approximately half of the nurses employed in the cancer centres were formally educated in oncology nursing (table 19).

At baseline, patients' characteristics showed significant differences for age, gender, living with family members needing care, cancer diagnosis, and treatment scheme (intravenous and oral). In the control group, more patients were treated with oral anticancer treatments, had reduced daily functioning based on the Karnofsky Index, and were diagnosed with cancers other than breast cancer. There were no significant differences between SNP and Control regarding mother-tongue, housing context, patients' education level, and co-morbidities (table 20).

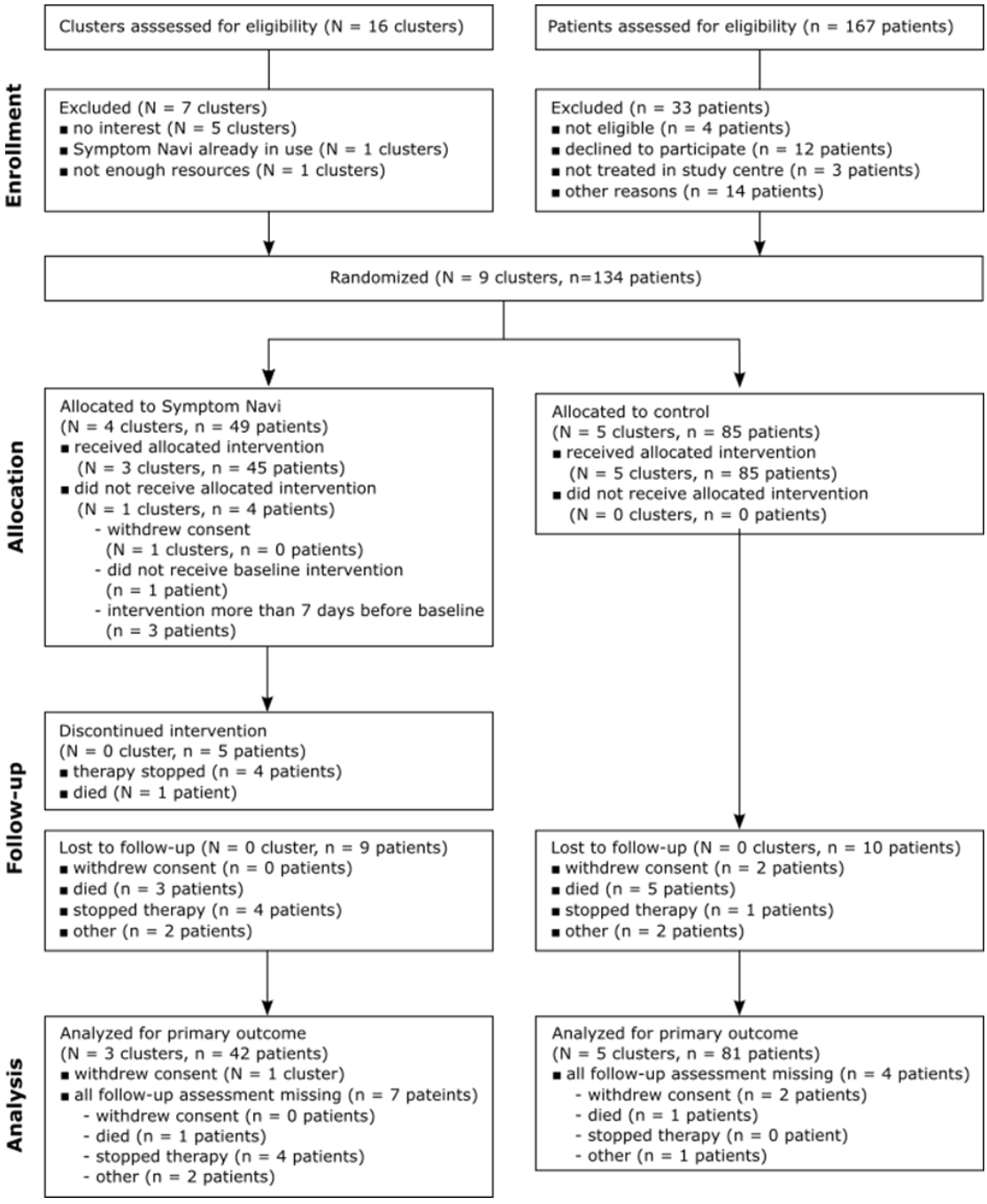


Figure 7: Cluster and Patient Flow

One cluster withdrew the consent before recruiting any patients.

Table 19: Cluster Baseline Characteristics

Participating clusters	SNP (N=3)	Control (N=5)
Outpatient Cancer Centre: n (%)*		
Independent oncological ambulatory	1 (33%)	2 (40%)
Ambulatory from a hospital network	0 (0%)	2 (40%)
Ambulatory from a cantonal hospital	1 (33%)	2 (40%)
Ambulatory from a tertiary hospital	1 (33%)	0 (0%)
Certificated oncological centre	3 (100%)	3 (60%)
Engaged Workforce: Median of total FTE [lq, uq]		
Oncologists	7.4 [2.0, 14.4]	4.6 [2.2, 7.4]
Nurses	3.1 [2.2, 7.1]	6.1 [2.6, 10.8]
Number Anticancer Treatments per Day		
Mean (sd)	26 (16)	22 (14)
Median [lq, uq]	22 [12, 44]	26 [9, 32]
Nurses Education: n/total (%)		
Graduated (higher education)	8/18 (44%)	27/54 (50%)
Graduated (BScN)	0/18 (0%)	1/54 (1.9%)
Graduated (MScN)	1/18 (5.6%)	1/54 (1.9%)
Education in oncology nursing, level I[a]	4/18 (22%)	20/54 (37%)
Education in oncology nursing, level II[b]	5/18 (28%)	5/54 (9.3%)

Abbreviations: FTE, Full Time Equivalent; BScN, Bachelor Science in Nursing; lq, lower quartile; MScN, Master Science in Nursing; sd, standard deviation; SNP, Symptom Navi Programme; uq, upper quartile;

Legend: *Numbers do not sum up as several entries are possible; [a]level I = education at non-university level; [b]level II = education at university level

Table 20: Patient Baseline Characteristics

	SNP (N=49)	Control (N=85)	P-Value
age: mean (sd)	59 (12)	66 (12)	.001
Women: n (%)	35 (71%)	44 (52%)	.030
Mother tongue*: n (%)			.37
German	46 (94%)	72 (85%)	
French	1 (2.0%)	1 (1.2%)	
Romansh	1 (2.0%)	3 (3.5%)	
Others	1 (2.0%)	8 (9.4%)	
Housing context*: n (%)			.43
Living alone	7 (14%)	15 (18%)	
Living with partner or spouse	42 (86%)	66 (78%)	
Other	0 (0%)	3 (3.5%)	
Caring for children or family members †: n (%)	14 (29%)	10 (12%)	.019
Highest education degree*: n (%)			.05
Compulsory school education (8 years)	5 (10%)	7 (8.2%)	
Completed vocational training	21 (43%)	55 (65%)	
Higher professional degree	19 (39%)	16 (19%)	
University degree	4 (8.2%)	6 (7.1%)	
Cancer diagnosis: n (%)			.013
Breast cancer	25 (51%)	24 (28%)	
Lung cancer	8 (16%)	12 (14%)	
Other	16 (33%)	49 (58%)	
Therapy scheme: n (%)			
intravenous	48 (98%)	68 (80%)	.003
subcutaneous	1 (2.0%)	6 (7.1%)	.42
oral	1 (2.0%)	19 (22%)	< .001
Co-Morbidities: n (%)			
Diabetes	6 (12%)	9 (11%)	.78
COPD	2 (4.1%)	6 (7.1%)	.71
Heart failure	1 (2.0%)	5 (5.9%)	.41
Mental diseases	0 (0%)	6 (7.1%)	.09
Dementia	1 (2%)	1 (1.2%)	1.0
Others	5 (10%)	17 (20%)	.16
Functional status based on Karnofsky Index: n (%)			.020
- unable to carry on normal activity or less (≤ 70%)	5 (10%)	13 (15.4%)	
- normal functionality with effort (80%)	8 (16%)	11 (13%)	
- minimal disease symptoms (90%)	9 (18%)	35 (41%)	
- normal condition, no manifest disease (100%)	27 (55%)	26 (31%)	

Legend: *Missing for one patient in Control group, †Missing for two patients in Control group, Other cancer diagnosis summarise prostate, colorectal, head and neck, pancreatic, hematologic, ovarial, and other cancers.

Intra-class correlation coefficient

Intra-class correlation coefficients (ICC) were overall very close to 0 in most situation, indicating that observations within the centres were not correlated (Appendix 7, supplementary tables 1 and 2).

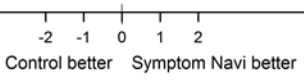
Effect on symptom outcomes and perceived self-efficacy

Descriptive plots of the outcomes are shown in the supplementary document (Appendix 7, supplementary figures 2 and 3). The primary analysis (SNP: 42 patients, Control: 81 patients), showed no significant effect on any of the assessed patient-reported symptom outcomes or self-efficacy at any time point (table 21). The SNP had no effect on SIDF over all time points (joint p-value: 0.59) nor at 16 weeks after baseline (mean difference: -0.50 (95% CI -1.38 to 0.38, p-value: 0.25) indicating that SNP interventions were not superior to usual care regarding the outcome of primary interest.

In both groups, patients reported mild symptom severity and burden scores (table **21**). Mean scores of symptom severity and burden increased from t1 to t3, and mean scores of self-efficacy decreased over this period, indicating that patients had to deal with more and/or more severe symptoms at t3, and concurrently they felt less confident to manage the situation. However, patients in the SNP rated their self-efficacy slightly higher compared to patients in the Control (mean difference at 16 weeks -0.14 (95% CI -0.79 to 1.07), joint p-value over all time points: 0.46, table 21).

Table 21: Mean Difference of Symptom Interference, Severity, Burden, and Self-Efficacy (MDASI and SES6G Items)

	Symptom Navi (SNP)		Control		Mean difference (95% CI)	P-value	Joint
	N	mean (95% CI)	N	mean (95% CI)			p-value
Mean symptom interference	42		81				.59
t1 (1-3 weeks)		2.77 (2.24 to 3.30)		2.37 (2.01 to 2.74)	-0.40 (-1.17 to 0.37)	.26	
t2 (4-6 weeks)		2.74 (2.14 to 3.35)		2.34 (1.93 to 2.75)	-0.40 (-1.21 to 0.41)	.30	
t3 (16 weeks)		3.26 (2.60 to 3.92)		2.76 (2.29 to 3.23)	-0.50 (-1.38 to 0.38)	.25	
Mean symptom severity	42		81				.65
t1 (1-3 weeks)		2.37 (1.96 to 2.78)		2.07 (1.78 to 2.36)	-0.30 (-0.90 to 0.30)	.28	
t2 (4-6 weeks)		2.43 (1.96 to 2.90)		2.15 (1.83 to 2.46)	-0.28 (-0.91 to 0.35)	.35	
t3 (16 weeks)		2.76 (2.24 to 3.27)		2.61 (2.24 to 2.97)	-0.15 (-0.83 to 0.53)	.65	
Mean symptom burden	42		81				.58
t1 (1-3 weeks)		5.11 (4.26 to 5.95)		4.40 (3.81 to 4.99)	-0.71 (-1.95 to 0.54)	.22	
t2 (4-6 weeks)		5.17 (4.19 to 6.14)		4.50 (3.84 to 5.16)	-0.67 (-1.99 to 0.64)	.29	
t3 (16 weeks)		5.90 (4.81 to 6.99)		5.37 (4.60 to 6.14)	-0.53 (-1.97 to 0.90)	.45	
Mean self-efficacy	41		81				.46
t1 (1-3 weeks)		7.66 (7.01 to 8.31)		7.27 (6.83 to 7.71)	0.39 (-0.48 to 1.27)	.35	
t2 (4-6 weeks)		7.69 (6.99 to 8.39)		7.03 (6.58 to 7.49)	0.66 (-0.26 to 1.57)	.15	
t3 (16 weeks)		7.01 (6.31 to 7.72)		6.87 (6.39 to 7.36)	0.14 (-0.79 to 1.07)	.75	



Legend: Primary analysis based on the full analysis set. Mean in each group and mean difference between groups (SNP vs Control) with 95% confidence intervals (CI) were derived from a linear mixed model. N refers to the number of non-missing observations.

The per-protocol and complete case analysis confirmed the results from the main analysis (Appendix 7, supplementary tables 3 and 4). Controlling for potential confounding variables (age, gender, living with persons who need care, education, type of cancer [breast, lung, others], Karnofsky Index, and mood) had small effects but the mean difference for SIDF somewhat increased in favour of the

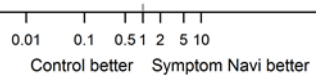
control (Appendix 7, supplementary table 5), e.g. - 0.83 (95% CI -1.62 to -0.04), p-value: 0.040 at 16 weeks). Simplified analysis for only the last follow-up visit (t3) showed a mean difference in SIDF of -0.68 (95% CI 1.76 to -0.40, p-value: 0.17, Appendix 7, supplementary table 6), and the comparison based on the cluster means confirmed that the SNP had no significant effect on any patient-reported outcome (Appendix 7, supplementary table 7).

Nurse support for symptom management

The primary analysis showed no significant difference on patients' reported nurse support for symptom management for any of the PR-CISE items (table 22). For three PR-CISE items, the evolution from t1 to t3 showed a more favourable trend in the SNP compared to the control. The proportion of patients reporting that nurses were aware about their symptom severity decreased from 94% to 86% in control, but increased in SNP at t3 to almost the results from t1, leading to an odds ratio of 1.39 (95% CI 0.21 to 9.27) at 16 weeks (joint p-value =.77). The proportion of patients reporting that they received useful information to manage their symptoms increased in the SNP from 79% to 85% between t1 and t3, whereas this proportion in the control decreased from 92% to 84%. In both groups, about one third of the patients was not confident managing their symptoms.

Table 22: Odds Ratio for Symptom Management Support (PR-CISE Items)

	Symptom Navi (SNP)		Control		Odds ratio (95% CI)	P-value	Joint
	N	n/N (%)	N	n/N (%)			p-value
Ask about symptoms	42		81				.95
t1 (1-3 weeks)		33/37 (89%)		74/79 (94%)	0.63 (0.07 to 5.72)	.68	
t2 (4-6 weeks)		25/31 (81%)		69/77 (90%)	0.58 (0.07 to 4.43)	.60	
t3 (16 weeks)		27/34 (79%)		60/70 (86%)	0.63 (0.09 to 4.21)	.63	
Aware of symptom severity	42		81				.77
t1 (1-3 weeks)		32/36 (89%)		74/79 (94%)	0.49 (0.06 to 3.71)	.49	
t2 (4-6 weeks)		25/31 (81%)		68/77 (88%)	0.56 (0.09 to 3.43)	.53	
t3 (16 weeks)		30/34 (88%)		60/70 (86%)	1.39 (0.21 to 9.27)	.74	
Information to manage symptoms	42		81				.17
t1 (1-3 weeks)		30/38 (79%)		73/79 (92%)	0.15 (0.02 to 1.26)	.08	
t2 (4-6 weeks)		24/31 (77%)		70/77 (91%)	0.15 (0.02 to 1.32)	.09	
t3 (16 weeks)		28/33 (85%)		59/70 (84%)	0.85 (0.10 to 7.04)	.88	
Practical advice to manage symptoms	42		81				.11
t1 (1-3 weeks)		28/38 (74%)		72/79 (91%)	0.14 (0.02 to 0.86)	.034	
t2 (4-6 weeks)		25/31 (81%)		69/77 (90%)	0.41 (0.06 to 2.98)	.38	
t3 (16 weeks)		28/33 (85%)		57/69 (83%)	1.48 (0.21 to 10.30)	.69	
Confident managing symptoms	42		81				.73
t1 (1-3 weeks)		25/38 (66%)		58/79 (73%)	0.52 (0.15 to 1.77)	.29	
t2 (4-6 weeks)		23/31 (74%)		61/77 (79%)	0.61 (0.16 to 2.44)	.49	
t3 (16 weeks)		21/33 (64%)		48/70 (69%)	0.69 (0.19 to 2.45)	.56	



Primary analysis based on the full analysis set. Odds ratios of SNP vs Control with 95% confidence intervals (CI) were derived from a generalised linear mixed model. N refers to the number of non-missing observations, n to the number of patients answering with yes.

Per-protocol analysis, complete case analyses, and adjustment for potential confounders (same variables used as for preliminary effectiveness analysis) confirmed results of primary analysis on symptom management support (Appendix 7, supplementary tables 8 - 10), as did the analysis of

only t3 and on comparison of the cluster-averaged data (Appendix 7, supplementary tables 11 and 12).

Subgroup and post-hoc analysis

We did not find any evidence that the effect of SNP on symptom interference at t3 (16 weeks) might be different in any of the pre-defined subgroups (centres' recruitment potential, combined chemo-radiotherapy, number of applied tumour therapies at the centres) (Appendix 7, supplementary figure 3). Including nurses' education level to the mixed-effect models had no influence on any patient-reported outcomes. Therefore, none of the added analysis changed the results of primary analysis of no significant difference between the SNP and control.

Patient safety

No adverse events were reported from any centre randomised to SNP during the study. Nurses did not report any observation of a critical behaviour of patients or signs of adverse events using the SN-Flyers. Based on national ethic committees' rules, we did not assess patient safety outcomes in the control.

Discussion

In this cluster-randomised pilot study, we evaluated whether the SNP could support patients' symptom self-management. Despite our promising descriptive results regarding acceptability of and satisfaction with the SNP, we did not find an effect of the SNP on the outcome of primary interest measure SIDF, or the measures of secondary interest symptom severity, burden, self-efficacy and perceived nursing support for symptom management. The SNP did not lead to any reported adverse events or delayed contact with health care providers.

To our best knowledge, interventions about SMS interventions developed for patients with any cancer diagnosis at the onset of anticancer treatment are scarce. A sequential before/after study tested a SMS intervention (CHEMO-SUPPORT) provided by trained nurses (two days training) for patients with different cancer diagnosis during ambulatory chemotherapy reported less symptom distress and severity, and improved self-efficacy in patients after the introduction of CHEMO-SUPPORT (93). The intervention included two tailored coaching sessions (in person and phone call) based on tailored symptom monitoring and patient diaries, complemented with a brochure and an online or on-call nursing service to answer patient's questions. Additional coaching sessions were added on request to support symptom management if needed. In our study, graduated nurses trained to use the SNP (6-hour training) provided semi-structured consultations with SN-Flyers. In contrast to the CHEMO-SUPPORT intervention, in our study symptom assessment was used to assess outcomes but was not included in semi-structured consultations. The SNP aimed to provide a *basic* SMS and therefore every patient in this study received intentionally this basic intervention independent of symptom severity and interference with daily functions. This approach of tailoring SMS to the therapy but not to individual needs does not fully comply with best practice recommendations for tailored SMS approaches (22, 23, 150) and should be reconsidered for further developing the SNP and SMS programs in general.

Face-to-face SMS interventions provided by trained health care professionals as the SNP require personal and institutional resources, whilst electronic tools are easy accessible and facilitate symptom monitoring. However, they are dependent on the patients engaging with and using the tool. Electronic tools usually facilitate monitoring of symptoms and reporting outcomes for health care providers and sometimes for patients (154-157). Recently, a study identified predictive factors for the use of an electronic tool for cancer survivors' (Toolkit). Higher symptom burden and better cognitive functions at the onset of the intervention and the increasing of symptom severity over time was associated with the continuation of using the Toolkit (156). The application of electronic tools without any in-person SMS showed no improvement of symptom outcomes (156) or self-

management behaviours (155), while the involvement of symptom management education provided by trained nurses complementary to the electronic tool reduced fatigue and improved sleep disturbances (154). We controlled for nurses' education level on patient-reported outcomes by performing post-hoc analysis without finding effects on any investigated outcome. Therefore, we conclude that the implementation of the SNP does not require specialised nurses per se. However, the inclusion of symptom monitoring in the SNP could facilitate the follow-up of patients with higher symptom intensity/burden who probably need SMS and therefore improve the impact of the SNP. Adding online access to SN-Flyers integrated in the SNP will be considered, but whether study results with electronic tools are transferable to the SNP should be further investigated.

Overall, patients in our study reported on average mild mean symptom severity and symptom burden that slightly increased over 16 weeks in both groups. This is in contrast to a survey reporting substantial numbers of patients with moderate or severe symptom severity (91). Patients with rather mild symptom severity and burden may probably have a higher capacity and motivation to manage their symptoms on their own. Therefore, some patients included in the intervention clusters of the study might not have used the SN-Flyers and might not have needed extra SMS from health care providers (156), but this element was not evaluated in our pilot study. However, symptom severity and burden scores varied largely in both groups of our study, emphasising the need of a tailored and stepwise care approach to provide patients with personalised SMS. The increase of symptom severity and burden over the treatment trajectory is well known (92) and evidence suggests that SMS including self-efficacy support is crucial to improve symptom outcomes and functional status (64, 142, 145, 147). Self-efficacy can fluctuate and supporting patients to foster self-efficacy can improve their emotional and functional well-being (106). However, symptom severity affects patients' self-efficacy (64, 98, 158) and this could explain the decrease of perceived self-efficacy in both groups concurrent to the increasing symptom severity and burden scores. We designed two semi-structured consultations for the SNP as a basic SMS intervention and this might have been insufficient to support self-efficacy effectively considering that approximately one third of all patients in our study indicated that they did not feel confident to manage their symptoms.

