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CASEMED

CAncer patients with pre-existing SEvere MEntal Disorders

- Inequalities, development, and feasibility of a supportive cancer care model

PhD Dissertation

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During the preparation of this dissertation, the author used ChatGPT to improve the readability and language of the work and has not replaced researcher tasks such as producing scientific insights, analysing and interpreting data, or drawing scientific conclusions. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

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Preface

This Dissertation is based on work conducted during my enrollment at the Graduate School of Health at Aarhus University and my employment at the Department of Oncology at Aarhus University Hospital from 2022 to 2025. The Dissertation is based on the following studies:

Study I

The Impact of Preexisting Severe Mental Disorders on Cancer Mortality: A Systematic Review and Meta-Analysis

Nikoline Riis, Malene Vestergaard, Mette Asbjoern Neergaard, Jan Alsner, Jesper Grau Eriksen, Poul Videbech, Anna Mygind, Søren Paaske Johnsen, Jan Brink Valentin, Louise Elkjær Fløe.

Acta Psychiatrica Scandinavica, published November 2025 [1]

Study II

Symptom burden and quality of life in patients with severe mental disorders initiating cancer treatment

Louise Elkjær Fløe, Anna Mygind, Jesper Grau Eriksen, Poul Videbech, Kirstine Bundsbæk Bøndergaard, Mette Asbjorn Neergaard.

Clinical Oncology, submitted December 2025 [2].

Study III

Development of a supportive cancer care model for patients with CAncer and pre-existing SEvere MEntal Disorders

Louise Elkjær Fløe, Josefine Maria Bruun, Jesper Grau Eriksen, Poul Videbech, Mette Asbjørn Neergaard, Anna Mygind.

European Journal of Oncology Nursing, 2025 [3].

Study IV

Feasibility of a supportive cancer care intervention for patients with pre-existing severe mental disorders – The CASEMED Model

Louise Elkjær Fløe, Anna Mygind, Jesper Grau Eriksen, Poul Videbech, Ana Lisa Martins Carmo, David Dines Gaardmand Jørgensen, Azza Ahmed Khalil, Hanne Melgaard Nielsen, Trine Brogaard, Mette Asbjoern Neergaard.

Psycho-Oncology, submitted September 2025 [4].

Additional papers published during the PhD

Patient and relative experiences with cancer and pre-existing mental disorders
Josefine Maria Bruun, Pernille Andreassen, Louise Elkjær Fløe, Jesper Grau Eriksen, Poul Videbech, Søren P. Johnsen, Trine Brogaard, Kelly Irwin, Mette Asbjorn Neergaard.
Danish Medical Journal, published 2025.

Professionals' perspectives on caring for cancer patients with pre-existing severe mental disorders
Josefine Maria Bruun, Pernille Andreassen, Louise Elkjær Fløe, Jesper Grau Eriksen, Poul Videbech, Søren P. Johnsen, Mette Asbjoern Neergaard.
Danish Medical Journal, published 2024.

Patients with cancer and pre-existing severe mental disorder
Louise Elkjær Fløe, Astrid Næraa Høeg Vendelsøe, Lars Henrik Jensen, Mette Stie, Peter Hjorth, Jens Søndergaard, Anna Mygind, Poul Videbech, Jesper Grau Eriksen, Terese Myhre Bentson, Josefine Maria Bruun, Søren Paaske Johnsen, Mette Asbjørn Neergaard.
Danish Medical Journal, published 2024 [in Danish].

End-of-life care for cancer patients with pre-existing severe mental disorders -a systematic review
Haukur Svansson, Kirstine Bøndergaard, Poul Videbech, Mette Kjærgaard Nielsen, Jane Ege Møller, Louise Elkjær Fløe, Terese Myhre Bentson, Mette Asbjoern Neergaad.
Annals of Palliative Medicine, published 2024.

Barriers in cancer trajectories of patients with pre-existing severe mental disorders-A systematic review
Terese Myhre Bentson, Louise Elkjær Fløe, Josefine M. Bruun, Jesper Grau Eriksen, Søren Paaske Johnsen, Poul Videbech, Trine Brogaard, Pernille Andreassen, Anna Mygind, Kirstine B. Bøndergaard, Mette Asbjoern Neergaard.
Psycho-Oncology, published 2023.