We asked graduated nurses to apply a complex self-management intervention by using MI techniques to support self-efficacy and to facilitate behaviour change if needed. MI is an advanced and sophisticated patient-centred behaviour change intervention that should be supervised (152). Supervising the nurses was not feasible in the pilot study and we therefore do not know how nurses implemented the trained skills into clinical practice. The level of complexity required to apply the SNP could have been too ambitious for nursing practice in chemotherapy units. As an alternative for MI, the '5 As' (brief primary care approach: Assess, Advise, Agree, Assist, Arrange) (159) may be another feasible option for all cancer nurses to use. Intensifying self-efficacy support by adding more follow-up consultations, or/and by emphasising dedicated approaches to foster self-efficacy during the consultations should be considered in future developments of the SNP.

Limitations

Our results have to be interpreted with caution due to limitations related to the study design. Randomisation of clusters was exclusively stratified on recruitment potential. As a result, the two breast cancer centres were randomised to the intervention group leading to an imbalance of more female patients receiving the intervention. On the other hand, none of the controlled confounding variables affected study results. Nevertheless, for a full-powered randomised study, stratification criteria on cluster level should be extended to better prevent recruitment imbalance.

Due to the withdrawal of one cluster, the statistical power was compromised by an unequal number of clusters in intervention and control group (160). To include nine centres was a feasibility decision based on the interest of centres to participate in the pilot study and other feasibility restrictions related to the pilot nature of the study. We therefore cannot exclude that the sample was too small to detect significant differences between the SNP and control assuming that the intervention effect would be

probably small (100); and we also cannot rule out that insufficient power caused non-significant results (161). The intervention effect depends on the successful implementation of the SNP leading to nurses' behaviour change in providing SMS and adopting a coaching role. We assume that nurses in both groups were motivated to best support patients. Therefore, SMS elements may have been integrated in usual care in the control group to a larger extend than in the care of the intervention group. The small intervention differences between the two groups may also have diluted the effect sizes in this pilot study.

Generalisability for pilot study results is limited (101). Because we could not show any superior effect for the SNP, sample and cluster size calculations are not yet possible, but a full powered randomised study would need considerably more participating centres and patients to achieve sufficient power (160). Further, eligibility of centres should be based on provided anticancer treatments and workforce resources than on estimated recruitment potential to avoid withdrawal of centres with too small patient numbers.

Implication and Conclusions

We perceived the SNP as a promising nurse-led intervention with confirmed acceptance and feasibility for patients regarding helpful written information and supportive nurse-led consultations, and nurses acceptability of the training (8). However, two semi-structured consultations with SN-Flyers may be insufficient to improve symptom interference with daily functions, patients' perceived self-efficacy, and their perceived nurse support for symptom management, over a period of 16 weeks after the onset of a first-line cancer treatment. Further investigations are needed to improve the SNP intervention content (e.g. including symptom assessments, facilitating self-efficacy) and intervention dose (tailored follow-up consultations for patients with low self-efficacy scores and an identified need for SMS).

Analysis of non-adjusted data

The reporting of the non-adjusted data was not included in the third article due to article length limitation. To complement this information to the thesis, these results are integrated in the Appendix 8.

Nurse fidelity to training manual (adoption)

Not all dimensions of the RE-AIM framework have been addressed in the published and submitted articles. Therefore, results related to the RE-AIM dimensions Adoption and Implementation will be described with the following paragraphs starting with nurse fidelity to training manual. A short summary on time and resources required to apply the SNP will complete the chapter Results.

Following each semi-structured consultation, nurses completed an online questionnaire to identify the core components (based on the training manual) applied during the SMS intervention. Overall, 92% of all defined core components were applied during semi-structured consultations (95% CI: 87% to 95%). Categorising the achieved proportions with applied core components showed that at least 70% of the core components were applied in every consultation (Table 23). Comparing the three intervention clusters, nurses at Centre 2 appeared to have lower adherence to the training manual compared with Centres 1 and 3.

Table 23: Proportion of adherence items answered "yes"

	N	n (%)	Proportion (95% CI)
Centre 1	20		
>80-90%		2 (10%)	10% (3 to 30%)
>90-100%		18 (90%)	90% (70 to 97%)
Centre 2	9		
>70-80%		1 (11%)	11% (2 to 43%)
>80-90%		5 (56%)	56% (27 to 81%)
>90-100%		3 (33%)	33% (12 to 65%)
Centre 3	20		
>70-80%		1 (5%)	5% (1 to 24%)
>80-90%		5 (25%)	25% (11 to 47%)
>90-100%		14 (70%)	70% (48 to 85%)
Overall	49		
>70-80%		2 (4%)	4% (1 to 14%)
>80-90%		12 (24%)	24% (15 to 38%)
>90-100%		35 (71%)	71% (58 to 82%)

Based on Wilson score 95% confidence intervals (CI). N refers to the total number of patients.

In addition to nurses' self-reported adherence to the training manual, we observed two semi-structured consultations at three SNP centres. Observations revealed that nurses most frequently discussed self-monitoring and self-management of symptoms with patients. We observed considerably less discussion of: coaching behaviours, facilitating communication with other health care professionals, tailoring recommendations to the individual context, and engaging patients as partners in discussions. Notably, self-management education components facilitating enhanced intervention tailoring to meet specific, individual patient needs were used approximately half as often as discussions on self-monitoring and symptom management. Further, self-manageIment education components aiding patients in setting goals and planning actions, or solving problems and making decisions were very seldom employed by nurses (Figure 8).

Figure 8: Frequency of use for self-management education core-elements

Time and resources required to apply the SNP (implementation)

Initial semi-structured consultations required more time than anticipated and were longer in duration than subsequent follow-up consultations. On average, initial consultations took 45.2 ±26.3 minutes (range 20 to 60 minutes) which was longer than the expected time (about 30 minutes). When considering additional time for preparation and documentation, initial consultations required 90.9 ±31.9 minutes (range 70 to 120 minutes) on average. In contrast, follow-up consultations were considerably shorter averaging 24.3 ±13.9 minutes (range 15 to 30 minutes/patient). Based on the training manual, about 40 minutes was expected for follow-up consultations as anticipated that active patient involvement would necessitate more time. The total time needed for follow-up consultations was 34.4 ±18.3 minutes (range 20 to 45 minutes).

Chapter 6: Discussion

This thesis is part of the Symptom Navi Pilot Study that aims to evaluate patient accrual and retention rates as well as assess preliminary impact of a nurse-led intervention supporting symptom self-management in patients with cancer. We developed a training manual and nurse education program for this pilot study. Therefore, additional aims were to evaluate the nurse training course and explore nurse fidelity to the SNP training manual. Several theoretical frameworks guided this thesis work. The implementation process was evaluated using the RE-AIM framework (4). The development and evaluation of the nurse training employed the COM-B model (130). The operationalization of patient-reported outcomes as indicators for SNP effectiveness were drawn from the TSSM (58, 64). The main purpose of the pilot testing of the SNP was to obtain information on feasibility to inform a multinational study formally testing SNP effectiveness in a larger context.

Main findings

The number of patients who consented and were included in the Symptom Navi Pilot study (accrual rate) differed significantly between the intervention and control groups - with notably more patients recruited into the control group. The considerable difference in accrual rates between groups may be explained by the fact that more centres considered to be 'fast' recruiters were in the control group compared to the intervention group (n=3 vs. 2 respectively).

Retention rates were high meaning that many patients received at least two semi-structured consultations with SN-Flyers. Cessation of therapy and death were primary reasons for the lower number of follow-up consultations. These observations suggest that patients included in the intervention group received the minimal intended number of semi-structured consultations with SN-Flyers. Neither nurse non-adherence to the SNP procedures nor contextual factors (e.g. high workload) contributed significantly to lack of follow-up consultations.

The evaluation of nurse training courses revealed that nurses accepted the training content with only minor suggestions (related to introduction and guidance through the training). Nurse confidence in implementing semi-structured consultations with SN-Flyers was positively correlated with perceived work-related situation. This finding may indicate that increased workload at the centre might reduce the likelihood that nurses would conduct semi-structured consultations. Further, it may indicate that nurses may prioritise other duties (rather than semi-structured consultations) in situations of increased workload. Thus, it seems that involving centre stakeholders is important for effective implementation (60, 76).

Self-reported nurse adherence to the training manual supported that semi-structured consultations were delivered as recommended in the training. However, the six consultation observations indicated that nurses primarily focused on facilitating symptom monitoring and management. Therefore, nurses seemed to continue using an approach emphasising informing and advising rather than integrating coaching patients on self-managing symptoms. Active patient involvement (i.e. individual goal setting, action planning, problem solving and decision making) were less often applied in consultations. Importantly, existing evidence suggests that such elements may be vital for helping patients achieve successful self-management behaviour (21, 22, 84).

The SNP showed no effect on the outcome of primary interest (symptom interference with daily functions). Similarly, the SNP did not affect any outcome of secondary interests (symptom severity and burden, self-efficacy and patients' perceived nursing support for symptom management). Overall scores of symptom severity and burden were mild at the onset of the systemic anticancer treatment (153) and trended towards increasing severity/burden over the 16-week period. In parallel, overall self-efficacy scores decreased over 16 weeks. These contrasting trends in symptom severity/burden and self-efficacy might indicate that patient need for SMS is relatively lower at the onset of the treatment compared to 16 weeks later. The increased symptom severity and burden

over time is consistent with prior reports showing symptoms increase during the treatment trajectory (80, 81, 92). Together, such observations underscore the need for SMS in outpatient settings as patients often have to manage their symptoms at home without immediate contact with a health care provider (83, 145, 162). No adverse events were reported indicating the SNP can be safely implemented in outpatient anti-cancer treatment settings.

Implications for further development of the SNP

A strength of the SNP is its rigorous, multistep development. The SNP focuses on supportive care for symptom self-management for patients starting anti-cancer treatment (15). All SNP components have been evaluated. Components not formally assessed in previous work were evaluated within the Symptom Navi Pilot Study. SN-Flyers have been evaluated by patients, family members, design experts and health care professionals - including nurses, oncologists and psycho-oncologists (2). In the present pilot study, we employed the revised second version of SN-Flyers. The SN-Flyers contain symptom specific self-management recommendations that are evidence-based with excellent Item –Content Validity Index ratings (75). The training manual developed for the pilot study defines training content facilitating standardised implementation of the SNP. The training manual explains all core elements of semi-structured consultations using SN-Flyers and describes the training procedures (8). We created the training manual in response of prior publications that either lack description or poorly describe interventions – making replication challenging if not impossible (163). Findings from our pilot study suggest that SNP components should be evaluated and adapted to improve semi-structured consultations and better incorporate certain elements of self-management education (22).

The training manual was based on theoretical underpinnings and evaluated by nursing experts prior to implementing SNP training. Therefore, developing training content and the didactic methods employed aligned with implementation research recommendations (76). One limitation of the training program is that only half of nurses completed both training courses. It is plausible that one training course (rather than two) was not sufficient to adequately prepare nurses to deliver semi-structured consultations and motivate them for behaviour change into a coaching role (22). Several nursing leaders at participating centres suggested a more flexible training approach - noting that it is not feasible to train all nurses together at the same time. Nurses confirmed that in-person training with learning from peers was helpful. Thus, future SNP training should pay more attention to centre-specific factors (i.e. staffing and culture) to reduce implementation barriers (164). Centre and culture specific factors emerged from nurses' narrative feedback obtained during and after training. Some nurses emphasised that video sequences did not adequately model supportive approaches for SMS. In contrast, other nurses stated the video examples were beneficial for learning. Such disparate attitudes may reflect the lack of standardised education programs and diversity of daily practice/responsibilities for oncology nursing in Switzerland. Consequently, we cannot assume uniform knowledge and competencies for oncology nursing which is the case in other European countries. A recently developed training program in the UK to prepare nurses to administer systemic anti-cancer therapies, deliver pre-treatment consultations and provide patient-centred care for symptom management (165). Based on our SNP training evaluation, it is important to assess nursing knowledge and tailor the training content to local contexts in order to respond to local SMS learning needs. Online modules on basic SMS knowledge and theoretical models to visualise self-management education could be added to create a more flexible training approach and facilitate nurse participation. Adding asynchronous pre-training modules could help reduce the time required for in-person training and facilitate a clear focus on SMS during face-to-face encounters. Such preparatory modules could also improve nurses' basic knowledge on SMS interventions and help mitigate imbalance of general knowledge prior to training.

Pilot study observations indicated that the targeted behaviour change in nursing practice regarding SMS was not entirely achieved. Rather, nurses continued using an informing and advising conversational approach and were less likely to actively include patients in discussions of patient's individual goals and behaviours. Given the limited number of observations (n=6), these observations regarding nurse fidelity to training should be interpreted with caution. Nevertheless, the nursing approach required for delivering SMS should be considered to improve and optimize nurse SNP adoption. Adoption of motivational interviewing (MI) principles may have been too challenging for nurses and thus nurses defaulted a more familiar conversation approaches. Originally, MI was developed to support people struggling with substance abuse (tobacco, drugs, alcohol) and chronic conditions (i.e. asthma, cardiovascular disease, mental health disorders) (104). Evidence support nursing SMS interventions consisting of MI, coaching for self-management, goal setting, and tailoring the intervention to individual patient experience resulted in significant decreases in symptom distress and severity. (93). This single-centre study used a pre-post design, and applied considerably more encounters over three months. Interventions included two initial in-person consultations followed by contact at each hospital visit and complemented with regular follow-up contacts (i.e. telephone and online). Therefore, the reported effects may be related to intervention strategies, intervention dose and/or the study design. Further, MI was one of three intervention strategies employed and nurse fidelity to MI was not evaluated (93). Besides MI, other SMS approaches have been applied and evaluated for chronic conditions. One approach, the brief primary care approach, may be a feasible alternative for SMS interventions in cancer settings (159). The approach includes "Five A's": Assess (patients' behaviour), Advise (encourage change), Agree (to set goals), Assist (to achieve knowledge, skills, confidence, and support), Arrange (referrals and follow-up contacts). The Five A's represent an easy to remember cue and nurses might feel more comfortable applying the brief primary approach. However, such changes to semi-structured consultations should be discussed with stakeholders (i.e. nurses who are experienced using the SNP) prior to future implementation (166). A complementary approach could be to involve local mentors to facilitate adoption and reduce barriers to SNP implementation into clinical practice (140). Masters-prepared clinical nurse specialists in oncology could play a role in supervising and supporting semi-structured consultations thereby facilitating SNP implementation.

Besides using a conversational approach, applying self-management education elements into semi-structured consultations affect whether or not patients effectively self-manage their symptoms (22). One important limitation of the SNP is that semi-structured consultations do not include dedicated symptom/needs assessment -potentially hindering tailoring to respond to individual patient needs. We observed a trend towards slightly increased symptom severity and burden along with decreased perceived self-efficacy at t3 (16 weeks into anti-cancer treatment). It is possible that patient need for SMS increases over the course of treatment. The variability in symptom burden between patients highlights the need for tailored SMS. Further, approximately one-third of patients did not feel confident in managing their symptoms 16 weeks after treatment initiation. This observation provides additional support for tailoring the SMS to the individual. A feasible symptom/needs assessment could help to tailor semi-structured consultations (21-23). Another opportunity for improving semi-structured consultations relates to supporting/facilitating patient self-efficacy (22, 71). Indeed, supporting self-efficacy is one of the six key elements of semi-structured consultations (8). Pilot study results showed decreased self-efficacy in both groups. Thus, basic SMS support with the SNP may not be sufficient for patients with relatively greater symptom burden. Our observation diverged from prior other RCT's. Previous studies testing nursing interventions supporting self-efficacy showed significant increases in patient self-efficacy for self-managing pain (147) and fatigue (64) respectively. Patients who are not supported in symptom management experience steady increases in symptom severity (92) and symptom burden (80, 81). Further, low self-efficacy scores are negatively correlated with anxiety and general symptom severity (167). It seems that self-efficacy can be successfully supported by nursing interventions if symptom-specific self-efficacy assessments are used (i.e. pain-related or fatigue-related self-efficacy assessment) (64, 147). In

contrast we used a general self-efficacy scale (SES6G) and therefore psychometric differences between the used instruments could partly explain that we could not show impact on patient perceived self-efficacy in the intervention group. Further, resources and time to train the nurses were limited. Why the current SNP nurse training and interventions did not effectively facilitate patient's self-efficacy merits further attention. Strengthening self-efficacy support in the nurse training could foster improved SMS application semi-structured SNP consultations and increased patient perceived self-efficacy. Future work may focus on specific techniques and pedagogy to enhance nurse training to facilitate patient self-efficacy.

Limitations and implications for research

A cluster-randomised design was chosen as SNP implementation would alter nursing care at participating centres thereby introducing a potential contamination effect and preventing randomisation at patient level (168). Using a cluster randomised design in a pilot study has limitations. Specifically, the number of included clusters will rarely be sufficient to achieve significant effects on outcomes – yet findings may inform implementation procedures for the specified intervention (77). Based on the MCR framework (62), pilot testing was needed because program effectiveness and safety data were lacking. Further, implementing a newly developed intervention can be hindered by barriers related to stakeholders and setting-specific cultures (76). Applying the RE-AIM framework supported a comprehensive evaluation of the implementation process (66, 124, 169).

A relative strength of the study design was the high accrual and retention rates observed in the pilot study. This observation indicates a full-powered RCT would be feasible as it seems sufficient clusters/centres could be enrolled. The overall accrual rate (80%) is comparable to a prior study evaluating a nursing SMS intervention for patients receiving chemotherapy (93). However, accrual rates in studies also may relate to intervention characteristics and patient population. For example, studies evaluating a nursing SMS intervention for pain demonstrated accrual rates between 46.6% (147) and 54.5% (145) whereas a study evaluating an electronic tool supporting adherence to oral anticancer treatment reported a 95% accrual rate (170). Based on the accrual rate in the Symptom Navi Pilot Study, sample size would need to be increased by 20% for a full-powered clinical trial.

A cluster randomised design seems to be feasible for a full-powered clinical trial testing SNP effectiveness. However, recruitment and randomisation methods would require adaptation. The clusters, trained nurses, and observations of semi-structured consultations represent a selection of cancer outpatient centres in the German-speaking part in Switzerland. The nine centres/clusters were selected based on their interest in implementing the SNP and not on a pre-defined sample size. Therefore, we cannot rule out potential selection bias (171). It is possible that participating centres may have existing high-quality standards of care and may not be representative of all centres. Selection bias could have limited our ability to detect a difference in SNP effect between groups. Second, despite stratifying randomisation (by blocks of two), we could not avoid an imbalance of included clusters and patients (172). Three of four clusters randomized to the intervention group adopted the SNP and implemented it at their centre. The withdrawal of the fourth centre created an imbalance in the number of clusters between intervention and control groups. The difference subsequently produced an imbalance in the number of patients included in each group. Therefore, particular attention should be given to achieve an equal number of clusters in both groups for a full-powered cluster randomised trial. A stepped wedge design (173) would potentially avoid this challenge as pre- and post-intervention assessments are conducted at all clusters. While developing the pilot study, several interested cancer centres noted that a stepped wedge design was not feasible, and they intended to withdraw participation given that particular design. Therefore, we opted to use a cluster randomised design. Best practices for cluster-randomised trials include three strategies to avoid methodological bias (174): 1) use individual allocation, 2) identify participants

before cluster randomisation (if cluster allocation is required), and 3), recruit participants through an independent recruiter (if prior patient identification is impossible). The first strategy was not used in this pilot study. However, we applied the second and third strategies: the inclusion and exclusion criteria of patients was defined prior to centre randomisation, and patient recruitment was delegated to local PIs and designated nurses at the clusters.

Another limitation of the pilot study was the homogeneity of the intervention group compared to the control group. The intervention group included a breast cancer centre and a gynaecological cancer centre. Consequently, patients in the control group were more varied and had significantly more cases of colorectal or lung cancer rather than breast cancer. Further, patients in the intervention and control group differed significantly at baseline. The intervention group included more younger patients, females, patients caring for family members and patients treated with intravenous anti-cancer therapies. In the control group, oral anti-cancer therapies were more frequent and patients had lower physical function (175). However, controlling for these potential confounding variables showed no effect on any patient-reported outcomes. Careful attention should be given to strategies for achieving evenly distributed patients when designing a full-powered clinical trial. Additional stratification (e.g. breast cancer centres, prostate cancer centres) could help alleviate this potential confounder.

We cannot rule out that SNP implementation differed across clusters. Nurse training was standardised to try to ensure that interventions were performed in the same way at each cluster. Evaluating nurse fidelity to training revealed variability in reaching target patients and nurse adherence to the training manual. At the intervention clusters, 75-100% of included patients received two semi-structured consultations as defined in the SNP training manual. Very few patients (n=5, 10%) received a third follow-up consultation. Receiving a third follow-up consultation indicates that patients with increased symptom burden received tailored SMS based on their individual needs. Therefore, it seems that some nurses might have limited their intervention to the minimal defined intervention, and we cannot rule out that patients with elevated SMS needs were not optimally supported. Such a dynamic could have made SNP measurement more challenging. As suggested in the previous chapter, a future study to improve nurse training may be warranted. Further, nurse self-reported adherence to the training manual ranged between 87-95%. This may indicate that nurse awareness of patient need (and nurse motivation to employ semi-structured consultations) might be centre-specific. On the other hand, patient-reported outcomes were neither related to centre nor nursing education. It may be that individual beliefs influence their behaviour change for SMS. This finding underlines also the importance to better train nurses to implement the SNP at the centres.