Abbreviations

Abbreviation	Meaning
95%CI	95% Confidence interval
CASEMED	CAncer patients with pre-existing SEvere MEntal Disorders
EORTC QLQ-C15-PAL	European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core-15 Palliative
EORTC QLQ-C30	European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core-30
GP	General practitioner
GSI	Global Severity Index
HCP	Healthcare professional
HRQoL	Health-Related Quality of Life
IQR	Inter quartile range
opMDT	Onco-psychiatric multidisciplinary team conference
PROM	Patient-reported outcome measure
PS	Performance status
SMD	Severe mental disorder
SMI	Severe mental illness
SLC-92	Symptom Checklist-92
QoL	Quality of Life

Terminology

Severe Mental Disorders

In this Dissertation, *severe mental disorder* (SMD) is defined, in accordance with the World Health Organization, as moderate to severe depression, bipolar affective disorder, or schizophrenia and other psychotic disorders [5]. The corresponding ICD-10 codes applied in this Dissertation are listed in Table 1. Another widely used term in the literature is *severe mental illness* (SMI). Although SMI and SMD are closely related and frequently used interchangeably, they represent conceptually distinct approaches. SMI is primarily a functional construct, referring to mental illnesses that cause substantial and persistent impairment in daily functioning, including limitations in social, occupational, and personal domains [6]. Thus, SMI emphasizes the degree of functional disability rather than the specific diagnosis. In contrast, SMD is fundamentally a diagnostic construct, referring to clearly defined psychiatric disorders classified as severe [5]. SMD therefore highlights the diagnostic category rather than functional impairment. Because this Dissertation integrates multiple methodological approaches and aims to align its findings with existing research, the diagnostic term SMD was chosen to ensure comparability and consistency across studies.

Patients

The persons included in Study II-IV are referred to as *patients*, as they were recruited in their function as patients in the healthcare system. This terminology reflects the clinical context under investigation and does not preclude a person-centred perspective. Throughout the Dissertation, persons diagnosed with an SMD before their cancer diagnosis, here termed "*patients with pre-existing SMDs*", are referred to as "*patients with SMDs*" or "*patients with cancer and SMDs*", hereby making it implicit that the SMD is prior to the cancer diagnosis.

Table 1: Definition of SMD by ICD-10

SMD	**ICD-10 code [7]**
Moderate to severe depression	F32.1 -9, F33.1-9
Bipolar affective disorder	F30-31
Schizophrenia and other psychoses	F20-25, F28-29

English summary

Patients with cancer and pre-existing severe mental disorders (SMDs) constitute a vulnerable population that is characterized by pronounced health inequalities, including increased mortality and reduced access to optimal cancer care. This Dissertation aimed to investigate cancer trajectories among patients with SMDs, focusing on mortality, health-related quality of life (HRQoL), and psychiatric symptom burden, and to develop and feasibility test a cross-sectoral intervention to support cancer care for patients with SMDs.

Study I comprised a systematic review and meta-analysis demonstrating that patients with cancer and pre-existing SMDs have a significantly increased risk of cancer-specific mortality compared with patients without SMDs. The excess mortality was most pronounced among patients with schizophrenia and other psychotic disorders, but was also evident among patients with affective disorders. These findings were consistent across cancer types and point to persistent structural and clinical barriers in cancer care for this population.

Study II was a matched case-control study examining HRQoL and psychiatric symptom burden at the initiation of cancer treatment. Patients with SMDs reported significantly lower HRQoL across all domains and a markedly higher psychiatric symptom burden compared with matched controls without psychiatric illness. The differences were both statistically significant and clinically meaningful, particularly for fatigue, pain, dyspnoea, sleep disturbance, and symptoms related to anxiety and depression. These results indicate that patients with SMDs enter cancer treatment with a substantially compromised physical and psychological state.

Study III focused on the development of a complex intervention, the CASEMED Model. Through a systematic barrier analysis, interviews, workshops, and co-production with patients, relatives, and healthcare professionals, key intervention components were identified: 1) Identification of psychiatric comorbidity, 2) Patient-centered approach, 3) Engagement of significant caregivers, 4) Enhanced collaboration between sectors, including the online multidisciplinary team meetings (opMDT) 5) Education of the oncological Healthcare professionals and 6) Continuity among HCPs.

Study IV feasibility tested the CASEMED Model. The results showed that the model was generally acceptable and feasible in clinical practice with limited resource use. Both patients and healthcare professionals experienced the intervention as meaningful, and the opMDT supported coordination, clinical decision-making, and open management of psychiatric issues. A small number of barriers to full implementation were identified.

In conclusion, this Dissertation documents substantial inequalities in cancer trajectories among patients with co-existing SMDs. It demonstrates that integrated, patient-centered, and cross-sectoral approaches such as the CASEMED Model have the potential to improve cancer care for this underserved population.

Dansk resume

Patienter med kræft og samtidig svær psykiatrisk sygdom udgør en særligt sårbar patientgruppe, som er kendetegnet ved markant ulighed i sundhed, herunder øget dødelighed og dårligere adgang til optimal kræftbehandling. Formålet med denne afhandling var at undersøge kræftforløb for patienter med svær psykiatrisk sygdom med fokus på dødelighed, livskvalitet og psykiatrisk symptom byrde samt at udvikle og afprøve en tværsektoriel intervention til at støtte dem igennem deres kræftforløb.

Studie I bestod af en systematisk litteraturgennemgang og metaanalyse, som viste, at patienter med kræft og samtidig svær psykiatrisk sygdom har en signifikant forhøjet risiko for kræftspecifik dødelighed sammenlignet med patienter uden samtidig psykiatrisk sygdom. Den øgede dødelighed var mest udtalt blandt patienter med skizofreni og andre psykotiske lidelser, men var også til stede hos patienter med affektive lidelser. Resultaterne var konsistente på tværs af kræfttyper, og peger på vedvarende strukturelle og kliniske barrierer i kræftbehandlingen for denne patientgruppe.

Studie II var et matchet case-kontrol-studie, der undersøgte livskvalitet og psykiatrisk symptom byrde ved opstart af kræftbehandling. Patienter med svær psykiatrisk sygdom rapporterede signifikant lavere livskvalitet på tværs af alle domæner samt en markant højere psykiatrisk symptombyrde sammenlignet med matchede kontroller uden samtidig psykiatrisk sygdom. Forskellene var både statistisk og klinisk relevante og omfattede især træthed, smerter, åndenød, søvnproblemer samt symptomer relateret til angst og depression. Fundene indikerer, at patienter med psykiatrisk sygdom allerede ved behandlingsstart har et væsentligt belastet fysisk og psykisk udgangspunkt.

Studie III fokuserede på udviklingen af en kompleks intervention; The CASEMED-Model. Gennem en barriereanalyse, interviews, workshops og samskabelse med patienter, pårørende og sundhedsprofessionelle blev centrale interventionselementer identificeret, herunder; 1) Identifikation af psykiatrisk komorbiditet, 2) patient-centeret tilgang 3) Inddragelse pårørende og ressourcer 4) Forbedre tværsektorielt samarbejde 5) Uddannelse af de sundhedsprofessionelle 6) Forbedre kontinuiteten på kræftafdelingen.

Studie IV afprøvede CASEMED-Modellen i et feasibility-studie. Resultaterne viste, at modellen generelt var acceptabel og gennemførlig i klinisk praksis med begrænset ressourceforbrug. Både patienter og sundhedsprofessionelle oplevede interventionen som meningsfuld, og at den bidrog til bedre koordinering, beslutningsstøtte og åben håndtering af psykiatriske problemstillinger. Enkelte barriere mod implementering blev identificeret.

Samlet set dokumenterer afhandlingen betydelige uligheder i kræftforløb for patienter med samtidig svær psykiatrisk sygdom og viser, at en integreret, patientcentreret og tværsektorielle tilgange som CASEMED-Modellen har potentiale til at forbedre kræftbehandling for denne patientgruppe.

1 Introduction

As a young oncologist, I have always been drawn to the intersection between cancer treatment and the people behind it. During my clinical work, I have repeatedly encountered patients who challenge our routines and our systems, patients with cancer and SMDs. They are often more complex, more fragile, and at times more frustrating to care for, not because they are unwilling, but because the system around them is not built to meet their needs. Too often, these patients fall between specialties, miss appointments, struggle to communicate, or are met with stigma and low expectations. Over time, this has left me with a deep sense of inequity: why should mental illness make surviving cancer harder?