According to the TSSM (71), we expected the SNP to improve patient functioning by fostering self-efficacy and his/her self-management behaviour. To measure patient-reported outcomes, we assessed 13 common symptoms related to anti-cancer treatments as well as symptom interference with daily functions (153). Several factors could have contributed to the lack of significant differences in outcomes between the two groups. First, the effect size of the intervention may have been small necessitating a larger sample to demonstrate statistical significance(i.e. more clusters, more patients (151). Second, relatively few patient-reported outcomes are proven to be nursing sensitive: nausea and vomiting, mucositis, safe oncological medication handling, and patient experience with chemotherapies (91, 134). Therefore, using outcomes that are not nursing sensitive could have influenced our ability to detect a SNP effect on patient-reported outcomes (91). Third, nursing SMS may have been already high in both groups and considerably more patients were included in the control group potentially diluting the SNP effect. Our observation that patients in the intervention group did not report better nursing support on symptom management was indeed contrary to our assumption. Therefore, nurses in the control group might have provided SMS that was equal to (or even superior) to nurses in the intervention group who applied the SNP. Evaluating nursing interventions in real life is particularly challenging because so many potentially confounding factors

have to be controlled for – and this is typically not possible in a pilot study (176). It may be worth considering use of proven, nursing-sensitive outcomes in a full-powered clinical trial. Such an approach could increase the likelihood of detecting an intervention effect and help evaluate nursing SMS in the control group.

Conclusions

Based on the data of our pilot study and available literature, we hypothesised that nurses must shift their orientation to achieve effective SMS in outpatient cancer settings. Rather than advising patients when symptoms occur, nurses must adopt a coaching role. To achieve this goal, the SNP should be adapted before implementing the basic SMS intervention at other outpatient cancer centres. Suggested adaptations include: 1) emphasising SMS techniques using a feasible approach for clinical practice, 2) extending nurse training with complementary e-learning opportunities, 3) including symptom assessment tools in semi-structured consultations to identify patients with elevated symptom burden, and 4) leveraging local mentors to support nurses implementing SNP at their respective centres. Local mentors are critical for long-term SNP implementation because they can provide key peer feedback supporting nurses' adaptation of a coaching role. The coaching role fosters active patient involvement in semi-structured consultations. Such patient activation is necessary for effective and comprehensive self-management behaviours.

No adverse events were noted during the Symptom Navi Pilot Study. In most cases, the program reached intended patients, and most received two basic SMS interventions. Nevertheless, the SNP did not have any statistically significant effects on symptom interference on daily function, symptom severity/burden or perceived nursing support for symptom management. Prior to launching a full-powered cluster RCT, feasible, realistic, nursing-sensitive primary outcomes need to be identified. Given the heterogeneity of the outpatient cancer setting, a valid and sensitive measure is needed to be able to detect measurable effect sizes. In addition, randomisation and implementation strategies will require considerable adaptation before conducting a full-powered cluster randomised study.

Outlook to further analyses of the Symptom Navi Pilot Study

This thesis is part of the Symptom Navi Pilot Study. Therefore, several analyses described in the study protocol (7) are not included in this dissertation. The examination of patient safety using qualitative focus groups was not part of this thesis. The overall study proposes to examine intervention clusters after completion of the final patient study. Focus group interviews may contribute further insights regarding nurse SNP adoption and can be used to explore facilitators/barriers to SNP implementation at individual centres. As the proposed qualitative analyses of focus group interviews was not part of the thesis, the results will be published elsewhere.

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Appendix 1: Consent of ethic committee

Gesundheits- und Fürsorgedirektion des Kantons Bern

Direction de la santé publique et de la prévoyance sociale du canton de Berne

Kantonale Ethikkommission für die Forschung

Commission cantonale d'éthique de la recherche

Murtenstrasse 31
3010 Bern
Telefon +41 31 633 70 70
Telefax +41 31 633 70 71
www.be.ch/kek
info.kek.kapa@gef.be.ch

Dorothy Pfiffner
Telefon +41 31 633 70 77
Telefax +41 31 633 70 71
dorothy.pfiffner@gef.be.ch

Frau
Prof. Dr. Manuela Eicher
Institut universitaire de formation et recherche en soins (IUFRS)
Universität Lausanne
Biopôle 2
Rte de la Corniche
1010 Lausanne

Bern, 29. März 2017, NR

Bewilligung der KEK Bern

Project-ID	2017-00020
Projekttitel	Implementation of the Symptom Navi© Program for cancer patients in ambulatory services: A cluster-randomized pilot study (Symptom Navi© Pilot Study)
Haupt-Prüfer / Koordinierender Prüfer	Prof. Dr. med. Daniel Betticher
Sponsor	University of Lausanne, Institut universitaire de formation et de recherche en soins, Prof. Dr. Manuela Eicher

Leit-Ethikkommission	**Zentren**
Kantonale Ethikkommission Bern	Prof. Dr. rer. medic. Manuela Eicher, Université de Lausanne Dr. med. Jean Marc Lüthi, Onkologiezentrum Thun-Berner Oberland, Spital Thun Dr. med. Katharina Buser, Brustzentrum Bern, Engeried

Lokalkommission/en	**Zentren**
EKNZ	Dr. med. Walter Mingrone, Solothurner Spitäler AG (soH), 4600 Oltern Dr. med. Thomas Egger, Bürgerspital Solothurn Prof. Dr. Viola Heinzelmann, Universitätsspital Basel
EKOS	Dr. med. Stefan Greuter, rundum Onkologie am Bahnhofpark, 7320 Sargans

I. Entscheidverfahren

☐ ordentliches Verfahren ☐ vereinfachtes Verfahren ☒ Präsidialverfahren

2016-01336

II. Entscheid

☒ Die Bewilligung wird mit Auflagen erteilt. Gilt für die Zentren:

Prof. Dr. rer. medic. Manuela Eicher, Université de Lausanne
Dr. med. Jean Marc Lüthi, Onkologiezentrum Thun-Berner Oberland, Spital Thun
Dr. med. Katharina Buser, Brustzentrum Bern, Engeried
Dr. med. Walter Mingrone, Solothurner Spitäler AG (soH), 4600 Olten
Dr. med. Thomas Egger, Bürgerspital Solothurn
Prof. Dr. Viola Heinzelmann, Universitätsspital Basel
Dr. med. Stefan Greuter, rundum Onkologie am Bahnhofpark, 7320 Sargans

Allgemeine Auflagen (sind innert 30 Tagen zu erfüllen)

1. Einreicheformular:
   Screen 1, Finanzierung: Bitte geben Sie die Forschungsassistenz von Frau Bana als Finanzierungsquelle an.

Auflagen der LeitEK BE, Onkologiezentrum Thun-Berner-Oberland, Dr. med. Jean Marc Lüthi

1. Patienteninformation (Zentrum Thun):
   S. 3, Kap. 10: Vertraulichkeit der Daten: Bitte den Passus: „innerhalb des IUFRS können die Daten und Proben durch berechtigte und klar bezeichnete Personen auch ohne Verschlüsselung eingesehen werden." korrigieren und IUFRS durch die lokale Institution Thun ersetzen.

2. GCP-Nachweis J. –M. Lüthi:
   Seit Beginn 2017 wird bei den TREE-online-Kursen auch das Modul Schweiz verlangt. Bitte reichen Sie das Modul Schweiz des TREE-online-Kurses nach

III. Klassifizierung

☒ klinische Studie gemäss KlinV, Kategorie: A

- ☐ mit Arzneimitteln
- ☐ mit Transplantatprodukten
- ☐ mit genetisch veränderten oder pathogenen Organismen
- ☒ anderer klinischer Versuch gemäss Kapitel 4 KlinV
- ☐ Umkategorisierung gemäss Art. 71, Abs. 3, KlinV
- ☐ mit Medizinprodukten
- ☐ der Gentherapie
- ☐ der Transplantation
- ☐ mit ionisierender Strahlung

IV. Gebühren

Betrag: CHF 0.-- **Tarifcode:**
Gemäss der geltenden Gebührenordnung von swissethics.

V. Rekursmöglichkeiten

Gegen diese Verfügung kann innert 30 Tagen seit Eröffnung bei der Gesundheits- und Fürsorgedirektion des Kantons Bern Beschwerde erhoben werden. Die Beschwerdefrist kann nicht verlängert werden. Die Beschwerdeschrift ist im Doppel bei der Gesundheits- und Fürsorgedirektion, Rathausgasse 1, 3011 Bern einzureichen.

Sie muss

(a) angeben, welche Entscheidung anstelle der angefochtenen Verfügung beantragt wird und
(b) aus welchen Gründen diese andere Entscheidung verlangt wird sowie
(c) die Unterschrift der beschwerdeführenden Partei oder der sie vertretenden Person enthalten.

Der Beschwerdeschrift beizulegen sind die Beweismittel, soweit sie greifbar sind, und die angefochtene Verfügung. (Art. 32 und 60 ff. des Gesetzes vom 23. Mai 1989 über die Verwaltungsrechtspflege [VRPG; BSG 155.21]).

Stand Dezember 2015

VI. Kopie an

☐ Swissmedic
☐ BAG
☒ Lokalkommission/en — Ethikkommission Nordwest- und Zentralschweiz EKNZ; Ethikkommission Ostschweiz (EKOS)
☐ Andere

Unterschriften

Prof. Dr. med. Christian Seiler
Präsident KEK Bern

Dr. sc. nat. Dorothy Pfiffner
Leiterin Wissenschaftliches Sekretariat

Gesundheits- und Fürsorgedirektion des Kantons Bern

Direction de la santé publique et de la prévoyance sociale du canton de Berne

Kantonale Ethikkommission für die Forschung

Commission cantonale d'éthique de la recherche

Murtenstrasse 31
3010 Bern
Tel. +41 31 633 70 70
Fax +41 31 633 70 71
www.be.ch/kek
info.kek.kapa@gef.be.ch

Dorothy Pfiffner
Tel. +41 31 633 70 77
Fax +41 31 633 70 71
dorothy.pfiffner@gef.be.ch

Frau
Prof. Dr. Manuela Eicher
Institut universitaire de formation et recherche en soins (IUFRS)
Universität Lausanne
Biopôle 2
Rte de la Corniche
1010 Lausanne

Bern, 16.11.2017 / YG

Zentrumsbewilligung Aarau, Sargans und Chur der KEK Bern

Project-ID	2017-00020
Projekttitel	Implementation of the Symptom Navi© Program for cancer patients in ambulatory services: A cluster-randomized pilot study (Symptom Navi© Pilot Study)
Master-/Doktorarbeit von	Bana, Marika
Haupt-Prüfer / Koordinierender Prüfer	Prof. Dr. Manuela Eicher
Sponsor	Universität Lausanne, Institut universitaire de formation et de recherche en soins, Prof. Dr. Manuela Eicher

Leit-Ethikkommission	**Zentren**
Kantonale Ethikkommission Bern	Prof. DrManuela Eicher, Université de Lausanne, Institut de Formation et de Recherche en Soins IUFRS, Lausanne Dr. med. Jean Marc Lüthi, Onkologiezentrum Thun-Berner Oberland, Spital Thun Dr. med. Katharina Buser, Brustzentrum Bern, Engeried, Bern

Lokalkommission/en	**Zentren**
EKNZ	Dr. med. Walter Mingrone, Solothurner Spitäler AG (soH), Olten Dr. med. Thomas Egger, Bürgerspital Solothurn, Solothurn Prof. Dr. Viola Heinzelmann, Universitätsspital Basel Dr. med. Nathan Cantoni, Kantonsspital Aarau
EKOS	Dr. med. Stefan Greuter, rundum Onkologie am Bahnhofpark, Sargans Dr. med. Rudolf Morant, ZeTuP Rapperswil
ZH	Dr. med. Michael Schwitter, Kantonsspital Graubünden, Chur

Entscheidverfahren

☐ ordentliches Verfahren ☐ vereinfachtes Verfahren ☒ Präsidialverfahren

Entscheid

Prof. Dr. Manuela Eicher, Université de Lausanne, Institut de Formation et de Recherche en Soins IUFRS, Lausanne

Dr. med. Jean Marc Lüthi, Onkologiezentrum Thun-Berner Oberland, Spital Thun

Dr. med. Katharina Buser, Brustzentrum Bern, Engeried, Bern

Dr. med. Walter Mingrone, Solothurner Spitäler AG (soH), Olten

Dr. med. Thomas Egger, Bürgerspital Solothurn

Prof. Dr. Viola Heinzelmann, Universitätsspital Basel

Dr. med. Nathan Cantoni, Kantonsspital Aarau

Dr. med. Stefan Greuter, rundum Onkologie am Bahnhofpark, Sargans

Dr. med. Rudolf Morant, ZeTuP Rapperswil

Dr. med. Michael Schwitter, Kantonsspital Graubünden, Chur

☒ Die Bewilligung wird mit Auflagen erteilt

Allgemeine Auflage (ist innert 30 Tage zu erfüllen):

1. Studieninformation:
   a. Einverständniserklärung, Z. 200: Es wird auf eine Version älteren Datums verwiesen. Die Studieninformation und die Einverständniserklärung werden als ein zusammenhängendes Dokument abgegeben. Ein Verweis auf die Studieninformation mit Datum und Version ist dann nicht mehr notwendig. Bitte streichen Sie den Verweis mit Datum und Version.

Allgemeine Bemerkung:

1. Die Änderungen werden zur Kenntnis genommen.

Dr. med. Jean Marc Lüthi, Onkologiezentrum Thun-Berner Oberland, Spital Thun

☒ Die Bewilligung wird mit Auflagen erteilt (Die Auflage vom 29.03.2017 wurde noch nicht erfüllt).

Auflage (ist innert 30 Tage zu erfüllen):

1. GCP-Nachweis:
   a. Seit Beginn 2017 wird bei den TRREE-online-Kursen auch das Modul Schweiz verlangt. Bitte reichen Sie das Modul Schweiz des TRREE-online-Kurses nach.

Dr. med. Nathan Cantoni, Kantonsspital Aarau

☒ Die Bewilligung wird mit Auflagen erteilt

Die lokalen Gegebenheiten sind erfüllt.

(Entscheid basierend auf der Beurteilung durch die Ethikkommission Nordwest- und Zentralschweiz EKNZ.)

Dr. med. Stefan Greuter, rundum Onkologie am Bahnhofpark, Sargans

☒ Die Bewilligung wird mit Auflagen erteilt

Die lokalen Gegebenheiten sind erfüllt.

(Entscheid basierend auf der Beurteilung durch die Ethikkommission Ostschweiz (EKOS).)

Dr. med. Michael Schwitter, Kantonsspital Graubünden, Chur

☒ Die Bewilligung wird mit Auflagen erteilt

Auflage:

- Bitte reichen Sie den geprüften und von allen Seiten unterzeichneten Studienvertrag nach. Teilnehmer dürfen erst eingeschlossen werden, wenn die (Leit-)Ethikkommission die Erfüllung der Auflagen bestätigt hat.

(Entscheid basierend auf der Beurteilung durch die Kantonale Ethikkommission Zürich.)

Klassifizierung

☒ klinische Studie gemäss KlinV, Kategorie: A

- ☐ mit Arzneimitteln
- ☐ mit Transplantatprodukten
- ☐ mit genetisch veränderten oder pathogenen Organismen
- ☒ anderer klinischer Versuch gemäss Kapitel 4 KlinV
- ☐ Umkategorisierung gemäss Art. 71, Abs. 3, KlinV
- ☐ mit Medizinprodukten
- ☐ der Gentherapie
- ☐ der Transplantation
- ☐ mit ionisierender Strahlung

Gebühren

Betrag: CHF 0.-- **Tarifcode:**

Gemäss der geltenden Gebührenordnung von swissethics.

Rekursmöglichkeiten

Gegen diese Verfügung kann innert 30 Tagen seit Eröffnung bei der Gesundheits- und Fürsorgedirektion des Kantons Bern Beschwerde erhoben werden. Die Beschwerdefrist kann nicht verlängert werden. Die Beschwerdeschrift ist im Doppel bei der Gesundheits- und Fürsorgedirektion, Rathausgasse 1, 3011 Bern einzureichen.

Sie muss

(a) angeben, welche Entscheidung anstelle der angefochtenen Verfügung beantragt wird und
(b) aus welchen Gründen diese andere Entscheidung verlangt wird sowie
(c) die Unterschrift der beschwerdeführenden Partei oder der sie vertretenden Person enthalten.

Der Beschwerdeschrift beizulegen sind die Beweismittel, soweit sie greifbar sind, und die angefochtene Verfügung. (Art. 32 und 60 ff. des Gesetzes vom 23. Mai 1989 über die Verwaltungsrechtspflege [VRPG; BSG 155.21]).

Stand Dezember 2015

Kopie an

☐ Swissmedic	
☐ BAG	
☒ Lokalkommission/en	Ethikkommission Nordwest- und Zentralschweiz EKNZ Ethikkommission Ostschweiz (EKOS) Kantonale Ethikkommission Zürich
☐ Andere	Marika Bana, marika.bana@hefr.ch

Unterschriften

Prof. Dr. med. Christian Seiler
Präsident KEK Bern

Dr. sc. nat. Dorothy Pfiffner
Vizepräsidentin
Leiterin Wissenschaftliches Sekretariat

Gesundheits- und Fürsorgedirektion des Kantons Bern

Direction de la santé publique et de la prévoyance sociale du canton de Berne

Kantonale Ethikkommission für die Forschung

Commission cantonale d'éthique de la recherche

Murtenstrasse 31
3010 Bern
Tel. +41 31 633 70 70
Fax +41 31 633 70 71
www.be.ch/kek
info.kek.kapa@gef.be.ch

Dorothy Pfiffner
Tel. +41 31 633 70 77
Fax +41 31 633 70 71
dorothy.pfiffner@gef.be.ch

Frau
Prof. Dr. Manuela Eicher
Institut universitaire de formation et recherche en soins (IUFRS)
Universität Lausanne
Biopôle 2
Rte de la Corniche
1010 Lausanne

Bern, 23.02.2017, NR

Bewilligung der KEK Bern für den Prüferwechsel am Brustzentrum in Bern (von Frau Dr. K. Buser zu Herr Prof. Borner)

Project-ID	2017-00020
Projekttitel	Implementation of the Symptom Navi© Program for cancer patients in ambulatory services: A cluster-randomized pilot study (Symptom Navi© Pilot Study)
Master-/Doktorarbeit von	Bana, Marika
Haupt-Prüfer / Koordinierender Prüfer	Prof. Dr. rer. medic. Manuela Eicher
Sponsor	University of Lausanne, Institut universitaire de formation et de recherche en soins, Prof. Dr. Manuela Eicher

Leit-Ethikkommission	Zentren
Kantonale Ethikkommission Bern	Prof. Dr. rer. medic. Manuela Eicher, Université de Lausanne, Institut de Formation et de Recherche en Soins IUFRS, Lausanne Dr. med. Jean Marc Lüthi, Onkologiezentrum Thun-Berner Oberland, Spital Thun, 3600 Thun **Prof. Dr. med. Markus Borner, Brustzentrum Bern, Engeried, 3012 Bern**

Lokalkommission/en	Zentren
EKNZ	Dr. med. Walter Mingrone, Solothurner Spitäler AG (soH), 4600 Oltern Dr. med. Thomas Egger, Bürgerspital Solothurn, 4500 Solothurn Prof. Dr. Viola Heinzelmann, Universitätsspital Basel, 4031 Basel Dr. med. Nathan Cantoni, Kantonsspital Aarau, Aarau
EKOS	Dr. med. Stefan Greuter, rundum Onkologie am Bahnhofpark, 7320 Sargans Dr. med. Rudolf Morant, ZeTuP Rapperswil, Rapperswil
ZH	Dr. med. Michael Schwitter, Kantonsspital Graubünden, Chur

Entscheidverfahren

☐ ordentliches Verfahren ☐ vereinfachtes Verfahren ☒ Präsidialverfahren

Entscheid

Prof. Dr. med. Markus Borner, Brustzentrum Bern

☒ Die Bewilligung wird erteilt

Bemerkungen:

1. Die Mitarbeiterliste ist nicht mehr aktuell und sollte aktualisiert werden.
2. Der Lebenslauf von Prof. Borner ist nicht aktuell, da die aktuelle Anstellung im Brustzentrum Bern nicht aufgelistet ist. Dies sollte im Zusammenhang mit einer nächsten Einreichung aktualisiert werden.

Klassifizierung

☒ klinischer Versuch gemäss KlinV, Kategorie A

- ☐ mit Arzneimitteln
- ☐ mit Transplantatprodukten
- ☐ mit genetisch veränderten oder pathogenen Organismen
- ☒ anderer klinischer Versuch gemäss Kapitel 4 KlinV
- ☐ Umkategorisierung gemäss Art. 71, Abs. 3, KlinV
- ☐ mit Medizinprodukten
- ☐ der Gentherapie
- ☐ der Transplantation
- ☐ mit ionisierender Strahlung

Gebühren

Betrag: CHF 200.-- **Tarifcode:3.3.1**
Gemäss der geltenden Gebührenordnung von swissethics.