When Professor Mette Asbjoern Neergaard announced this as a future PhD project, I immediately recognized it as a unique opportunity to lead the development of the study together with my supervisors and to combine my clinical experience with my passion for improving cancer care for patients with SMDs and reducing inequalities.

This question - *How do we improve our healthcare system to support patients with cancer and SMDs better?* Has become the driving force behind my research. I want to understand how cancer care can be improved for patients living with mental illness. This is not only about better treatment outcomes but also about dignity, trust, and inclusion. These patients remind us that modern oncology must be not only evidence-based but also patient-centered.

This PhD project is part of the broader **CASEMED initiative** (*Cancer Patients with Pre-existing Severe Mental Disorders*), a multidisciplinary, nationwide Danish research and development program dedicated to improving cancer care for patients with cancer and SMDs throughout their cancer trajectory, from entry into treatment to end-of-life care. By contributing to CASEMED, this project aims to bridge the gap between psychiatric and oncology healthcare, moving towards an oncology that not only treats cancer but also honestly treats the patient.

2 Background

2.1 Population, incidence, and mortality

Approximately 5% of the global adult population lives with a mental illness that substantially impairs daily functioning, posing a significant challenge for healthcare systems worldwide [6]. Patients with SMDs constitute a particularly vulnerable population with a two-to threefold higher all-cause mortality compared with the general population [5]. The excess mortality is multifactorial, but the majority of years of life lost are attributable to poor physical health, with cardiometabolic disease being the leading cause [8,8,10]. Several behavioural and metabolic risk factors, such as smoking, excessive alcohol consumption, and obesity, are more prevalent across a broad range of mental disorders and are also well-established risk factors for cancer development [8]. However, when focusing specifically on cancer-specific mortality, existing studies reveal notable inconsistencies in mortality among patients with SMDs [9,10,11,12]. Nevertheless, a consistent pattern of inequality across the cancer trajectory has been documented. Patients with SMDs are more often diagnosed at advanced stages of disease [13,14], participate less frequently in cancer screening programs [15,16], and are less likely to be diagnosed through standard cancer referral pathways. Instead, patients with SMDs are more often identified through unplanned hospital admissions, which are associated with poorer prognosis [17,18]. Furthermore, they are less likely to receive guideline-concordant cancer treatment [19,20]. Together, these findings suggest that competing risk factors, psychiatric diagnosis, time of diagnosis, cancer diagnosis, or study design influence the association between SMDs and cancer mortality.

2.2 Symptom burden

Receiving a cancer diagnosis is psychologically demanding for many patients [21]. Even in the absence of pre-existing SMD, substantial distress is common, related to the life-threatening nature of the disease, uncertainty, and social and practical disruptions [21,22]. Evidence on psychological responses at the time of cancer diagnosis is, however, heterogeneous. Patients with greater internal resources and resilience tend to report less distress, more adaptive coping, and better quality of life. Coping with a diagnosis has been linked to psychological growth and meaning-making [21]. Whether similar processes apply to patients with pre-existing SMD is unclear. However, qualitative findings suggest varied responses, ranging from worsening depressive symptoms to improved emotional stability and adaptive coping following a terminal cancer diagnosis [23].

As patients with SMDs remain historically underrepresented in clinical research in general [24], which also counts for studies based on patient-reported outcome measures (PROMs), in oncology, PROMs are widely used to monitor treatment-related toxicity, assess HRQoL,

guide symptom management, and support shared decision-making, but consequently, the missing research evidence is limited regarding how mental illness influences self-reporting of symptoms and health-related quality of life (HRQoL) [25]. And on whether patients with SMDs experience a higher symptom burden than patients without SMDs at the time of cancer treatment initiation [25].

2.3 Barriers towards optimal cancer care

Patients with SMDs face barriers to optimal cancer care at patient-, provider- and system level. The levels are defined in Table 2 [26,27].

Patient-level barriers

Patients with SMDs face multiple patient-related barriers to achieving optimal cancer trajectories. Cognitive impairment, negative symptoms, and unstable psychiatric symptoms may compromise the capacity for informed consent and the ability to understand diagnoses and complex treatment plans [26,27,28,29]. Studies indicate that more than 25% of patients with SMDS experience difficulties adhering to treatment, and more than 50% are reluctant to take recommended medications [30,31]. Healthcare professionals further report that many patients with SMDs have a reduced ability to provide self-care and to recognize physical symptoms [32,22].

Impaired self-care and reduced symptom recognition increase the risk of postoperative complications and unmanaged treatment-related toxicity, particularly when timely reporting of adverse effects is required [30] . For example, chemotherapy requires patients to recognize and promptly report side effects such as diarrhea, bleeding, or fever, as delayed help-seeking may lead to life-threatening complications [16,33]. However, some patients with SMDs does not seek the necessary support, placing them at increased risk of severe treatment-related adverse effects [23,33]. In addition, an anthropological CASEMED study revealed internalized stigma as a significant barrier, illustrated by patients expressing gratitude for receiving cancer treatment as if it were undeserved, reflecting diminished self-worth and societal marginalization [28]. Such internal stigma may further reduce help-seeking behaviour and engagement with care, thereby reinforcing disparities in treatment intensity and continuity among patients with cancer and SMDs [28].

Provider-level barriers

Under-detection of psychiatric comorbidity, lack of continuity among healthcare professionals, difficulties in assessing decision-making capacity, external stigma, and diagnostic overshadowing (i.e., misattributing physical symptoms to psychiatric illness) have been reported [26,27,32,33]. These barriers are further supported by a study done by the Danish Psychiatry foundation, where 35% of persons with a psychiatric diagnosis stated that

they had experienced discrimination to a very high, high, or moderate degree due to their mental illness, and 27% of this discrimination had occurred within the healthcare system [34]. This indicates that stigma remains a significant challenge in healthcare. In addition, healthcare professionals frequently report feeling insufficiently prepared to manage patients with SMDs, indicating a general lack of training and confidence in addressing mental illness within somatic healthcare settings [32]. Altogether, these provider-level issues highlight the need for reducing stigma through education of healthcare professionals and limited cooperation between somatic and mental healthcare services.

System-level barriers

Fragmented care, limited cross-sectoral coordination, restricted access to psychiatric expertise, and constrained time and resources within oncology services remain significant challenges in the healthcare system for delivering optimal cancer care for patients with SMDs [26,27,32]. One of the most persistent system-level barriers is the division between somatic and mental healthcare services[26]. When a mental illness is noted in the medical journal, patients tend to be routed to psychiatric care through emergency services, regardless of whether their current symptoms are physical or psychological [35]. When new psychiatric symptoms emerge during the cancer trajectory, responsibility between oncology and mental healthcare services is often poorly defined, resulting in delays in assessment and treatment and also increased uncertainty for the patient [22,35]. Hospitalization for acute psychiatric episodes can also postpone cancer treatment, further worsening cancer outcomes [36].

Limited resources intensify these coordination problems. Caring for patients with cancer and SMDs requires explicit commitment at the hospital level, as these patients often need additional time, coordination, and multidisciplinary resources. Without institutional prioritization and organizational support, efforts to improve care for patients with mental illness are unlikely to be sustainable [33]. At the same time, insufficient in-hospital training leaves healthcare professionals underprepared to manage psychiatric needs [26]. Outside the hospital, additional barriers, including physical distance between somatic and mental healthcare services, transportation difficulties, area-based inequalities in mental healthcare service access, and broader socioeconomic constraints, further exacerbate disparities. [26,27,32] Collectively, these systemic barriers, both within the hospital setting and in the broader social context, continue to compromise the quality of cancer care for patients with SMDs.

Table 2: Barriers and definition of patient-, provider-, and system-level

Level	Patient	Provider	System
Definition	Factors affecting cancer trajectories, concerning the patient, their mental disease, for example, what patients can manage at the given moment. Psychological and physical resources.	Factors affecting cancer trajectories, as perceived by health care professionals, their thoughts and actions, and possible bias toward the patient.	Factors affecting cancer trajectories, concerning how the system is organized, for example, distance and collaboration between locations of oncology and mental healthcare services, accessibility to insurance coverage, etc.
Barriers	Unstable psychiatric symptoms. Social isolation. Poor compliance. Mistrust towards the system and HCPs. Limited illness understanding and cognitive deficits. Internal stigma.	Limited time to coordinate with other sectors. Lack of assessing a patient's decision-making capacity. Difficulties in determining whether cancer or psychiatric illness should be prioritised. Confusion about who is responsible for the different parts of the treatment. Diagnostic overshadowing. External stigma.	Fragmentation of mental health and somatic services. Lack of coordination between health care sectors. Limited access to mental health services Limited time and resources. Lack of continuity among HCPs. Lack of education.