Rekursmöglichkeiten

Gegen diese Verfügung kann innert 30 Tagen seit Eröffnung bei der Gesundheits- und Fürsorgedirektion des Kantons Bern Beschwerde erhoben werden. Die Beschwerdefrist kann nicht verlängert werden. Die Beschwerdeschrift ist im Doppel bei der Gesundheits- und Fürsorgedirektion, Rathausgasse 1, 3011 Bern einzureichen.

Sie muss

(a) angeben, welche Entscheidung anstelle der angefochtenen Verfügung beantragt wird und
(b) aus welchen Gründen diese andere Entscheidung verlangt wird sowie
(c) die Unterschrift der beschwerdeführenden Partei oder der sie vertretenden Person enthalten.

Der Beschwerdeschrift beizulegen sind die Beweismittel, soweit sie greifbar sind, und die angefochtene Verfügung. (Art. 32 und 60 ff. des Gesetzes vom 23. Mai 1989 über die Verwaltungsrechtspflege [VRPG; BSG 155.21]).

Stand Dezember 2015

Kopie an

- ☐ BAG
- ☐ DLF
- ☐ Lokalkommission/en
- ☐ Andere

Unterschriften

Prof. Dr. med. Christian Seiler
Präsident KEK Bern

Dr. sc. nat. Dorothy Pfiffner
Vizepräsidentin
Leiterin Wissenschaftliches Sekretariat

Anhang: -Pflichten des Gesuchstellers
-Eingereichte Dokumente vom 13.02.2018

Appendix 2: EJON Confirmation of online publication

De : Elsevier - Article Status <Article_Status@elsevier.com>
Envoyé : mercredi 15 janvier 2020 22:50
À : Marika Bana
Objet : Share your article [YEJON_101714] published in European Journal of Oncology Nursing

ELSEVIER

Share your article!

Dear Mrs. Bana,

We are pleased to let you know that the final version of your article *Development and implementation strategies of a nurse-led symptom self-management program in outpatient cancer centres: The Symptom Navi© Programme* is now available online, containing full bibliographic details.

To help you access and share this work, we have created a Share Link – a personalized URL providing **50 days' free access** to your article. Anyone clicking on this link before March 05, 2020 will be taken directly to the final version of your article on ScienceDirect, which they are welcome to read or download. No sign up, registration or fees are required.

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Kind regards,
Elsevier Researcher Support

Appendix 3: Submission confirmation of the Journal Cancer Nursing

Feb 28 2020 09:42AM

Dear Mrs. Bana,

Your submission entitled "Pilot-testing of a Nurse-led basic Symptom Self-Management Support for Patients Receiving First-line Systemic Outpatient Anticancer Treatment: A Cluster-randomised Study" has been received by the journal editorial office.

You will be able to check on the progress of your paper by logging on to Editorial Manager as an author.

https://www.editorialmanager.com/cn/

Your username is: marika.bana@hefr.ch
click here to reset your password

Your manuscript will be given a reference number once an Editor has been assigned.

Thank you for submitting your work to this journal.

Kind Regards,

CANCER NURSING: An International Journal for Cancer Care

In compliance with data protection regulations, you may request that we remove your personal registration details at any time. (Remove my information/details). Please contact the publication office if you have any questions.

Appendix 4 Example of Symptom Navi Flyer

krebsliga

Tipps

Unterstützung durch Psychoonkologie

Die psychische Belastung durch die Krankheit kann möglicherweise nicht ohne fachliche Hilfe bewältigt werden. Psychoonkologinnen/ Psychoonkologen unterstützen Sie und Ihre Angehörigen ergänzend mittels Gesprächen bei der Krankheitsverarbeitung. Fragen Sie Ihr Behandlungsteam nach einer Empfehlung.

Weitere Informationen zu diesem Thema

- «Wenn auch die Seele leidet», Krebsliga Schweiz
- «Krebs trifft auch die Nächsten», Krebsliga Schweiz
- «Krebs – wenn Hoffnung auf Heilung schwindet», Krebsliga Schweiz
- «Wenn Eltern an Krebs erkranken – Mit Kindern darüber reden», Krebsliga Schweiz
- «Krebs – was leisten Sozialversicherungen?», Krebsliga Schweiz

Die Flyer Symptom Navi wurden entwickelt durch:

- Lindenhofgruppe Bern
- Hochschule für Gesundheit Freiburg
- Freiburger Spital
- Onkologiepflege Schweiz
- Solothurner Spitäler
- Schweizerischer Verein für Pflegewissenschaft
- Centre hospitalier universitaire vaudois
- Université de Lausanne

Angst

Gut zu wissen

Angst ist eine normale Reaktion auf eine schwierige und bedrohliche Situation. Die Angst kann sich mit körperlichen und seelischen Beschwerden zeigen. Veränderungen der Lebenssituation können Angst auslösen.

Bei einer Krebserkrankung kann zum Beispiel Angst aufkommen

- bei der Diagnosestellung,
- beim Start der Therapie,
- bei einer Umstellung der Therapie,
- bei der Anpassung an die neue Lebenssituation oder
- bei einer Verschlechterung der Gesundheit.

Oft tritt Angst auch eher unerwartet auf, beispielsweise beim Abschluss der Therapie oder bei der Rückkehr in den Alltag.

Angst

Sie fühlen sich …	Oder Sie stellen fest …	Was Sie selbst für sich tun können …
	• Leichte Ängstlichkeit	• Versuchen Sie, schwierige Momente nicht allein durchzustehen. Die Bewältigung fällt Ihnen leichter, wenn Sie solche Momente mit vertrauten Menschen teilen können. • Scheuen Sie sich nicht, Fragen an das Behandlungsteam zu stellen. Bereiten Sie sich auf den nächsten Kontakt vor und notieren Sie sich alle Fragen, die Sie stellen möchten. • Besprechen Sie anstehende Entscheidungen auch mit Ihren Nächsten. • Sorgen Sie für regelmässige Bewegung. Körperliche Aktivität kann die innere Ausgeglichenheit stärken.
	• Innere Unruhe, Herzklopfen • Schwindel, Schwitzen, Zittern • Sie können Alltagsaufgaben nur noch eingeschränkt wahrnehmen • Sie haben Schlafprobleme • Sie haben das Gefühl, die Kontrolle über Ihre Situation zu verlieren • Sie haben das Gefühl, dass Sie «nicht mehr sich selbst sind»	• Klären Sie mit dem Behandlungsteam offene Fragen zu Therapie und Krankheit. • Versuchen Sie, sich bei wiederkehrenden negativen Gedanken abzulenken mit etwas, was Ihnen Freude bereitet. • Entspannungsübungen mittels Yoga oder Muskelrelaxation können beruhigen. Ebenfalls entspannend wirken Massagen (evtl. ärztlich verordnet), Musik hören. • Zögern Sie nicht, mit Ärzten, Pflegefachkräften, Psychoonkologen oder in Selbsthilfegruppen über Ihre Angst zu sprechen. • Informieren Sie sich im Voraus, an wen Sie sich in Notfallsituationen wenden können.
	Plötzlich auftretende körperliche Anzeichen wie: • Brustschmerzen • erschwerte Atmung • ohne Anstrengung Schwindel Oder: • Sie wissen weder aus noch ein • Sie haben Panikgefühle	• Nehmen Sie mit dem Behandlungsteam Kontakt auf.

Appendix 5 Questionnaires for evaluating nurse training

Initial nurse training

Evaluation der ersten Schulungs-Sequenz für Pflegefachpersonen Symptom Navi© Pilotstudie

Liebe Teilnehmerin, lieber Teilnehmer

Wir möchten Ihnen gerne eine unterstützende Schulung zur Einführung des SN©P bieten. Deshalb bitten wir Sie folgende Fragen zu beantworten.

Ich arbeite am: _____ ID-Nummer Pflege ☐☐

Bitte umkreisen Sie bei den folgenden Fragen die für Sie am besten zutreffende Zahl.

1) Die erste Schulungssequenz hat das SN©P umfassend eingeführt

Überhaupt nicht 1 2 3 4 5 6 7 grösstmöglich

2) Die Präsentation zum SN©P war informativ und verständlich

Überhaupt nicht 1 2 3 4 5 6 7 grösstmöglich

3) Ich konnte von den Videosequenzen beispielhaft lernen

Überhaupt nicht 1 2 3 4 5 6 7 grösstmöglich

4) Ich traue mir zu Edukationsgespräche im Alltag auszuprobieren

Überhaupt nicht 1 2 3 4 5 6 7 grösstmöglich

5) Ich traue mir zu die Motivierende Gesprächsführung während der Edukationsgespräche anzuwenden

Überhaupt nicht 1 2 3 4 5 6 7 grösstmöglich

6) **Besonders positiv war für mich während der ersten Schulung (in Stichworten):**

7) **Eher unpassend war für mich während der ersten Schulung (in Stichworten):**

Bitte wenden!

Wir wissen, dass die Umsetzung von Edukationsgesprächen auch von der allgemeinen Arbeitssituation abhängig ist. Deshalb bitten wir Sie, folgende Fragen zu beantworten:

Wie empfinden Sie persönlich Ihre momentane Arbeit bzw. Arbeitssituation im Allgemeinen?
(Kreuzen Sie auf jeder Zeile an, was Ihren Empfindungen am ehesten entspricht)

		(1)	(2)	(3)	(4)	(5)	(6)	(7)	
s31_01	bewältigbar	○1	○2	○3	○4	○5	○6	○7	nicht bewältigbar
s31_02	sinnlos	○1	○2	○3	○4	○5	○6	○7	sinnvoll
s31_03	strukturiert	○1	○2	○3	○4	○5	○6	○7	chaotisch
s31_04	beeinflussbar	○1	○2	○3	○4	○5	○6	○7	unbeeinflussbar
s31_05	unbedeutend	○1	○2	○3	○4	○5	○6	○7	bedeutend
s31_06	übersichtlich	○1	○2	○3	○4	○5	○6	○7	unübersichtlich
s31_07	steuerbar	○1	○2	○3	○4	○5	○6	○7	nicht steuerbar
s31_08	nicht lohnend	○1	○2	○3	○4	○5	○6	○7	lohnenswert
s31_09	vorhersehbar	○1	○2	○3	○4	○5	○6	○7	nicht vorhersehbar

Follow-up nurse training

Evaluation der zweiten Schulungs-Sequenz für Pflegefachpersonen Symptom Navi©
Pilotstudie

Liebe Teilnehmerin, lieber Teilnehmer der Schulung zum SN©P

Wir möchten Ihnen eine angepasste Schulung bieten und sicher gehen, dass Sie von der Schulung profitiert haben. Deshalb bitten wir Sie, folgende Fragen für uns zu beantworten: bitte umkreisen Sie die für Sie am besten Zutreffende Zahl zu den Fragen.

Ich arbeite am: _____ ID-Nummer Pflege ☐☐

1) Ich konnte meine Fragen zur Praxisanwendung vom SN©P einbringen

Überhaupt nicht 1 2 3 4 5 6 7 Grösstmöglich

2) Meine Fragen wurden zufriedenstellend beantwortet

Überhaupt nicht 1 2 3 4 5 6 7 Grösstmöglich

3) Ich fühle mich befähigt, Edukationsgespräche in meinem Arbeitsalltag anzuwenden

Überhaupt nicht 1 2 3 4 5 6 7 Grösstmöglich

4) Ich fühle mich sicher, dem Patienten die SN©Flyer zu erklären und deren Anwendung zu Hause zu vermitteln

Überhaupt nicht 1 2 3 4 5 6 7 Grösstmöglich

5) Ich bin mir sicher, dass ich Edukationsgespräche in meinen Arbeitsalltag integrieren kann

Überhaupt nicht 1 2 3 4 5 6 7 Grösstmöglich

5) Besonders positiv war für mich während der zweiten Schulung (in Stichworten):

6) Eher unpassend war für mich während der zweiten Schulung (in Stichworten):

Bitte wenden!

Wie Sie in Ihrem Alltag Edukationsgespräche anwenden können, hängt auch von der allgemeinen Arbeitssituation ab. Wir bitten Sie deshalb folgende Fragen in Bezug auf die Einführung vom SN©P und der Anwendung von Edukationsgesprächen mit SN©Flyern zu beantworten:

Wie empfinden Sie persönlich Ihre momentane Arbeit bzw. Arbeitssituation?
(Kreuzen Sie auf jeder Zeile an, was Ihren Empfindungen am ehesten entspricht)

		(1)	(2)	(3)	(4)	(5)	(6)	(7)	
s31_01	bewältigbar	O_1	O_2	O_3	O_4	O_5	O_6	O_7	nicht bewältigbar
s31_02	sinnlos	O_1	O_2	O_3	O_4	O_5	O_6	O_7	sinnvoll
s31_03	strukturiert	O_1	O_2	O_3	O_4	O_5	O_6	O_7	chaotisch
s31_04	beeinflussbar	O_1	O_2	O_3	O_4	O_5	O_6	O_7	unbeeinflussbar
s31_05	unbedeutend	O_1	O_2	O_3	O_4	O_5	O_6	O_7	bedeutend
s31_06	übersichtlich	O_1	O_2	O_3	O_4	O_5	O_6	O_7	unübersichtlich
s31_07	steuerbar	O_1	O_2	O_3	O_4	O_5	O_6	O_7	nicht steuerbar
s31_08	nicht lohnend	O_1	O_2	O_3	O_4	O_5	O_6	O_7	lohnenswert
s31_09	vorhersehbar	O_1	O_2	O_3	O_4	O_5	O_6	O_7	nicht vorhersehbar

Appendix 6 Questionnaires for patient-reported outcomes

Baseline assessment

Datum: ☐☐☐ Patient Add ID: ☐☐☐

Name des Ambulatoriums (Ort):_____

Messzeitpunkt: Vor erster Medikamentengabe ❑

Sehr geehrter Patient, sehr geehrte Patientin,

Wir danken Ihnen, dass Sie sich Zeit nehmen den Fragebogen für die Symptom Navi© Pilotstudie auszufüllen.

Dieser Fragebogen besteht aus vier Teilen. Wir bitten Sie, alle Fragen zu beantworten.

Bitte setzen Sie pro Frage immer nur ein Kreuz ein.

Wenn Sie den Fragebogen in der Papierversion ausgefüllt haben, wird das Pflegeteam Ihren Fragebogen mit einem vorfrankierten und adressierten Couvert an uns zurück zu senden.

Wir bedanken uns vielmals, dass Sie sich die Zeit nehmen, alle Fragen zu beantworten.

Die Studienleiterin: Prof. Dr. Manuela Eicher

MD Anderson Symptominventar (MDASI-Score)

Teil 1. Wie **stark** sind Ihre Beschwerden?
Menschen mit Krebs leiden häufig unter Beschwerden, die durch die Krankheit selbst oder durch deren Behandlung verursacht werden. Wir bitten Sie, zu beurteilen, wie stark die folgenden Beschwerden **in den letzten 24 Stunden** waren. Bitte füllen Sie zu jeder Frage einen der Kreise aus, von 0 (nicht vorhanden) bis 10 (die stärksten Beschwerden, die Sie sich vorstellen können).

	Nicht vorhanden										Die stärksten Beschwerden, die Sie sich vorstellen können
	0	1	2	3	4	5	6	7	8	9	10
1. Ihre **Schmerzen** im SCHLIMMSTEN Fall?	○	○	○	○	○	○	○	○	○	○	○
2. Ihre **Abgeschlagenheit** (**Müdigkeit**) im SCHLIMMSTEN Fall?	○	○	○	○	○	○	○	○	○	○	○
3. Ihre **Übelkeit** im SCHLIMMSTEN Fall?	○	○	○	○	○	○	○	○	○	○	○
4. Ihre **Schlafstörungen** im SCHLIMMSTEN Fall?	○	○	○	○	○	○	○	○	○	○	○
5. Ihre Sorgen (**Ihr Kummer**) im SCHLIMMSTEN Fall?	○	○	○	○	○	○	○	○	○	○	○
6. Ihre **Kurzatmigkeit** im SCHLIMMSTEN Fall?	○	○	○	○	○	○	○	○	○	○	○
7. Ihre **Gedächtnisprobleme** im SCHLIMMSTEN Fall?	○	○	○	○	○	○	○	○	○	○	○
8. Ihre **Appetitlosigkeit** im SCHLIMMSTEN Fall?	○	○	○	○	○	○	○	○	○	○	○
9. Ihre **Schläfrigkeit** (**Benommenheit**) im SCHLIMMSTEN Fall?	○	○	○	○	○	○	○	○	○	○	○
10. Ihre **Mundtrockenheit** im SCHLIMMSTEN Fall?	○	○	○	○	○	○	○	○	○	○	○

	Nicht vorhanden										Die stärksten Beschwerden, die Sie sich vorstellen können
	0	1	2	3	4	5	6	7	8	9	10
11. Ihre **Traurigkeit** im SCHLIMMSTEN Fall?	○	○	○	○	○	○	○	○	○	○	○
12. Ihr **Erbrechen** im SCHLIMMSTEN Fall?	○	○	○	○	○	○	○	○	○	○	○
13. Ihre **Taubheitsgefühle** oder Ihr **Kribbeln** im SCHLIMMSTEN Fall?	○	○	○	○	○	○	○	○	○	○	○

Teil 2. Wie haben die Beschwerden Ihr Leben **beeinträchtigt**?
Beschwerden beeinträchtigen häufig wie wir uns fühlen und wie wir im Alltag zurechtkommen. Wie sehr haben Ihre Beschwerden **in den letzten 24 Stunden** die folgenden Dinge beeinträchtigt? Bitte füllen Sie zu jeder Frage einen der Kreise aus, von 0 (keine Beeinträchtigung) bis 10 (die stärkste Beeinträchtigung, die Sie sich vorstellen können).

	Nicht beeinträchtigt										Völlig beeinträchtigt
	0	1	2	3	4	5	6	7	8	9	10
14. **Alltagstätigkeiten**?	○	○	○	○	○	○	○	○	○	○	○
15. **Ihre Stimmung**?	○	○	○	○	○	○	○	○	○	○	○
16. **Arbeit oder Hausarbeit (einschliesslich Arbeiten ums Haus)**?	○	○	○	○	○	○	○	○	○	○	○
17. **Ihre Beziehung zu anderen Menschen**?	○	○	○	○	○	○	○	○	○	○	○
18. **Zu Fuss gehen**?	○	○	○	○	○	○	○	○	○	○	○
19. **Ihre Freude am Leben**?	○	○	○	○	○	○	○	○	○	○	○

Fragebogen zum Selbstvertrauen im Umgang mit der Krebskrankheit (SES6G)

Wir möchten gerne erfahren, wie **zuversichtlich** Sie sind, gut mit Ihrer Krebserkrankung umgehen zu können.
Es ist wichtig, dass Sie alle Fragen beantworten, lassen Sie keine aus. Kreuzen Sie diejenige Antwortmöglichkeit an, die Ihnen spontan in den Sinn kommt.

Bitte kreuzen Sie bei jeder Frage die Zahl an, die dem Grad Ihrer **Zuversicht** entspricht.										
	Überhaupt nicht zuversichtlich									Völlig zuversichtlich
Wie zuversichtlich sind Sie, dass Sie es derzeit schaffen…	1	2	3	4	5	6	7	8	9	10
…mit der Erschöpfung, die Ihre Krankheit verursacht, so umzugehen, dass diese Sie nicht stört Dinge zu tun, die Sie gerne tun möchten?	○	○	○	○	○	○	○	○	○	○
…mit den körperlichen Beschwerden oder Schmerzen, die ihre Krankheit verursacht, so umzugehen, dass diese Sie nicht stören Dinge zu tun, die Sie gerne tun möchten?	○	○	○	○	○	○	○	○	○	○
…mit dem Kummer, den Ihre Krankheit verursacht, so umzugehen, dass dieser Sie nicht stört Dinge zu tun, die Sie gerne tun möchten?	○	○	○	○	○	○	○	○	○	○
…mit allen übrigen Beschwerden oder Gesundheitsproblemen so umzugehen, dass diese Sie nicht stören Dinge zu tun, die Sie gerne tun möchten?	○	○	○	○	○	○	○	○	○	○

Bitte kreuzen Sie bei jeder Frage die Zahl an, die dem Grad Ihrer **Zuversicht** entspricht.										
	Überhaupt nicht zuversichtlich									Völlig zuversichtlich
Wie zuversichtlich sind Sie, dass Sie es derzeit schaffen...	1	2	3	4	5	6	7	8	9	10
...all die Dinge zu tun, die für den Umgang mit Ihrer Krankheit notwendig sind, damit Sie nicht so oft zum Arzt müssen?	○	○	○	○	○	○	○	○	○	○
...andere Dinge zu tun – ausser einfach Medikamente zu nehmen – damit Ihre Krankheit Sie im Alltag weniger einschränkt?	○	○	○	○	○	○	○	○	○	○
...ihre Symptome so zu managen, dass diese Sie nicht stören Dinge zu tun, die Sie gerne tun möchten?	○	○	○	○	○	○	○	○	○	○

Einschätzung von Ihrer Stimmung (Mood LASA Scale)

Wie schätzen Sie Ihre Stimmung **während den letzten zwei Wochen** ein?
Bitte setzen Sie auf der Linie von *glücklich* bis *unglücklich* **ein Kreuz** an dem Ort, der Ihre Stimmung während den letzten zwei Wochen darstellt.