Modified from Bentson et al [26]

2.4 Healthcare interventions in cancer trajectories

Despite clear evidence of multiple barriers to cancer treatment among patients with cancer and SMDs, few structured interventions have been developed. The only known intervention is the American BRIDGE intervention [37]. BRIDGE combined proactive identification of psychiatric comorbidity, person-centered care by a psychiatrist, case management, and enhanced collaboration between oncology and psychiatry. The intervention was feasible in an American context and demonstrated a reduction in both disruptions of cancer treatment and psychiatric symptom severity in a randomized controlled trial [37,38].

Other healthcare interventions have also proven to improve cancer trajectories for patients with mental illness, e.g., a randomised trial from Japan showed increased participation in colorectal cancer screening among people with schizophrenia when assigned to a case-manager. A study from America showed increased rates of breast and cervical cancer screening when people with SMDs were assigned to a psychiatric rehabilitation program [39,40]. Despite this, no interventions to support patients with SMDs during cancer trajectories have previously been developed within a European healthcare system.

2.5 Development of complex interventions

A validated approach to addressing multifaceted barriers across many levels of the healthcare system is the development of complex interventions. Complex interventions are particularly well-suited to situations in which outcomes are influenced by interactions among patients, healthcare professionals, and organizational structures [41]. A prominent one is the UK Medical Research Council (MRC) framework for complex interventions [41]. The MRC framework emphasizes iterative development, theory-informed design, feasibility testing, and evaluation within real-world clinical contexts to enhance both effectiveness and implementation potential [41]. By systematically integrating evidence, stakeholder perspectives, and contextual adaptation in a co-creation approach, complex interventions can address barriers at patient, provider, and system levels simultaneously, throughout all phases of development, from conceptualisation to pilot testing. The participatory process facilitates ownership, feasibility, and long-term sustainability, thereby increasing the likelihood of meaningful and durable improvements in care applicable to everyday clinical practices [41].

2.6 Background conclusion

As outlined above, substantial gaps remain in the evidence regarding the extent to which SMDs influence cancer-specific mortality, how HRQoL and psychiatric symptom burden affect patients with cancer and SMDs when entering cancer treatment, and which supportive strategies are most effective and sustainable for supporting this vulnerable population across cancer trajectories within a European healthcare context.

3 Aims and hypotheses

We hypothesize that patients with cancer and SMDs experience inequalities in both mortality, symptom burden, and support during cancer trajectories, and that cancer care can be improved through cross-sectoral, multidisciplinary interventions.

Therefore, this PhD project aimed to investigate and improve cancer trajectories for patients with cancer and pre-existing SMDs. The specific aims of the four studies were:

Study I: To investigate the evidence of cancer-specific mortality among patients with pre-existing SMDs compared to those without.

Study II: To examine Health-related quality of life (HRQoL) and psychiatric symptom burden among patients with cancer and SMDs.

Study III: To develop a patient-centered, interdisciplinary, cross-sectoral, collaborative care model for patients with cancer and SMDs.

Study IV: To assess the feasibility of the CASEMED Model.

4 Materials and methods

In the following sections, the main elements of the materials and methods used in the four studies are outlined. Full methodological descriptions are provided in the individual papers included at the end of this Dissertation. All the patients in Study II, III and IV are included at Department of Oncology at Aarhus University Hospital in Denmark.

4.1 Setting

In Denmark, about 74% of the population will, at some point in life, either be prescribed medication for psychiatric symptoms and/or receive treatment within the psychiatric healthcare system [42]. Approximately 6.6% of the Danish adult population lives with SMDs, corresponding to roughly 3,200 newly diagnosed cancer patients with SMDs each year, and this incidence is rising [42,43].

The Danish healthcare system is based on equal, free-of-charge access to somatic and mental healthcare, funded through taxes [44]. Furthermore, all Danish citizens are entitled to compensation for loss of income due to unemployment, disability, or illness [44]. National cancer pathways are implemented for Non-specific Symptoms and Signs of Cancer (NSSC-CPP) to ensure standardised, early diagnosis for patients suspected of having cancer [45]. The NSSC-CPPs thereby facilitate early and fast diagnosis, reducing waiting time and ultimately improving prognosis [45]. Medical oncology and radiotherapy are centralized at large hospitals and are primarily delivered in an outpatient setting [45].