Glücklich ——————————————— Unglücklich

Zum Abschluss bitten wir Sie, folgende vier Fragen zu beantworten:

Meine Muttersprache ist:	◯ Deutsch ◯ Französisch ◯ Italienisch ◯ Rätoromanisch ◯ Andere:_____
Mein Familienstand:	◯ Alleinstehend ◯ In Partnerschaft lebend (verheiratet oder Konkubinat) ◯ Andere Form von gemeinschaftlichem Zusammenleben (zB. In Wohngemeinschaft oder betreute Wohnform)
Im gleichen Haushalt mit betreuungsbedürftigen Kindern oder pflegebedürftigen Angehörigen lebend	◯ Ja ◯ Nein
Bildungsstand: höchster Bildungsabschluss	◯ Obligatorische Schulbildung ◯ Abgeschlossene Berufsausbildung ◯ Höherer Fachabschluss ◯ Universitärer Abschluss

Assessments t1-t3

Datum: ☐☐☐ Patient Add ID: ☐☐☐

Code des Ambulatoriums (Ort):_____

Messzeitpunkt: Zwischen zweiter und dritter Medikamentengabe ❑
Zwischen dritter und vierter Medikamentengabe ❑
16 Wochen nach erster Messung ❑

(Messzeitpunkt wird vom Studienteam ausgefüllt)

Sehr geehrter Patient, sehr geehrte Patientin,

Wir danken Ihnen, dass Sie sich Zeit nehmen den Fragebogen für die Symptom Navi© Pilotstudie auszufüllen.

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Wenn Sie den Fragebogen ausgefüllt haben, bitten wir Sie, diesen im beigelegten, vorfrankierten und adressierten Couvert an uns zurück zu senden.

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	Nicht vorhanden										Die stärksten Beschwerden, die Sie sich vorstellen können
	0	1	2	3	4	5	6	7	8	9	10
1. Ihre **Schmerzen** im SCHLIMMSTEN Fall?	○	○	○	○	○	○	○	○	○	○	○
2. Ihre **Abgeschlagenheit (Müdigkeit)** im SCHLIMMSTEN Fall?	○	○	○	○	○	○	○	○	○	○	○
3. Ihre **Übelkeit** im SCHLIMMSTEN Fall?	○	○	○	○	○	○	○	○	○	○	○
4. Ihre **Schlafstörungen** im SCHLIMMSTEN Fall?	○	○	○	○	○	○	○	○	○	○	○
5. Ihre Sorgen (**Ihr Kummer**) im SCHLIMMSTEN Fall?	○	○	○	○	○	○	○	○	○	○	○
6. Ihre **Kurzatmigkeit** im SCHLIMMSTEN Fall?	○	○	○	○	○	○	○	○	○	○	○
7. Ihre **Gedächtnisprobleme** im SCHLIMMSTEN Fall?	○	○	○	○	○	○	○	○	○	○	○
8. Ihre **Appetitlosigkeit** im SCHLIMMSTEN Fall?	○	○	○	○	○	○	○	○	○	○	○
9. Ihre **Schläfrigkeit (Benommenheit)** im SCHLIMMSTEN Fall?	○	○	○	○	○	○	○	○	○	○	○
10. Ihre **Mundtrockenheit** im SCHLIMMSTEN Fall?	○	○	○	○	○	○	○	○	○	○	○

	Nicht vorhanden										Die stärksten Beschwerden, die Sie sich vorstellen können
	0	1	2	3	4	5	6	7	8	9	10
11. Ihre **Traurigkeit** im SCHLIMMSTEN Fall?	○	○	○	○	○	○	○	○	○	○	○
12. Ihr **Erbrechen** im SCHLIMMSTEN Fall?	○	○	○	○	○	○	○	○	○	○	○
13. Ihre **Taubheitsgefühle** oder Ihr **Kribbeln** im SCHLIMMSTEN Fall?	○	○	○	○	○	○	○	○	○	○	○

Teil 2. Wie haben die Beschwerden Ihr Leben **beeinträchtigt**?
Beschwerden beeinträchtigen häufig wie wir uns fühlen und wie wir im Alltag zurechtkommen. Wie sehr haben Ihre Beschwerden **in den letzten 24 Stunden** die folgenden Dinge beeinträchtigt? Bitte füllen Sie zu jeder Frage einen der Kreise aus, von 0 (keine Beeinträchtigung) bis 10 (die stärkste Beeinträchtigung, die Sie sich vorstellen können).

	Nicht beeinträchtigt										Völlig beeinträchtigt
	0	1	2	3	4	5	6	7	8	9	10
14. **Alltagstätigkeiten**?	○	○	○	○	○	○	○	○	○	○	○
15. **Ihre Stimmung**?	○	○	○	○	○	○	○	○	○	○	○
16. **Arbeit oder Hausarbeit (einschliesslich Arbeiten ums Haus)**?	○	○	○	○	○	○	○	○	○	○	○
17. **Ihre Beziehung zu anderen Menschen**?	○	○	○	○	○	○	○	○	○	○	○
18. **Zu Fuss gehen**?	○	○	○	○	○	○	○	○	○	○	○
19. **Ihre Freude am Leben**?	○	○	○	○	○	○	○	○	○	○	○

Fragebogen zum Selbstvertrauen im Umgang mit der Krebskrankheit (SES6G)

Wir möchten gerne erfahren, wie **zuversichtlich** Sie sind, gut mit Ihrer Krebserkrankung umgehen zu können.
Es ist wichtig, dass Sie alle Fragen beantworten, lassen Sie keine aus. Kreuzen Sie diejenige Antwortmöglichkeit an, die Ihnen spontan in den Sinn kommt.

Bitte kreuzen Sie bei jeder Frage die Zahl an, die dem Grad Ihrer **Zuversicht** entspricht.										
	Überhaupt nicht zuversichtlich									Völlig zuversichtlich
Wie zuversichtlich sind Sie, dass Sie es derzeit schaffen…	1	2	3	4	5	6	7	8	9	10
…mit der Erschöpfung, die Ihre Krankheit verursacht, so umzugehen, dass diese Sie nicht stört Dinge zu tun, die Sie gerne tun möchten?	○	○	○	○	○	○	○	○	○	○
…mit den körperlichen Beschwerden oder Schmerzen, die ihre Krankheit verursacht, so umzugehen, dass diese Sie nicht stören Dinge zu tun, die Sie gerne tun möchten?	○	○	○	○	○	○	○	○	○	○
…mit dem Kummer, den Ihre Krankheit verursacht, so umzugehen, dass dieser Sie nicht stört Dinge zu tun, die Sie gerne tun möchten?	○	○	○	○	○	○	○	○	○	○
…mit allen übrigen Beschwerden oder Gesundheitsproblemen so umzugehen, dass diese Sie nicht stören Dinge zu tun, die Sie gerne tun möchten?	○	○	○	○	○	○	○	○	○	○

Bitte kreuzen Sie bei jeder Frage die Zahl an, die dem Grad Ihrer **Zuversicht** entspricht.										
	Überhaupt nicht zuversichtlich									Völlig zuversichtlich
Wie zuversichtlich sind Sie, dass Sie es derzeit schaffen...	1	2	3	4	5	6	7	8	9	10
...all die Dinge zu tun, die für den Umgang mit Ihrer Krankheit notwendig sind, damit Sie nicht so oft zum Arzt müssen?	○	○	○	○	○	○	○	○	○	○
...andere Dinge zu tun – ausser einfach Medikamente zu nehmen – damit Ihre Krankheit Sie im Alltag weniger einschränkt?	○	○	○	○	○	○	○	○	○	○
...ihre Symptome so zu managen, dass diese Sie nicht stören Dinge zu tun, die Sie gerne tun möchten?	○	○	○	○	○	○	○	○	○	○

5 Fragen zu Ihrer Einschätzung der Betreuung durch Pflegefachpersonen

Bitte beantworten Sie alle folgenden fünf Fragen mit Ihrer persönlichen Einschätzung, wie Sie die **Betreuung durch die Pflegefachpersonen** während Ihrem Aufenthalt im Ambulatorium **erlebt haben.**
Bitte füllen Sie zu jeder Frage einen der Kreise aus, von ja – teilweise – nein.

	ja	teilweise	nein
Werden Sie von den Pflegefachpersonen, die Ihnen die Therapie verabreichen, nach Ihren Symptomen gefragt?	○	○	○
Sind sich die Pflegefachpersonen, die Ihnen die Therapie verabreichen, der Schwere Ihrer Symptome bewusst?	○	○	○
Geben Ihnen die Pflegefachpersonen, die Ihnen die Therapie verabreichen, nützliche Informationen für den Umgang mit Ihren Symptomen?	○	○	○
Geben Ihnen die Pflegefachpersonen, die Ihnen die Therapie verabreichen, praktische Ratschläge für den Umgang mit Ihren Symptomen?	○	○	○
Sind Sie zuversichtlich, mit auftretenden Symptomen umgehen zu können?	○	○	○

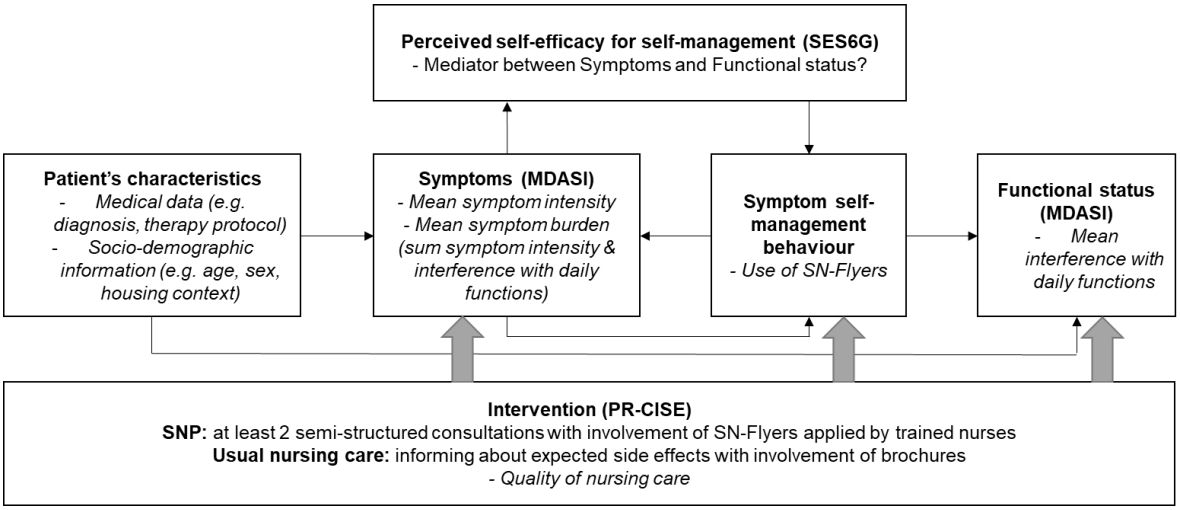
PR-CISE Questionnaire (Prof. Peter Griffiths and Dr. Richard Wagland, Southamptom UK)
Übersetzung durch die Hochschule für Gesundheit, Fribourg HES-SO

Einschätzung von Ihrer Stimmung (Mood LASA Scale)

Wie schätzen Sie Ihre Stimmung **während den letzten zwei Wochen** ein?
Bitte setzen Sie auf der Linie von *glücklich* bis *unglücklich* **ein Kreuz** an dem Ort, der Ihre Stimmung während den letzten zwei Wochen darstellt.

Glücklich ——————————————— Unglücklich

Appendix 7: Supplementary file from third article



Supplementary figure 1: Theoretical framework for pilot study and semi-structured consultations

Abbreviations: MDASI, MD Anderson Symptom Inventory; PR-CISE, Patient-reported Chemotherapy Indicators for Symptoms and Experience; SES6G, Self-efficacy for Chronic Disease 6 item Scale; SN-Flyers, Symptom Navi Flyers; SNP, Symptom Navi Programme;

Symptom specific SN-Flyers: Alopecia, Anxiety, Breathlessness, Diarrhoea, Emesis and nausea, Fatigue, Increased susceptibility: infections and bleeding, Irradiated skin, Loss of appetite, Inflamed oral mucosa, Obstipation, Pain, Peripheral neuropathy, Sexuality, Skin alteration: feet and hand, and Skin alterations related to target therapies.

General SN-Flyers: information how to use the flyers, complementary information on pain management and on Oxaliplatin, useful addresses for support at home, and a list of all available flyers.

Supplementary table 1:

Intra-class correlation coefficient (ICC) for continuous efficacy outcomes at every visit and overall

	N	n	Adjusted ICC (95% CI)	Crude ICC (95% CI)
Mean symptom interference				
t1 (1-3 weeks)	8	118	0.0 (n.e.)	0.03 (0.00 to 0.54)
t2 (4-6 weeks)	8	108	0.001 (0.00 to 0.96)	0.00 (0.00 to 1.00)
t3 (16 weeks)	8	106	0.00 (n.e.)	0.00 (n.e.)
Overall	8	332	0.00 (n.e.)	0.02 (0.00 to 0.52)
Mean symptom severity				
t1 (1-3 weeks)	8	117	0.00 (n.e.)	0.02 (0.00 to 0.84)
t2 (4-6 weeks)	8	109	0.03 (0.00 to 0.63)	0.03 (0.00 to 0.48)
t3 (16 weeks)	8	105	0.00 (n.e.)	0.00 (n.e.)
Overall	8	331	0.00 (n.e.)	0.02 (0.00 to 0.71)
Mean symptom burden				
t1 (1-3 weeks)	8	117	0.00 (n.e.)	0.06 (0.00 to 0.41)
t2 (4-6 weeks)	8	108	0.03 (0.00 to 0.77)	0.02 (0.00 to 0.84)
t3 (16 weeks)	8	105	0.00 (n.e.)	0.00 (n.e.)
Overall	8	330	0.00 (n.e.)	0.03 (0.00 to 0.45)
Mean self-efficacy				
t1 (1-3 weeks)	8	118	0.01 (0.00 to 1.00)	0.01 (0.00 to 1.00)
t2 (4-6 weeks)	8	108	0.00 (n.e.)	0.01 (0.00 to 1.00)
t3 (16 weeks)	8	104	0.00 (n.e.)	0.00 (n.e.)
Overall	8	330	0.00 (n.e.)	0.00 (n.e.)

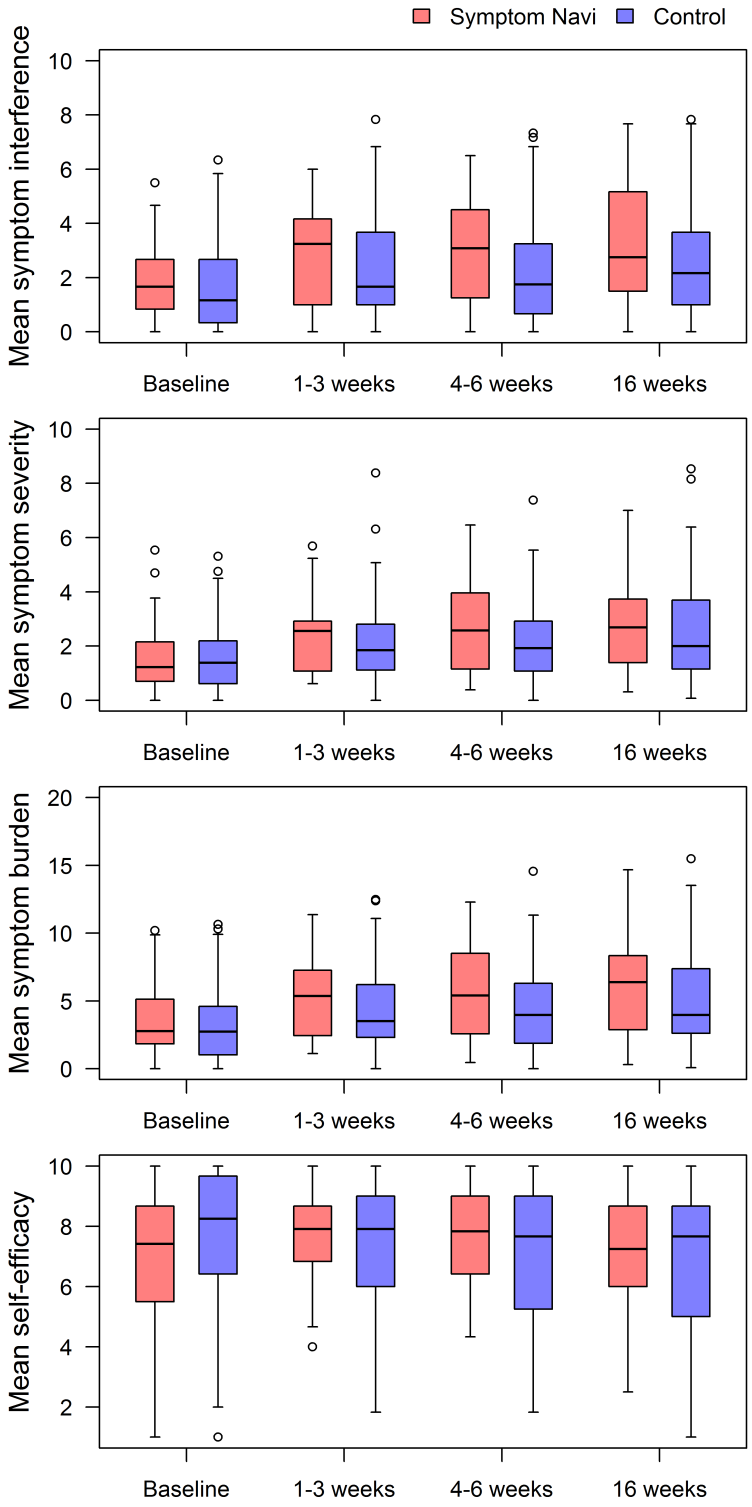
Calculated from linear mixed-effects regression models. The adjusted ICC is based on models with group and stratum (and visits for the overall estimate) as fixed effects and centre (and patient for the overall estimate) as random effect. The crude ICC is based on models with random effects only. N: number of clusters; n: number of observations; n.e. not estimable.

Supplementary table 2:

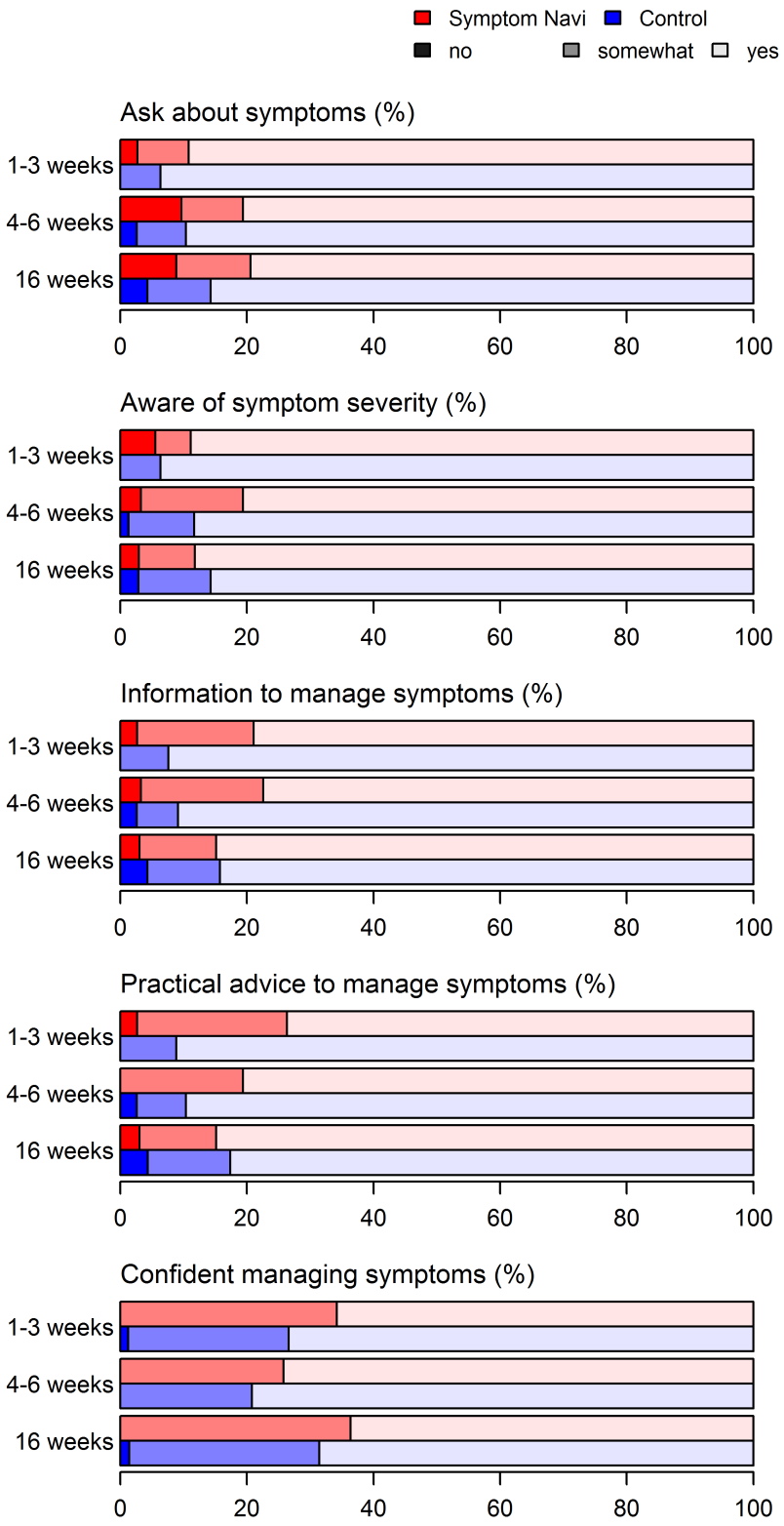
Intra-class correlation coefficient (ICC) for binary efficacy outcomes (PR-CISE items) at every visit and overall

	N	n	Adjusted ICC (95% CI)	Crude ICC (95% CI)
Nurses ask about symptoms				
t1 (1-3 weeks)	8	116	0.00 (n.e.)	0.00 (n.e.)
t2 (4-6 weeks)	8	108	0.10 (0.00 to 0.78)	0.14 (0.00 to 0.72)
t3 (16 weeks)	8	104	0.00 (n.e.)	0.02 (0.00 to 1.00))
Overall	8	328	0.04 (0.00 to 0.67)	0.07 (0.01 to 0.48)
Nurses are aware of symptom severity				
t1 (1-3 weeks)	8	115	0.00 (n.e.)	0.00 (n.e.)
t2 (4-6 weeks)	8	109	0.00 (n.e.)	0.00 (n.e.)
t3 (16 weeks)	8	104	0.00 (n.e.)	0.00 (n.e.)
Overall	8	327	0.00 (n.e.)	0.00 (n.e.)
Nurses provide useful information to manage symptoms				
t1 (1-3 weeks)	8	117	0.00 (n.e.)	0.18 (0.02 to 0.73)
t2 (4-6 weeks)	8	108	0.07 (0.00 to 0.86)	0.17 (0.01 to 0.75)
t3 (16 weeks)	8	103	0.00 (n.e.)	0.00 (n.e.)
Overall	8	328	0.02 (0.00 to 0.90)	0.08 (0.01 to 0.52)
Nurses provide practical advice to manage symptoms				
t1 (1-3 weeks)	8	117	0.00 (n.e.)	0.14 (0.01 to 0.70)
t2 (4-6 weeks)	8	108	0.00 (n.e.)	0.00 (n.e.)
t3 (16 weeks)	8	102	0.00 (n.e.)	0.00 (n.e.)
Overall	8	327	0.00 (n.e.)	0.00 (n.e.)
Are you confident to manage symptoms				
t1 (1-3 weeks)	8	117	0.00 (n.e.)	0.00 (n.e.)
t2 (4-6 weeks)	8	108	0.00 (n.e.)	0.00 (n.e.)
t3 (16 weeks)	8	103	0.05 (0.00 to 0.51)	0.06 (0.00 to 0.47)
Overall	8	328	0.00 (n.e.)	0.00 (0.00 to 1.00)

Calculated from logistic mixed-effects regression models. The adjusted ICC is based on models with group and stratum (and visits for the overall estimate) as fixed effects and centre (and patient for the overall estimate) as random effect. The crude ICC is based on models with random effects only. N: number of clusters; n: number of observations; n.e. not estimable.



Supplementary figure 2:
Descriptive Boxplots for continuous efficacy outcomes based on MDASI and SES6G questionnaires at each visit



Supplementary figure 3:
Descriptive bar charts for patients' perceived nursing support for symptom management based on PR-CISE items

Supplementary table 3:

Per protocol analysis for continuous efficacy outcome effects at each time point. A positive mean difference indicates an improvement in the Symptom Navi group (SNP).

	SNP		Control			
	N	Mean (95% CI)	N	Mean (95% CI)	Mean difference (95% CI)	P-value	Joint p-value
Mean symptom interference	29		64				.72
t1 (1-3 weeks)		2.72 (1.94 to 3.50)		2.17 (1.62 to 2.71)	-0.55 (-1.71 to 0.61)	.30	
t2 (4-6 weeks)		2.49 (1.61 to 3.37)		2.07 (1.49 to 2.64)	-0.43 (-1.62 to 0.77)	.44	
t3 (16 weeks)		3.04 (2.17 to 3.91)		2.51 (1.90 to 3.12)	-0.54 (-1.74 to 0.67)	.35	
Mean symptom severity	29		64				.97
t1 (1-3 weeks)		2.12 (1.65 to 2.60)		2.06 (1.75 to 2.38)	-0.06 (-0.73 to 0.61)	.84	
t2 (4-6 weeks)		2.27 (1.71 to 2.82)		2.10 (1.76 to 2.44)	-0.17 (-0.88 to 0.55)	.62	
t3 (16 weeks)		2.56 (2.01 to 3.12)		2.44 (2.07 to 2.81)	-0.12 (-0.85 to 0.61)	.73	
Mean symptom burden	29		64				.85
t1 (1-3 weeks)		4.81 (3.71 to 5.92)		4.26 (3.50 to 5.01)	-0.56 (-2.17 to 1.06)	.44	
t2 (4-6 weeks)		4.79 (3.51 to 6.07)		4.20 (3.39 to 5.00)	-0.60 (-2.30 to 1.10)	.46	
t3 (16 weeks)		5.48 (4.18 to 6.78)		4.98 (4.09 to 5.86)	-0.50 (-2.24 to 1.24)	.54	
Mean self-efficacy	28		64				.32
t1 (1-3 weeks)		7.77 (6.96 to 8.57)		7.31 (6.77 to 7.84)	0.46 (-0.62 to 1.54)	.37	
t2 (4-6 weeks)		8.04 (7.12 to 8.96)		7.10 (6.55 to 7.64)	0.95 (-0.21 to 2.10)	.10	
t3 (16 weeks)		7.00 (6.15 to 7.84)		6.96 (6.41 to 7.51)	0.04 (-1.07 to 1.15)	.94	

Symptom interference and symptom severity scores 0 – 10 (higher ratings indicating higher symptom interference and higher symptom severity); symptom burden scores 0 – 20 (higher ratings indicating higher symptom burden); self-efficacy sores 1 – 10 (higher ratings indicating higher/better self-efficacy); CI = confidence interval; N refers to non-missing observations. Means in each group and mean differences between groups with 95% CI were derived from linear mixed-effects regression models.

Supplementary table 4:

Complete case analysis of continuous efficacy outcomes at each time point. A positive mean difference indicates an improvement in the Symptom Navi group (SNP).

	N	SNP Mean (95% CI)	N	Control Mean (95% CI)	Mean difference (95% CI)	P-value	Joint p-value
Mean symptom interference	23		67				.55
t1 (1-3 weeks)		2.74 (2.05 to 3.42)		2.23 (1.83 to 2.64)	-0.50 (-1.43 to 0.42)	.25	
t2 (4-6 weeks)		2.70 (1.95 to 3.45)		2.18 (1.73 to 2.62)	-0.52 (-1.48 to 0.45)	.27	
t3 (16 weeks)		3.22 (2.38 to 4.07)		2.57 (2.07 to 3.07)	-0.66 (-1.71 to 0.40)	.21	
Mean symptom severity	23		67				.75
t1 (1-3 weeks)		2.29 (1.77 to 2.82)		2.00 (1.69 to 2.30)	-0.30 (-0.99 to 0.40)	.37	
t2 (4-6 weeks)		2.33 (1.76 to 2.90)		2.03 (1.70 to 2.36)	-0.30 (-1.03 to 0.43)	.39	
t3 (16 weeks)		2.79 (2.15 to 3.42)		2.41 (2.04 to 2.78)	-0.38 (-1.17 to 0.41)	.33	
Mean symptom burden	23		66				.56
t1 (1-3 weeks)		4.99 (3.93 to 6.05)		4.17 (3.55 to 4.80)	-0.82 (-2.25 to 0.61)	.23	
t2 (4-6 weeks)		4.99 (3.81 to 6.17)		4.19 (3.50 to 4.89)	-0.80 (-2.31 to 0.71)	.27	
t3 (16 weeks)		5.97 (4.61 to 7.33)		4.97 (4.17 to 5.77)	-1.00 (-2.68 to 0.68)	.23	
Mean self-efficacy	21		67				.19
t1 (1-3 weeks)		7.92 (6.93 to 8.90)		7.32 (6.74 to 7.90)	0.59 (-0.69 to 1.88)	.33	
t2 (4-6 weeks)		8.20 (7.20 to 9.21)		7.11 (6.52 to 7.70)	1.09 (-0.20 to 2.39)	.09	
t3 (16 weeks)		6.99 (5.95 to 8.02)		6.96 (6.35 to 7.57)	0.03 (-1.29 to 1.35)	.96	

Symptom interference and symptom severity scores 0 – 10 (higher ratings indicating higher symptom interference and higher symptom severity); symptom burden scores 0 – 20 (higher ratings indicating higher symptom burden); self-efficacy sores 1 – 10 (higher ratings indicating higher/better self-efficacy); CI = confidence interval; N refers to non-missing observations. Means in each group and mean differences between groups with 95% CI were derived from linear mixed-effects regression models.

Supplementary table 5:

Sensitivity analysis of continuous efficacy outcomes adjusted for potential confounders based on the FAS at each time point. A positive mean difference indicates an improvement in the Symptom Navi group (SNP).

	SNP		Control		Mean difference	P-value	Joint p-value
	N	Mean (95% CI)	N	Mean (95% CI)	(95% CI)		
Mean symptom interference	42		80				.19
t1 (1-3 weeks)		2.84 (2.36 to 3.32)		2.36 (2.03 to 2.68)	-0.48 (-1.22 to 0.26)	.17	
t2 (4-6 weeks)		2.94 (2.41 to 3.47)		2.29 (1.94 to 2.65)	-0.65 (-1.40 to 0.11)	.09	
t3 (16 weeks)		3.45 (2.89 to 4.02)		2.62 (2.23 to 3.02)	-0.83 (-1.62 to -0.04)	.040	
Mean symptom severity	42		80				.76
t1 (1-3 weeks)		2.31 (1.95 to 2.68)		2.09 (1.85 to 2.34)	-0.22 (-0.80 to 0.36)	.38	
t2 (4-6 weeks)		2.45 (2.03 to 2.88)		2.19 (1.90 to 2.47)	-0.27 (-0.87 to 0.33)	.35	
t3 (16 weeks)		2.80 (2.31 to 3.29)		2.56 (2.22 to 2.90)	-0.23 (-0.89 to 0.42)	.46	
Mean symptom burden	42		80				.35
t1 (1-3 weeks)		5.13 (4.40 to 5.86)		4.40 (3.91 to 4.90)	-0.72 (-1.88 to 0.44)	.18	
t2 (4-6 weeks)		5.39 (4.54 to 6.23)		4.47 (3.91 to 5.03)	-0.92 (-2.11 to 0.28)	.12	
t3 (16 weeks)		6.18 (5.23 to 7.14)		5.19 (4.53 to 5.85)	-0.99 (-2.29 to 0.31)	.12	
Mean self-efficacy	41		80				.43
t1 (1-3 weeks)		7.48 (6.82 to 8.15)		7.42 (6.97 to 7.87)	0.06 (-0.89 to 1.01)	.89	
t2 (4-6 weeks)		7.44 (6.74 to 8.15)		7.25 (6.79 to 7.71)	0.19 (-0.77 to 1.15)	.67	
t3 (16 weeks)		6.65 (5.94 to 7.36)		7.18 (6.70 to 7.66)	-0.53 (-1.50 to 0.44)	.26	

Symptom interference and symptom severity scores 0 – 10 (higher ratings indicating higher symptom interference and higher symptom severity); symptom burden scores 0 – 20 (higher ratings indicating higher symptom burden); self-efficacy sores 1 – 10 (higher ratings indicating higher/better self-efficacy); CI = confidence interval; N refers to non-missing observations. Means in each group and mean differences between groups with 95% CI were derived from linear mixed-effects regression models.

Supplementary table 6:

Sensitivity analysis of continuous efficacy outcomes using only the last follow-up visit (t3, 16 weeks). A positive mean difference indicates an improvement in the Symptom Navi group (SNP).

	SNP		Control		Mean difference (95% CI)	P-value
	N	mean (95% CI)	N	mean (95% CI)		
Mean symptom interference	36	3.33 (2.64 to 4.01)	70	2.65 (2.16 to 3.13)	-0.68 (-1.76 to 0.40)	.17
Mean symptom severity	35	2.65 (2.11 to 3.20)	70	2.60 (2.22 to 2.99)	-0.05 (-0.90 to 0.79)	.89
Mean symptom burden	35	5.81 (4.68 to 6.95)	70	5.28 (4.48 to 6.07)	-0.54 (-2.30 to 1.23)	.48
Mean self-efficacy	34	7.16 (6.42 to 7.90)	70	6.80 (6.30 to 7.31)	0.35 (-0.76 to 1.47)	.47

Symptom interference and symptom severity scores 0 – 10 (higher ratings indicating higher symptom interference and higher symptom severity); symptom burden scores 0 – 20 (higher ratings indicating higher symptom burden); self-efficacy sores 1 – 10 (higher ratings indicating higher/better self-efficacy); CI = confidence interval; N refers to non-missing observations. N refers to non-missing observations. Mean in each group and mean difference between groups with 95% CI were derived from a simplified linear mixed-effects regression model with treatment group and stratification factor as fixed covariates and cluster as random intercept.

Supplementary table 7:

Sensitivity analysis of continuous efficacy outcomes based on the comparison of cluster means of the change score from baseline to t3 (16 weeks). The effects are presented as mean difference or Mann-Whitney statistic (the probability that a random patient in the Symptom Navi group (SNP) has better outcome than a random patient from the Control group) with 95% confidence intervals (CI). A positive mean difference and a Mann-Whitney statistic larger than 0.5 indicates an improvement in SNP. N refers to the number of clusters.

	SNP (N=3)	Control (N=5)	Effect measures (95%CI)	P-value
Change of mean symptom interference				
Parametric†	1.21 (0.67)	0.91 (1.04)	-0.26 (-2.04 to 1.53)	.73
Non-parametric*	1.45 [0.45, 1.73]	0.97 [0.95, 1.59]	0.47 (0.16 to 0.80)	.81
Change of mean symptom severity				
Parametric†	0.94 (0.37)	0.99 (0.59)	0.07 (-0.94 to 1.09)	.86
Non-parametric*	0.81 [0.66, 1.36]	1.15 [0.97, 1.34]	0.60 (0.24 to 0.88)	.48
Change of mean symptom burden				
Parametric†	2.00 (1.00)	1.90 (1.59)	-0.04 (-2.79 to 2.71)	.97
Non-parametric*	1.80 [1.11, 3.08]	2.47 [1.92, 2.74]	0.60 (0.24 to 0.88)	.48
Change of mean self-efficacy				
Parametric†	-0.05 (0.28)	-0.76 (1.00)	0.70 (-1.01 to 2.42)	.34
Non-parametric*	-0.18 [-0.24, 0.27]	-1.10 [-1.32, 0.20]	0.67 (0.28 to 0.91)	.35

†Mean (sd), mean difference (95% CI) and p-value from linear regression adjusted for stratum used in randomisation.
*Median (lower, upper quartile), Mann-Whitney statistic (95% CI) and p-value from van Elteren test with stratum used in randomisation.

Supplementary table 8:

Per-protocol analysis of binary outcomes (PR-CISE items) at each time point. An odds ratio larger than one indicates an improvement in the Symptom Navi group (SNP).

	SNP		Control		Odds ratio	P-value	Joint p-value
	N	n/N (%)	N	n/N (%)	(95% CI)		
Nurses ask about symptoms	29		64				n.e.
t1 (1-3 weeks)		27/27 (100%)		58/62 (94%)	n.e.	n.e.	
t2 (4-6 weeks)		17/19 (89%)		57/63 (90%)	1.43 (0.08 to 25.43)	.81	
t3 (16 weeks)		22/27 (81%)		54/64 (84%)	0.95 (0.01 to 9.28	.97	
Nurses are aware of symptom severity	29		64				.78
t1 (1-3 weeks)		26/27 (96%)		58/62 (94%)	5.25 (0.12 to 233.44)	.39	
t2 (4-6 weeks)		16/19 (84%)		55/63 (87%)	1.62 (0.08 to 33.85)	.75	
t3 (16 weeks)		24/27 (89%)		54/64 (84%)	3.38 (0.19 to 60.92)	.41	
Nurses provide useful information to manage symptoms	29		64				.68
t1 (1-3 weeks)		24/28 (86%)		58/62 (94%)	0.26 (0.01 to 4.67)	.36	
t2 (4-6 weeks)		16/19 (84%)		57/63 (90%)	0.35 (0.02 to 7.00)	.49	
t3 (16 weeks)		22/26 (85%)		54/64 (84%)	1.06 (0.07 to 15.35)	.97	
Nurses provide practical advice to manage symptoms	29		64				.11
t1 (1-3 weeks)		21/28 (75%)		58/62 (94%)	0.08 (0.01 to 0.76)	.028	
t2 (4-6 weeks)		16/19 (84%)		56/63 (89%)	0.67 (0.05 to 8.40)	.76	
t3 (16 weeks)		22/26 (85%)		52/63 (83%)	1.40 (0.16 to 12.27)	.76	
Are you confident to manage symptoms	29		64				.73
t1 (1-3 weeks)		18/28 (64%)		46/62 (74%)	0.49 (0.12 to 2.02)	.32	
t2 (4-6 weeks)		15/19 (79%)		52/63 (83%)	0.60 (0.10 to 3.52)	.57	
t3 (16 weeks)		18/26 (69%)		43/64 (67%)	1.05 (0.25 to 4.42)	.95	

Only including patients treated per-protocol. Number and percentage in each group are raw data. N refers to the number of non-missing observations (overall and per time point), n to the number of patients answering with yes. Odds ratios of SNP vs Control with 95% confidence intervals (CI) were derived from logistic mixed-effects regression models. Odds ratios and joint p-values were not estimable (n.e.) if all patients in one group hat the same outcome at a specific time point.

Supplementary table 9:

Complete case analysis of binary efficacy outcomes (PR-CISE items). An odds ratio larger than one indicates an improvement in the Symptom Navi group (SNP).

	SNP		Control		Odds ratio	P-value	Joint p-value
	N	n (%)	N	n (%)	(95% CI)		
Nurses ask about symptoms	23		67				.87
t1 (1-3 weeks)		21 (91%)		63 (94%)	0.69 (0.05 to 9.19)	.78	
t2 (4-6 weeks)		19 (83%)		60 (90%)	0.45 (0.05 to 3.81)	.47	
t3 (16 weeks)		18 (78%)		57 (85%)	0.52 (0.07 to 3.73)	.51	
Nurses are aware of symptom severity	23		67				.86
t1 (1-3 weeks)		20 (87%)		63 (94%)	0.33 (0.03 to 4.31)	.40	
t2 (4-6 weeks)		19 (83%)		58 (87%)	0.71 (0.08 to 6.48)	.76	
t3 (16 weeks)		19 (83%)		57 (85%)	0.86 (0.10 to 7.73)	.89	
Nurses provide useful information to manage symptoms	23		67				.44
t1 (1-3 weeks)		19 (83%)		62 (93%)	0.20 (0.01 to 3.15)	.25	
t2 (4-6 weeks)		18 (78%)		60 (90%)	0.20 (0.02 to 2.41)	.20	
t3 (16 weeks)		19 (83%)		56 (84%)	1.01 (0.08 to 12.76)	.99	
Nurses provide practical advice to manage symptoms	23		67				.37
t1 (1-3 weeks)		18 (78%)		62 (93%)	0.13 (0.01 to 1.43)	.10	
t2 (4-6 weeks)		18 (78%)		59 (88%)	0.29 (0.03 to 2.79)	.28	
t3 (16 weeks)		18 (78%)		55 (82%)	0.63 (0.07 to 5.59)	.68	
Are you confident to manage symptoms	23		67				.96
t1 (1-3 weeks)		16 70%)		49 (73%)	0.70 (0.16 to 3.02)	.64	
t2 (4-6 weeks)		18 (78%)		54 (81%)	0.74 (0.16 to 3.57)	.71	
t3 (16 weeks)		16 (70%)		47 (70%)	0.86 (0.20 to 3.66)	.84	

Only including patients with complete follow-up of the respective outcome. Number and percentage in each group are raw data. N refers to the number of non-missing observations, n to the number of patients answering with yes. Odds ratios of SNP vs Control with 95% confidence intervals (CI) were derived from logistic mixed-effects regression models.

Supplementary table 10:

Sensitivity analysis of binary efficacy outcomes (PR-CISE items) adjusted for potential confounders. An odds ratio larger than one indicates an improvement in the Symptom Navi group (SNP).