The treatment of patients with mental illness is primarily a public task and is managed by the regional authorities. Patients with SMDs are treated in hospital-based psychiatric services, whereas milder psychiatric conditions are typically handled by general practitioners (GPs), psychiatrists in private practice, or psychologists [46].

GPs anchor the psychiatric treatment of more than 90% of patients, and they serve as gatekeepers to the healthcare system [47]. Hence, the choice between referral to hospital-based mental health care or private psychiatrists is based on the severity and the complexity of the mental disorder. GPs, psychiatrists, and psychologists work closely with community nurses and social services [48]. GPs in Study III and IV received remuneration for participating in the online opMDTs, developed in Study III and IV, as compensation for participation in online conferences without patients, which is not standard in Denmark [3,4]

4.2 Study I

Search strategy and selection process

The systematic review and meta-analysis were performed according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines [49] and were reported to the International Prospective Register of Systematic Reviews (PROSPERO) with ID: CRD42023475227 [50]. A comprehensive search in the PubMed, Embase, PsycINFO, and Scopus databases was conducted, using a combination of MeSH terms and keywords related to cancer, severe mental disorders, and survival/mortality, to identify relevant studies published from 1st January 2003 to the 19th of October 2024. A professional research librarian modeled the search string, and the final search strings are shown in Appendix S1.

Studies investigating cancer-specific mortality among adult patients with cancer and pre-existing SMDs were included. Studies were excluded if they met any of the following criteria: 1) Studies in which psychiatric disorder were diagnosed after the cancer diagnosis, 2) Studies reporting other association measurements than Mortality rate ratio (MRR), Standardized mortality ratio (SMR) and Hazard rate ratio (HR) incl. subdistribution hazard rate ratio (SHR), 3) Studies not available in English; 4) Study types: systematic reviews, meta-analyses, and reviews, 5) Statistical issues. The identified studies were independently screened by the first two authors (NR and MV) for titles and subsequent abstracts. Later, full texts of potentially eligible studies were obtained, and disagreements were resolved through discussion with the remaining group of authors.

Risk of bias assessment

Study quality was assessed using the Newcastle-Ottawa Scale (NOS, scores of 0-9) for the included studies [51]. The first two and last authors independently conducted quality assessment, and disagreements were resolved by consensus. Consensus was achieved in all cases. Studies with a total NOS-score ≥ 7 were considered to have low risk of bias, whereas a total score of 4-6 indicated a moderate risk, and 0-3 indicated a high risk of bias.

Data analysis

A random effects model was employed for the analysis, with heterogeneity across studies quantified using the I^2 statistic. To investigate potential sources of heterogeneity, subgroup analyses were performed based on cancer type and three psychiatric diagnosis categories: affective disorders (encompassing moderate to severe depression, mood disorders, mania, and bipolar disorders), schizophrenia, and other psychotic disorders, including non-affective psychotic disorders (NAPD) and SMDs representing a mix of the two combined. Each study accounted for various confounding factors, and for the meta-analysis, we utilised the simplest models, which controlled for at least age and sex. All statistical analyses were performed in Stata version 18.0 (Stata Corp LLC, Texas, USA).

4.3 Study II

Inclusion

The included participants were newly referred patients to the Department of Oncology who had lung-, breast, or head and neck cancer and a record of an SMD within the last 10 years in their hospital record. SMDs were defined as moderate to severe depression (ICD-10: F32.1-9, F33.1-9), bipolar affective disorder (ICD-10: F30–31), or schizophrenia and other psychoses (ICD-10: F20–25, F28–29). The included patients with cancer and SMDs were matched 1:2 with patients without SMDs. The matches were made on age, sex, cancer type, and treatment (curative/palliative).

Data collection

PROMs were collected according to two validated questionnaires. The first measures health-related quality of life using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core-15 Palliative (EORTC QLQC15-PAL) [52], and the other measures a broad perspective of psychiatric symptoms using the Symptom Checklist-92 (SCL-92) [53]. The data were collected electronically or on paper and entered into a REDCap database [54,55]. Patient characteristics were obtained from questionnaires, and missing values were obtained from the medical record by the first author (LEF).