	SNP		Control		Odds ratio	P-value	Joint p-value
	N	n/N (%)	N	n/N (%)	(95% CI)		
Nurses ask about symptoms	42		80				1.00
t1 (1-3 weeks)		33/37 (89%)		73/78 (94%)	1.12 (0.07 to 18.12)	.94	
t2 (4-6 weeks)		25/31 (81%)		68/76 (89%)	0.99 (0.07 to 14.05)	1.00	
t3 (16 weeks)		26/33 (79%)		59/69 (86%)	1.07 (0.08 to 13.76)	.96	
Nurses are aware of symptom severity	42		80				.79
t1 (1-3 weeks)		32/36 (89%)		73/78 (94%)	0.45 (0.03 to 5.92)	.54	
t2 (4-6 weeks)		25/31 (81%)		67/76 (91%)	0.50 (0.05 to 5.47)	.57	
t3 (16 weeks)		29/33 (88%)		59/69 (84%)	1.21 (0.10 to 14.16)	.88	
Nurses provide useful information to manage symptoms	42		80				.36
t1 (1-3 weeks)		30/38 (79%)		72/78 (92%)	0.22 (0.01 to 4.03)	.31	
t2 (4-6 weeks)		24/31 (77%)		69/76 (91%)	0.22 (0.01 to 4.08)	.31	
t3 (16 weeks)		28/33 (85%)		58/69 (84%)	1.19 (0.07 to 21.08)	.88	
Nurses provide practical advice to manage symptoms	42		80				.11
t1 (1-3 weeks)		28/38 (74%)		71/78 (91%)	0.12 (0.02 to 0.84)	.032	
t2 (4-6 weeks)		25/31 (81%)		68/76 (89%)	0.37 (0.05 to 2.88)	.35	
t3 (16 weeks)		28/33 (85%)		56/68 (82%)	1.22 (0.16 to 9.05)	.85	
Are you confident to manage symptoms	42		80				.11
t1 (1-3 weeks)		25/38 (66%)		58/78 (74%)	0.35 (0.11 to 1.12)	.08	
t2 (4-6 weeks)		23/31 (74%)		60/76 (79%)	0.34 (0.09 to 1.24)	.10	
t3 (16 weeks)		21/33 (64%)		47/69 (68%)	0.37 (0.11 to 1.21)	.10	

Adjusted for potential confounders based on the full analysis set. Number and percentage in each group are raw data. N refers to the number of non-missing observations (overall and per time point), n to the number of patients answering with yes. Odds ratios of SNP vs Control with 95% confidence intervals (CI) were derived from logistic mixed-effects regression models.

Supplementary table 11:

Sensitivity analysis of binary efficacy outcomes (PR-CISE items) using only the last follow-up (16 weeks) based on the FAS. An odds ratio larger than one indicates an improvement in the Symptom Navi group (SNP)

	SNP n/N (%)	Control n/N (%)	Odds ratio (95% CI)	P-value
Nurses ask about symptoms	27/34 (79%)	60/70 (86%)	0.68 (0.23 to 2.04)	.50
Nurses are aware of symptom severity	30/34 (88%)	60/79 (86%)	1.29 (0.36 to 4.57)	.69
Nurses provide useful information to manage symptoms	28/33 (85%)	59/70 (84%)	0.94 (0.29 to 3.05)	.92
Nurses provide practical advice to manage symptoms	28/33 (85%)	57/69 (83%)	1.22 (0.38 to 3.92)	.74
Are you confident to manage symptoms	21/33 (64%)	48/70 (69%)	0.74 (0.25 to 2.17)	.58

Number and percentage in each group are raw data. N refers to the number of non-missing observations, n to the number of patients answering with yes. The analysis was done with a simplified logistic mixed-effects regression model with treatment group and stratification factor as fixed covariates and cluster as random intercept.

Supplementary table 12:

Sensitivity analysis of binary efficacy outcomes (PR-CISE items) based on the comparison of data summarized on cluster level (i.e. the number of patients answering with yes and no per cluster). An odds ratio larger than one indicates an improvement in the Symptom Navi group (SNP).

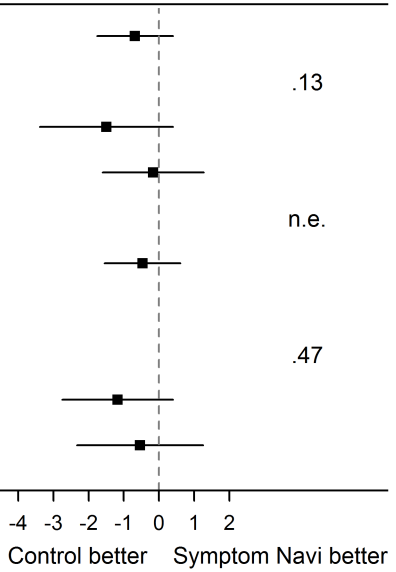
	SNP (N=3) n/N (%)	Control (N=5) n/N (%)	Odds ratio (95% CI)	P-value
Nurses ask about symptoms	27/34 (79%)	60/70 (86%)	0.68 (0.23 to 2.04)	.50
Nurses are aware of symptom severity	30/34 (88%)	60/79 (86%)	1.29 (0.36 to 4.57)	.69
Nurses provide useful information to manage symptoms	28/33 (85%)	59/70 (84%)	0.94 (0.29 to 3.05)	.92
Nurses provide practical advice to manage symptoms	28/33 (85%)	57/69 (83%)	1.22 (0.38 to 3.92)	.74
Are you confident to manage symptoms	21/33 (64%)	48/70 (69%)	0.74 (0.30 to 1.81)	.51

Number and percentage in each group are raw data. N refers to the number of non-missing observations, n to the number of patients answering with yes. The analysis was done with a logistic regression with treatment group and stratification factor as fixed covariates.

Supplementary figure 3:

Forest plot for subgroup analysis of the primary outcome for binary subgroups. A positive mean difference indicates an improvement in the Symptom Navi group (SNP).

	Symptom Navi (SNP)		Control		Mean difference (95% CI)	P-value for
	N	mean (95% CI)	N	mean (95% CI)		interaction
Overall	36	3.33 (2.64 to 4.01)	70	2.65 (2.16 to 3.13)	-0.68 (-1.76 to 0.40)	
Recruitment potential						.13
Slow	16	3.47 (2.47 to 4.48)	19	1.98 (1.05 to 2.90)	-1.50 (-3.39 to 0.40)	
Fast	20	3.11 (2.20 to 4.01)	51	2.94 (2.37 to 3.51)	-0.17 (-1.61 to 1.27)	
Combined chemo-radiotherapy						n.e.
No	36	3.28 (2.60 to 3.95)	61	2.81 (2.29 to 3.33)	-0.47 (-1.55 to 0.61)	
Yes	0	n.e.	9	1.76 (0.42 to 3.10)	n.e.	
Tumor therapies per day						.47
≤ 25	23	3.16 (2.32 to 4.00)	19	1.98 (1.06 to 2.91)	-1.18 (-2.75 to 0.39)	
>25	13	3.47 (2.35 to 4.60)	51	2.93 (2.37 to 3.50)	-0.54 (-2.34 to 1.26)	



Means in each group and mean differences between groups (SNP vs Control) with 95% confidence intervals (CI) were derived from linear mixed-effects regression models with the subgroup and its interaction with treatment group as covariates. Only the last follow-up (t3, 16 weeks) was taken into account. The p-values for interaction were derived from likelihood ratio test of models with and without interaction. The treatment effect was not estimable (n.e.) in patients with combined chemo-radiotherapy. N refers to the number of non-missing observations.

Appendix 8: Analysis of unadjusted data

Symptom interference at each visit assessed by MDASI

	Symptom Navi (N = 49)		Control (N = 85)		Mean difference (95% CI)	P-value
	Non-missing	*mean (sd)*	*Non-missing*	*mean (sd)*		
General activities						
Baseline	49	2.4 (2.2)	84	1.9 (2.2)	0.57 (-0.22 to 1.4)	.16
t1 (1-3 weeks)	38	3.2 (2.4)	80	2.6 (2.5)	0.52 (-0.44 to 1.5)	.29
t2 (4-6 weeks)	32	3.6 (2.6)	76	2.5 (2.5)	1.1 (0.03 to 2.1)	.043
t3 (16 weeks)	36	4.1 (2.8)	70	2.8 (2.4)	1.3 (0.27 to 2.3)	.013
Mood						
Baseline	49	2.7 (2.1)	83	2.3 (2.3)	0.32 (-0.48 to 1.1)	.43
t1 (1-3 weeks)	37	2.9 (1.8)	78	2.4 (2.1)	0.50 (-0.31 to 1.3)	.22
t2 (4-6 weeks)	32	3.3 (2.1)	76	2.5 (2.3)	0.79 (-0.13 to 1.7)	.09
t3 (16 weeks)	35	3.5 (2.6)	70	3.0 (2.4)	0.44 (-0.58 to 1.5)	.39
Work (including work around the house)						
Baseline	49	2.6 (2.4)	83	2.1 (2.5)	0.52 (-0.37 to 1.4)	.25
t1 (1-3 weeks)	38	3.9 (2.8)	79	3.0 (2.7)	0.97 (-0.08 to 2.0)	.07
t2 (4-6 weeks)	31	4.3 (2.9)	76	2.7 (2.6)	1.5 (0.42 to 2.7)	.008
t3 (16 weeks)	36	4.6 (2.8)	70	3.2 (2.9)	1.3 (0.18 to 2.5)	.024
Relations with other people						
Baseline	49	0.98 (1.5)	84	1.0 (2.1)	-0.02 (-0.69 to 0.65)	.95
t1 (1-3 weeks)	38	2.1 (2.0)	80	1.5 (1.9)	0.58 (-0.19 to 1.3)	.14
t2 (4-6 weeks)	32	2.0 (1.8)	76	1.4 (1.9)	0.60 (-0.19 to 1.4)	.13
t3 (16 weeks)	36	2.8 (2.5)	70	1.5 (1.8)	1.3 (0.44 to 2.1)	.003
Walking						
Baseline	48	1.4 (2.1)	84	1.4 (2.2)	-0.00 (-0.78 to 0.77)	.99
t1 (1-3 weeks)	38	2.6 (2.5)	80	2.6 (2.4)	0.01 (-0.95 to 0.97)	.99
t2 (4-6 weeks)	32	3.0 (2.7)	76	2.7 (2.7)	0.32 (-0.81 to 1.4)	.57
t3 (16 weeks)	36	3.3 (2.8)	70	2.8 (2.5)	0.48 (-0.57 to 1.5)	.37
Enjoyment of life						
Baseline	49	1.4 (2.0)	84	1.2 (2.0)	0.19 (-0.51 to 0.90)	.59
t1 (1-3 weeks)	38	2.1 (1.9)	80	1.8 (2.0)	0.27 (-0.50 to 1.5)	.49
t2 (4-6 weeks)	32	2.0 (2.1)	76	1.7 (1.9)	0.33 (-0.50 to 1.2)	.43
t3 (16 weeks)	36	2.1 (2.3)	70	2.3 (2.6)	-0.20 (-1.2 to 0.81)	.69
Mean symptom interference						
Baseline	49	1.9 (1.5)	84	1.6 (1.7)	0.26 (-0.30 to 0.83)	.36
t1 (1-3 weeks)	38	2.8 (1.7)	80	2.3 (1.9)	0.47 (-0.24 to 1.2)	.19
t2 (4-6 weeks)	32	3.0 (2.0)	76	2.2 (1.9)	0.76 (-0.03 to 1.6)	.06
t3 (16 weeks)	36	3.4 (2.3)	70	2.6 (2.0)	0.76 (-0.09 to 1.6)	.08

Variables are presented as mean (standard deviation) and were compared using mean difference with 95% confidence interval (CI) and Student's t-test. MDASI scores from 0 (did not interfere) to 10 (interfered completely).

Symptom severity at each visit assessed by MDASI

	Symptom Navi (N = 49)		Control (N = 85)		Mean difference (95% CI)	P-value
	Non-missing	*mean (sd)*	*Non-missing*	*mean (sd)*		
Pain						
Baseline	49	1.2 (1.9)	83	1.7 (2.4)	-0.45 (-1.2 to 0.33)	.26
t1 (1-3 weeks)	38	1.5 (1.7)	78	1.9 (2.5)	-0.35 (-1.2 to 1.54)	.44
t2 (4-6 weeks)	32	2.4 (2.8)	76	1.8 (2.1)	0.60 (-0.38 to 1.6)	.22
t3 (16 weeks)	35	2.6 (2.7)	70	2.2 (2.4)	0.37 (-0.66 to 1.6)	.48
Fatigue						
Baseline	49	2.8 (2.4)	84	2.6 (2.5)	0.24 (-0.63 to 1.1)	.59
t1 (1-3 weeks)	38	4.8 (2.3)	79	3.9 (2.2)	0.85 (-0.02 to 1.7)	.06
t2 (4-6 weeks)	31	4.9 (3.0)	75	4.0 (2.6)	0.87 (-0.28 to 2.0)	.14
t3 (16 weeks)	35	5.0 (2.6)	70	4.1 (2.5)	0.91 (-0.14 to 2.0)	.09
Nausea						
Baseline	49	0.92 (2.2)	83	2.3 (2.5)	0.46 (-0.18 to 1.1)	.15
t1 (1-3 weeks)	38	1.9 (2.2)	79	2.4 (2.5)	0.28 (-0.57 to 1.1)	.52
t2 (4-6 weeks)	32	2.2 (2.6)	77	2.4 (2.4)	0.73 (-0.19 to 1.6)	.12
t3 (16 weeks)	35	1.6 (2.2)	70	3.0 (2.8)	-0.04 (-0.98 to 0.90)	.93
Disturbed sleep						
Baseline	49	2.0 (2.2)	83	2.3 (2.5)	-0.28 (-1.1 to 0.57)	.52
t1 (1-3 weeks)	37	2.6 (2.6)	79	2.4 (2.5)	0.19 (-0.80 to 1.2)	.71
t2 (4-6 weeks)	32	3.1 (2.8)	77	2.4 (2.4)	0.77 (-0.28 to 1.8)	.15
t3 (16 weeks)	35	2.7 (2.9)	70	3.0 (2.8)	-0.31 (-1.5 to 0.85)	.59
Distress						
Baseline	49	3.7 (2.3)	83	3.0 (2.6)	0.69 (-0.20 to 1.6)	.13
t1 (1-3 weeks)	37	2.7 (2.3)	79	2.6 (2.3)	0.10 (-0.78 to 0.99)	.82
t2 (4-6 weeks)	32	2.9 (2.0)	77	2.4 (2.3)	0.43 (-0.48 to 1.4)	.35
t3 (16 weeks)	35	3.2 (2.2)	69	3.5 (2.8)	-0.34 (-1.4 to 0.75)	.54
Shortness of breath						
Baseline	49	1.3 (2.0)	84	1.4 (2.1)	-0.07 (-0.81 to 0.66)	.84
t1 (1-3 weeks)	38	2.1 (2.0)	79	1.5 (2.1)	0.64 (-0.17 to 1.4)	.12
t2 (4-6 weeks)	32	2.4 (2.8)	76	1.6 (1.9)	0.79 (-0.14 to 1.7)	.09
t3 (16 weeks)	35	2.7 (2.6)	70	2.4 (2.4)	0.30 (-0.73 to 1.3)	.56
Difficulty remembering						
Baseline	49	1.5 (2.1)	84	1.1 (1.5)	0.41 (-0.22 to 1.0)	.20
t1 (1-3 weeks)	38	2.0 (2.0)	79	1.4 (2.0)	0.62 (-0.16 to 1.4)	.12
t2 (4-6 weeks)	32	2.3 (2.3)	77	1.7 (2.0)	0.61 (-0.26 to 1.5)	.17
t3 (16 weeks)	35	3.1 (2.4)	70	2.0 (2.5)	1.1 (0.07 to 1.2)	.036
Poor appetite						
Baseline	49	1.7 (2.8)	84	1.5 (2.5)	0.19 (-0.74 to 1.1)	.69
t1 (1-3 weeks)	38	2.4 (2.2)	79	2.1 (2.5)	0.35 (-0.61 to 1.3)	.47
t2 (4-6 weeks)	32	2.9 (2.8)	77	2.0 (2.4)	0.96 (-0.10 to 2.0)	.08
t3 (16 weeks)	35	1.9 (2.4)	70	2.3 (2.8)	-0.39 (-1.5 to 0.70)	.48

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	Symptom Navi (N = 49)		Control (N = 85)		Mean difference (95% CI)	P-value
	Non-missing	*mean (sd)*	*Non-missing*	*mean (sd)*		
Drowsiness						
Baseline	49	1.5 (2.0)	84	1.6 (2.3)	-0.05 (-0.83 to 0.72)	.89
t1 (1-3 weeks)	38	2.9 (2.6)	79	2.5 (2.3)	0.32 (-0.63 to 1.3)	.50
t2 (4-6 weeks)	32	2.9 (2.7)	77	2.6 (2.5)	0.29 (-0.79 to 1.4)	.60
t3 (16 weeks)	35	2.9 (2.5)	70	2.9 (2.7)	0.00 (-1.1 to 1.1)	1.0
Dry mouth						
Baseline	49	0.96 (2.1)	84	1.3 (2.3)	-0.36 (-1.1 to 0.41)	.36
t1 (1-3 weeks)	38	3.2 (2.6)	79	2.4 (2.4)	0.79 (-0.17 to 1.8)	.10
t2 (4-6 weeks)	32	3.3 (2.6)	77	2.5 (2.4)	0.84 (-0.19 to 1.9)	.11
t3 (16 weeks)	35	3.2 (2.8)	70	2.9 (3.0)	0.37 (-0.84 to 1.6)	.54
Sadness						
Baseline	49	2.7 (2.4)	83	2.3 (2.5)	0.36 (-0.53 to 1.3)	.42
t1 (1-3 weeks)	38	2.4 (2.2)	80	2.2 (2.4)	0.18 (-0.74 to 1.1)	.70
t2 (4-6 weeks)	32	2.6 (2.3)	76	2.4 (2.3)	0.24 (-0.73 to 1.2)	.63
t3 (16 weeks)	36	2.9 (2.5)	70	2.9 (2.7)	-0.04 (-1.1 to 1.0)	.94
Vomiting						
Baseline	49	0.65 (1.9)	84	0.24 (0.89)	0.41 (-0.07 to 0.90)	.09
t1 (1-3 weeks)	38	0.68 (1.7)	80	0.52 (1.5)	0.16 (-0.45 to 0.77)	.61
t2 (4-6 weeks)	32	0.53 (1.2)	76	0.46 (1.2)	0.07 (-0.42 to 0.57)	.78
t3 (16 weeks)	36	0.44 (1.2)	69	0.64 (1.5)	-0.20 (-0.78 to 0.39)	.50
Numbness or tingling						
Baseline	49	0.59 (1.2)	84	0.80 (1.3)	-0.21 (-0.66 to 0.25)	.37
t1 (1-3 weeks)	37	1.2 (1.6)	80	1.6 (2.0)	-0.38 (-1.1 to 0.37)	.32
t2 (4-6 weeks)	32	1.5 (2.2)	76	1.9 (2.2)	-0.39 (-1.3 to 0.52)	.40
t3 (16 weeks)	36	3.3 (2.6)	69	3.0 (2.8)	0.26 (-0.87 to 1.4)	.65
Mean symptom severity						
Baseline	49	1.6 (1.3)	84	1.5 (1.2)	0.10 (-0.34 to 0.54)	.65
t1 (1-3 weeks)	38	2.3 (1.3)	79	2.0 (1.4)	0.30 (-0.25 to 0.85)	.28
t2 (4-6 weeks)	32	2.6 (1.7)	77	2.1 (1.4)	0.52 (-0.09 to 1.1)	.09
t3 (16 weeks)	35	2.7 (1.6)	70	2.6 (1.9)	0.13 (-0.60 to 0.87)	.72

Variables are presented as mean (standard deviation) and were compared using mean difference with 95% confidence interval (CI) and Student's t-test. MDASI score from 0 (not present) to 10 (as bad as you can imagine).

MDASI summary scores: symptom interference, severity and burden at each visit

	Symptom Navi (N = 49)		Control (N = 85)		Mean difference (95% CI)	P-value
	Non-missing	*mean (sd)*	*Non-missing*	*mean (sd)*		
Mean symptom interference						
Baseline	49	1.9 (1.5)	84	1.6 (1.7)	0.26 (-0.30 to 0.83)	.36
t1 (1-3 weeks)	38	2.8 (1.7)	80	2.3 (1.9)	0.47 (-0.24 to 1.2)	.19
t2 (4-6 weeks)	32	3.0 (2.0)	76	2.2 (1.9)	0.76 (-0.03 to 1.6)	.06
t3 (16 weeks)	36	3.4 (2.3)	70	2.6 (2.0)	0.76 (-0.09 to 1.6)	.08
Mean symptom severity						
Baseline	49	1.6 (1.3)	84	1.5 (1.2)	0.10 (-0.34 to 0.54)	.65
t1 (1-3 weeks)	38	2.3 (1.3)	79	2.0 (1.4)	0.30 (-0.25 to 0.85)	.28
t2 (4-6 weeks)	32	2.6 (1.7)	77	2.1 (1.4)	0.52 (-0.09 to 1.1)	.09
t3 (16 weeks)	35	2.7 (1.6)	70	2.6 (1.9)	0.13 (-0.60 to 0.87)	.72
Mean symptom burden						
Baseline	49	3.6 (2.6)	84	3.2 (2.7)	0.36 (-0.58 to 1.3)	.45
t1 (1-3 weeks)	38	5.1 (2.7)	79	4.3 (2.9)	0.84 (-0.27 to 2.0)	.14
t2 (4-6 weeks)	32	5.6 (3.5)	76	4.3 (3.0)	1.3 (-0.05 to 2.6)	.06
t3 (16 weeks)	35	6.0 (3.5)	70	5.2 (3.7)	0.79 (-0.69 to 2.3)	.29

Variables are presented as mean (standard deviation) and were compared using mean difference with 95% confidence interval (CI) and Student's t-test. MDASI score from 0 (not present) to 10 (as bad as you can imagine). Symptom burden is the sum of symptom interference and symptom severity scores.

Patients' perceived self-efficacy at each visit assessed by SES6G

	Symptom Navi (N = 49)		Control (N = 85)		Mean difference (95% CI)	P-value
Perceived self-efficacy for:	*Non-missing*	*mean (sd)*	*Non-missing*	*mean (sd)*		
managing fatigue						
Baseline	48	6.6 (2.8)	84	7.8 (2.4)	-1.1 (-2.1 to 0.24)	.013
t1 (1-3 weeks)	38	7.3 (1.8)	80	7.2 (2.3)	0.12 (-0.72 to 0.95)	.78
t2 (4-6 weeks)	32	7.3 (1.9)	76	7.0 (2.5)	0.31 (-0.67 to 1.3)	.53
t3 (16 weeks)	34	6.3 (2.4)	70	6.8 (2.5)	-0.43 (-1.4 to 0.58)	.40
managing physical discomfort						
Baseline	48	6.4 (2.7)	84	7.5 (2.3)	-1.2 (-2.0 to -0.28))	.01
t1 (1-3 weeks)	38	7.3 (1.9)	80	7.0 (2.4)	0.23 (-0.65 to 1.1)	.61
t2 (4-6 weeks)	32	7.4 (1.9)	76	6.8 (2.6)	0.56 (-0.45 to 1.6)	.28
t3 (16 weeks)	34	6.6 (2.3)	70	6.6 (2.6)	0.02 (-1.0 to 1.1)	.97
managing emotional distress						
Baseline	48	6.8 (2.8)	84	7.6 (2.4)	-0.85 (-1.8 to 0.06)	.07
t1 (1-3 weeks)	38	7.7 (1.8)	80	7.4 (2.3)	0.31 (-0.54 to 1.2)	.47
t2 (4-6 weeks)	32	7.8 (1.6)	76	7.0 (2.6)	0.79 (-0.20 to 1.8)	.12
t3 (16 weeks)	34	7.3 (2.2)	70	6.8 (2.6)	0.49 (-0.53 to 1.5)	.34
keeping symptoms from interfering with daily activities						
Baseline	48	6.4 (2.8)	84	7.6 (2.4)	-1.2 (-2.1 to -0.27)	.011
t1 (1-3 weeks)	38	7.2 (1.9)	80	7.2 (2.3)	0.05 (-0.79 to 0.89)	.91
t2 (4-6 weeks)	32	7.3 (1.9)	76	6.9 (2.6)	0.46 (-0.54 to 1.5)	.36
t3 (16 weeks)	33	6.9 (2.2)	70	6.6 (2.5)	0.25 (-0.77 to 1.3)	.63
managing health conditions						
Baseline	48	7.3 (2.7)	82	8.2 (2.2)	-0.89 (-1.8 to -0.02)	.045
t1 (1-3 weeks)	38	8.1 (1.7)	80	7.6 (2.4)	0.49 (-0.36 to 1.3)	.25
t2 (4-6 weeks)	32	8.1 (1.6)	76	7.7 (2.3)	0.34 (-0.54 to 1.2)	.45
t3 (16 weeks)	36	7.8 (2.0)	70	7.2 (2.5)	0.56 (-0.39 to 1.5)	.25
generally feeling confident						
Baseline	48	7.2 (2.7)	82	8.0 (2.2)	-0.84 (-1.7 to 0.03)	.06
t1 (1-3 weeks)	38	8.2 (1.7)	80	7.5 (2.3)	0.68 (-0.16 to 1.5)	.11
t2 (4-6 weeks)	32	8.1 (1.7)	76	7.6 (2.3)	0.46 (-0.44 to 1.4)	.32
t3 (16 weeks)	36	7.4 (2.4)	70	7.2 (2.5)	0.12 (-0.88 to 1.1)	.81
Mean self-efficacy						
Baseline	48	6.8 (2.6)	84	7.8 (2.1)	-1.00 (-1.8 to -0.18)	.017
t1 (1-3 weeks)	38	7.6 (1.5)	80	7.3 (2.2)	0.31 (-0.46 to 1.1)	.43
t2 (4-6 weeks)	32	7.7 (1.6)	76	7.2 (2.3)	0.49 (-0.39 to 1.4)	.28
t3 (16 weeks)	34	7.0 (2.0)	70	6.9 (2.4)	0.17 (-0.76 to 1.1)	.72

Variables are presented as mean (standard deviation) and were compared using mean difference with 95% confidence interval (CI) and Student's t-test. SES6G score from 1 (not at all confident) to 10 (totally confident).

Patients' perceived quality of nursing symptom management support at each visit assessed by PR-CISE

		Symptom Navi (N = 49		Control (N = 85)		Risk difference (95% CI)	P-value
		Non-missing	*n (%)*	*Non-missing*	*n (%)*		
Ask about symptoms	t1 (1-3 weeks)	37		79			.30
No			1 (2.0%)		0 (0%)	2.0% (-1.9 to 6.0%)	
Somewhat			3 (6.1%)		5 (5.9%)	0.2% (-8.1 to 8.6%)	
Yes			33 (67%)		74 (87%)	-20% (-35 to -4.8%)	
Ask about symptoms	t2 (4-6 weeks)	31		77			.23
No			3 (6.1%)		2 (2.4%)	3.8% (-3.7 to 11%)	
Somewhat			3 (6.1%)		6 (7.1%)	-0.9 (-10 to 7.7%)	
Yes			25 (51%)		69 (81%)	-30% (-46 to -14%)	
Ask about symptoms	t3 (16 weeks)	34		70			.53
No			3 (6.1%)		3 (3.5%)	2.6% (-5.2 to 10%)	
Somewhat			4 (8.2%)		7 (8.2%)	-0.1% (-10 to 10%)	
Yes			27 (55%)		60 (71%)	-15% (-32 to 1.5%)	
Aware of symptom severity	t1 (1-3 weeks)	36		79			.18
No			2 (4.1%)		0 (0%)	4.1% (-1.5 to 10%)	
Somewhat			2 (4.1%)		5 (5.9%)	-1.8% (-9.3 to 5.7%)	
Yes			32 (65%)		74 (87%)	-22% (-37 to - 6.6%)	
Aware of symptom severity	t2 (4-6 weeks)	31		77			.39
No			1 (2.0%)		1 (1.2%)	0.9% (-3.7 to 5.4%)	
Somewhat			5 (10%)		8 (9.4%)	0.8% (-10 to 11%)	
Yes			25 (51%)		68 (80%)	-29% (-45 to -13%)	
Aware of symptom severity	t3 (16 weeks)	34		70			1.00
No			1 (2.0%)		2 (2.4%)	.0.3% (-5.4 to 4.8%)	
Somewhat			3 (6.1%)		8 (9.4%)	-3.3% (-12 to 5.9%)	
Yes			30 (61%)		60 (71%)	-9.4% (-26 to 7.4%)	

Continued on next page

		Symptom Navi (N = 49		Control (N = 85)		Risk difference (95% CI)	P-value
		Non-missing	*n (%)*	*Non-missing*	*n (%)*		
Information to manage symptoms	t1 (1-3 weeks)	38		79			.05
No			1 (2.0%)		0 (0%)	2.0% (-1.9 to 6.0%)	
Somewhat			7 (14%)		6 (7.1%)	7.2% (-4.0 to 18%)	
Yes			30 (61%)		73 (86%)	-25% (-40 to -9.1%)	
Information to manage symptoms	t2 (4-6 weeks)	31		77			.11
No			1 (2.0%)		2 (2.4%)	-0.3% (-5.4 to 4.8%)	
Somewhat			6 (12%)		5 (5.9%)	6.4% (-4.1 to 17%)	
Yes			24 (49%)		70 (82%)	-33% (-50 to -17%)	
Information to manage symptoms	t3 (16 weeks)	33		70			1.00
No			1 (2.0%)		3 (3.5%)	-1.5% (-7.1 to 4.1%)	
Somewhat			4 (8.2%)		8 (9.4%)	-1.2% (-11 to 8.6%)	
Yes			28 (57%)		59 (69%)	-12% (-29 to 4.7%)	
Practical advice to manage symptoms	t1 (1-3 weeks)	38		79			.026
No			1 (2.0%)		0 (0%)	2.0% (-1.9 to 6.0%)	
Somewhat			9 (18%)		7 (8.2%)	10% (-2.2 to 22%)	
Yes			28 (57%)		72 (85%)	-28% (-46 to -14%)	
Practical advice to manage symptoms	t2 (4-6 weeks)	31		77			.20
No			0 (0%)		2 (2.4%)	-2.4% (-5.6 to 0.9%)	
Somewhat			6 (12%)		6 (7.1%)	5.2% (-5.5 to 16%)	
Yes			25 (51%)		69 (81%)	-30% (-46 to -14%)	
Practical advice to manage symptoms	t3 (16 weeks)	33		69			1.00
No			1 (2.0%)		3 (3.5%)	-1.5% (-7.1 to 401%)	
Somewhat			4 (8.2%)		9 (11%)	-2.4% (-13 to 7.7%)	
Yes			28 (57%)		57 (67%)	-10% (-27 to 7.2)	

		Symptom Navi (N = 49		Control (N = 85)		Risk difference (95% CI)	P-value
		Non-missing	*n (%)*	*Non-missing*	*n (%)*		
Confident managing symptoms	t1 (1-3 weeks)	38		79			.58
No			0 (0%)		1 (1.2%)	-1.2% (-3.5 to 1.1%)	
Somewhat			13 (27%)		20 (24%)	3.0% (-12 to 18%)	
Yes			25 (51%)		58 (68%)	-17% (-34 to -0.1%)	
Confident managing symptoms	t2 (4-6 weeks)	31		77			.61
No			0 (0%)		0 (0%)	0.0% (0.0 to 0.0%)	
Somewhat			8 (16%)		16 (19%)	-2.5% (-16 to 11%)	
Yes			23 (47%)		61 (72%)	-25% (-42 to -7.9%)	
Confident managing symptoms	t3 (16 weeks)	33		70			.76
No			0 (0%)		1 (1.2%)	-1.2% (-3.5 to 1.1%)	
Somewhat			12 (24%)		21 (25%)	-0.2% (-15 to 15%)	
Yes			21 (43%)		48 (56%)	-14% (-31 to 3.8%)	

Variables are presented as number and percentage of patients and were compared using risk difference (in%) with 95% confidence interval (CI) and Student's t-test.

Appendix 9: Co-authors consent to insert article in thesis

First article: study protocol submitted to BMJ-Open:

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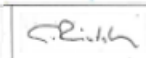
F470 Autorisation des coauteurs pour l'insertion d'un article dans une thèse

Lorsqu'un article, prévu pour être inséré dans une thèse, a été rédigé par plus d'un auteur, le ou la doctorant-e doit faire signer le présent formulaire par tous les coauteurs de l'article. Par leur signature, les coauteurs attestent avoir donné leur accord quant à la diffusion de l'article dans la thèse et indiquent le type de contribution.

DOCTORANT-E	
NOM : BANA	**Prénom : Marika**
No d'immatriculation : 10195634	**Année d'inscription au programme : 2016**
Titre de la thèse: **Implementation of the Symptom Navi Program for cancer patients in ambulatory services: A cluster randomised pilot study (Symptom Navi Pilot Study)**	
Titre de l'article à insérer : **Implementation of the Symptom Navi© Programme for cancer patients in the Swiss outpatient setting: a study protocol for a cluster randomised pilot study (Symptom Navi© Pilot Study)**	

Autorisation du ou des coauteurs de l'article et indication du type de contribution
Par la présente, j'autorise le ou la doctorant-e à insérer dans sa thèse l'article mentionné plus haut (sous la rubrique « Titre de l'article à insérer ») et j'indique le type de contribution justifiant de figurer comme coauteur : 1) contribution substantielle liée à la conception et au design de la recherche et/ou à l'analyse et à l'interprétation des données, et 2) participation à la rédaction de l'article ou à la révision critique et constructive de ses versions préliminaires et approbation de la version finale en vue de sa publication et, éventuellement, tout autre contribution majeure (à spécifier).
Les éléments indiqués au point 1) et au point 2) doivent être réunis pour justifier de figurer comme coauteur.

DATE	NOM ET PRÉNOM DU COAUTEUR	TYPE DE CONTRIBUTION	SIGNATURE
19.02.2020	KARIN RIBI	STUDY CONDUCT, MANUSCRIPT WRITING	K. Ribi
5.02.20	SUSANNE KROPF-STAUB	SNCP DEVELOPMENT, STUDY DESIGN AND CONDUCT, MANUSCRIPT REVIEW	S. Kropf Staub
10.2.2020	SABIN ZÜRCHER-FLORIN	SNCP DEVELOPMENT, STUDY DESIGN, MANUSCRIPT REVIEW	S. Zürcher
5.2.2020	ERNST NÄF	SNCP DEVELOPMENT, STUDY DESIGN AND CONDUCT, MANUSCRIPT REVIEW	E. Näf
12.2.2020	TANJA MANSER	STUDY DESIGN, MANUSCRIPT REVIEW	Tanja Manser

DATE	NOM ET PRÉNOM DU COAUTEUR	TYPE DE CONTRIBUTION	SIGNATURE
24.1.20	LUKAS BÜTIKOFER	STUDY DESIGN AND STATISTICAL SUPPORT, MANUSCRIPT REVIEW	
5.2.2020	FELIX RINTELEN	STUDY DESIGN, MANUSCRIPT REVIEW	
24.02.2020	SOLANGE PETERS	STUDY DESIGN, MANUSCRIPT REVIEW	
19.02.2020	MANUELA EICHER	SNCP DEVELOPMENT, STUDY DESIGN AND CONDUCT, OBTAINED FUNDING, MANUSCRIPT WRITING	

Svp, ajouter un feuillet ou utiliser le verso si d'autres coauteurs sont concernés.

Second article: development and implementation strategies of the SNP submitted to the EJON:

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Ecole doctorale

Doctorat ès sciences infirmières (PhD)

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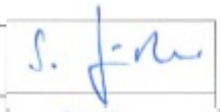
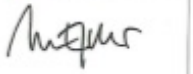
Lorsqu'un article, prévu pour être inséré dans une thèse, a été rédigé par plus d'un auteur, le ou la doctorant-e doit faire signer le présent formulaire par tous les coauteurs de l'article. Par leur signature, les coauteurs attestent avoir donné leur accord quant à la diffusion de l'article dans la thèse et indiquent le type de contribution.

DOCTORANT-E	
NOM : BANA	**Prénom : Marika**
No d'immatriculation : 10195634	**Année d'inscription au programme : 2016**
Titre de la thèse: **Implementation of the Symptom Navi Program for cancer patients in ambulatory services: A cluster randomised pilot study (Symptom Navi Pilot Study)**	
Titre de l'article à insérer : **Development and implementation strategies of a nurse-led symptom self-management program in outpatient cancer centres: The Symptom Navi© Programme**	

Autorisation du ou des coauteurs de l'article et indication du type de contribution
Par la présente, j'autorise le ou la doctorant-e à insérer dans sa thèse l'article mentionné plus haut (sous la rubrique « Titre de l'article à insérer ») et j'indique le type de contribution justifiant de figurer comme coauteur : 1) contribution substantielle liée à la conception et au design de la recherche et/ou à l'analyse et à l'interprétation des données, et 2) participation à la rédaction de l'article ou à la révision critique et constructive de ses versions préliminaires et approbation de la version finale en vue de sa publication et, éventuellement, tout autre contribution majeure (à spécifier).
Les éléments indiqués au point 1) et au point 2) doivent être réunis pour justifier de figurer comme coauteur.

DATE	NOM ET PRÉNOM DU COAUTEUR	TYPE DE CONTRIBUTION	SIGNATURE
19.02.2020	KARIN RIBI	CONCEPTUALISATION, WRITING-REVIEWING & EDITING, VALIDATION, SUPERVISION, PROJECT ADMINISTRATION	K. Ribi
05.02.20	SUSANNE KROPF-STAUB	CONCEPTUALISATION, METHODOLOGY, INVESTIGATION, WRITING REIVIEW & EDITING	S. Kropf-Staub
5.2.2020	ERNST NÄF	CONCEPTUALISATION, METHODOLOGY, INVESTIGATION, WRITING REIVIEW & EDITING	E. Näf
11.2.2020	MONIQUE SAILER SCHRAMM	CONCEPTUALISATION, METHODOLOGY, FORMAL ANALYSIS, INVESTIGATION, WRITING-REVIEWING & EDITING	M. Sailer Schramm

10.2.2020	SABIN ZÜRCHER-FLORIN	CONCEPTUALISATION, WRITING REIVIEW & EDITING	
24.02.2020	SOLANGE PETERS	CONCEPTUALISATION, METHODOLOGY, WRITING REIVIEW & EDITING	
19.02.2020	MANUELA EICHER	CONCEPTUALISATION, METHODOLOGY, INVESTIGATION, VALIDATION, WRITING-REVIEW & EDITING, PROJECT ADMINISTRATION, FUNDING ACQUISITION	

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Third article: pilot-testing of the SNP submitted to the Journal Cancer Nursing

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Ecole doctorale

Doctorat ès sciences infirmières (PhD)

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Lorsqu'un article, prévu pour être inséré dans une thèse, a été rédigé par plus d'un auteur, le ou la doctorant-e doit faire signer le présent formulaire par tous les coauteurs de l'article. Par leur signature, les coauteurs attestent avoir donné leur accord quant à la diffusion de l'article dans la thèse et indiquent le type de contribution.

DOCTORANT-E	
NOM : BANA	**Prénom : Marika**
No d'immatriculation : 10195634	**Année d'inscription au programme : 2016**
Titre de la thèse: **Implementation of the Symptom Navi Program for cancer patients in ambulatory services: A cluster randomised pilot study (Symptom Navi Pilot Study)**	
Titre de l'article à insérer : **Pilot Testing of a Nurse-led basic Symptom Self-Management Support for Patients Receiving First-line Systemic Outpatient Anticancer Treatment using a Cluster-randomised Design (Symptom Navi Pilot Study)**	

Autorisation du ou des coauteurs de l'article et indication du type de contribution
Par la présente, j'autorise le ou la doctorant-e à insérer dans sa thèse l'article mentionné plus haut (sous la rubrique « Titre de l'article à insérer ») et j'indique le type de contribution justifiant de figurer comme coauteur : 1) contribution substantielle liée à la conception et au design de la recherche et/ou à l'analyse et à l'interprétation des données, et 2) participation à la rédaction de l'article ou à la révision critique et constructive de ses versions préliminaires et approbation de la version finale en vue de sa publication et, éventuellement, tout autre contribution majeure (à spécifier).
Les éléments indiqués au point 1) et au point 2) doivent être réunis pour justifier de figurer comme coauteur.

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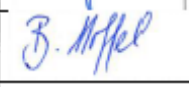
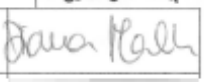
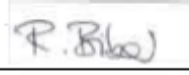
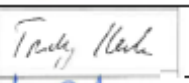
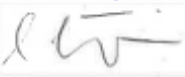
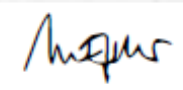
19.02.2020	KARIN RIBI	CONCEPTUALISATION, WRITING-REVIEWING & EDITING, VALIDATION, SUPERVISION, PROJECT ADMINISTRATION	K. Ribi
24.02.2020	SOLANGE PETERS	CONCEPTUALISATION, METHODOLOGY, WRITING REVIEW & EDITING	
05.02.20	SUSANNE KROPF-STAUB	CONCEPTUALISATION, METHODOLOGY, INVESTIGATION, WRITING REVIEW & EDITING	S. Kropf Staub
5. 2.2020	ERNST NÄF	CONCEPTUALISATION, METHODOLOGY, INVESTIGATION, WRITING REVIEW & EDITING	E. Näf

DATE	NOM ET PRÉNOM DU COAUTEUR	TYPE DE CONTRIBUTION	SIGNATURE
10.2.2020	SABIN ZÜRCHER-FLORIN	CONCEPTUALISATION, WRITING REVIEW & EDITING	
5.2.20	BARBARA STOFFEL	INVESTIGATION, WRITING REVIEW & EDITING	
5.2.2020	CORNELIA BLÄUER	INVESTIGATION, WRITING REVIEW & EDITING	
4/2/20	MARKUS BORNER	INVESTIGATION, WRITING REVIEW & EDITING	
10.2.20	DIANA MALIN	INVESTIGATION, WRITING REVIEW & EDITING	
6.2.20	REBECCA BIBER	INVESTIGATION, WRITING REVIEW & EDITING	
6.2.2020	DANIEL BETTICHER	INVESTIGATION, WRITING REVIEW & EDITING	
13.2.20	TRUDY KUHN-BÄCHLER	INVESTIGATION, WRITING REVIEW & EDITING	
06.02.20	NATHAN CANTONI	INVESTIGATION, WRITING REVIEW & EDITING	
05.02.2020	THOMAS SEEGER	INVESTIGATION, WRITING REVIEW & EDITING	
24.1.20	LUKAS BÜTIKOFER	STUDY DESIGN AND STATISTICAL SUPPORT, MANUSCRIPT WRITING AND EDITING	
19.02.2020	MANUELA EICHER	CONCEPTUALISATION, METHODOLOGY, INVESTIGATION, SUPERVISION, VALIDATION, WRITING-REVIEW & EDITING, PROJECT ADMINISTRATION, FUNDING ACQUISITION	

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