Data analysis

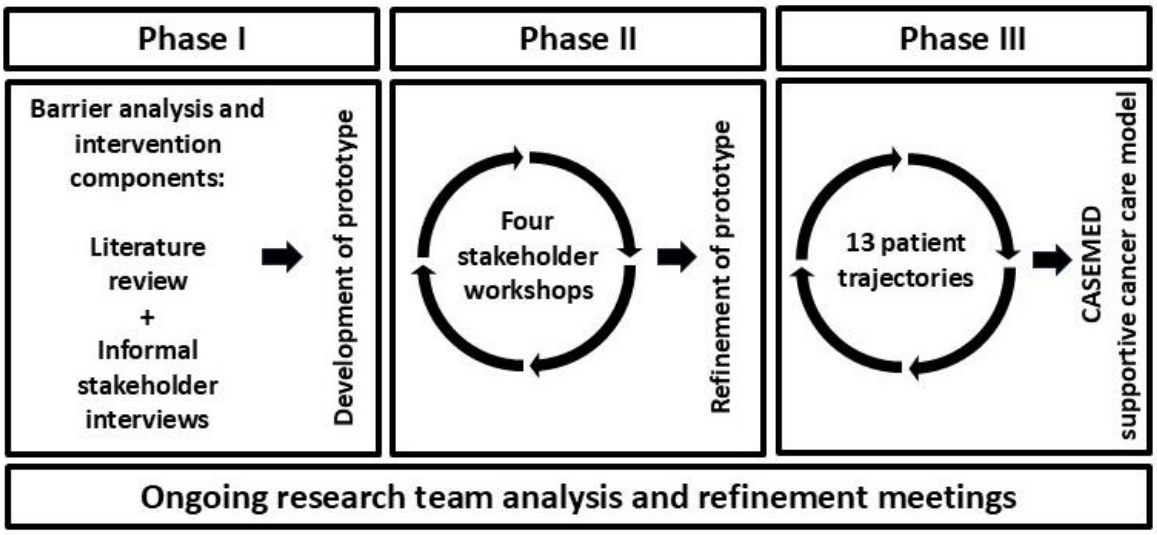
Patients with SMDs were compared with patients without SMDs concerning questionnaires and patient characteristics. Descriptive statistics were used to characterize the cohort, and the EORTC QLQ-C15-PAL items were transformed to standardized 0-100 scores following the official scoring manual, where higher scores reflect better functioning or HRQoL, and for symptom scales, a higher symptom burden [52,56,57]. SCL-92 responses were converted into the ten predefined symptom dimensions specified in the scoring manual: Global Severity Index, somatization, anxiety, interpersonal sensitivity, phobic anxiety, obsessive–compulsive symptoms, depression, anger, hostility, and psychoticism [53].

For all continuous outcomes (EORTC QLQ-C15-PAL and SCL-92 domains), mean values and corresponding 95% confidence intervals (CIs) were calculated to enable comparison with available normative data from the EORTC QLQ-C30 and SCL-92. Between-group differences were expressed as mean ratios with 95% CIs to quantify relative differences between patients with and without SMDs. All statistical analyses were conducted using Stata version 18.0 (Stata Corp LLC, Texas, USA).

4.4 Study III

The CASEMED Model was developed in line with the MRC guidelines [41], designed to facilitate sustainable adoption and implementation in a real-world setting [58]. A co-creative, participatory methodology was applied, emphasizing development, adaptation, and rapid evaluation cycles, with continuous refinement based on dialogue between the research team and stakeholders [59,60]. The development process was divided into three phases, as shown in Figure 1.

Figure 1: Development phases of the CASEMED supportive cancer care model



Data collection and analysis

Data were collected from March 2022 to April 2023. A detailed overview of the 162 participants is shown in Table 3. The first author conducted all interviews, and the qualitative data were analysed thematically, focusing on acceptability, feasibility, mechanisms of change, and key uncertainties. During this process, continuous adaptations were made to the preliminary model.

In Phase I, as a basis for this study, the research team conducted a systematic literature review [26] and two anthropological studies [28,32] to explore barriers and facilitators to optimal cancer care for patients with cancer and SMDs, focusing on patient, provider, and system levels. These findings were discussed in informal interviews, held as eight group and six single interviews with a total of 102 participants. The participants consisted of healthcare professionals, including oncologists, psychiatrists, oncological and psychiatric nurses, GPs, psychologists, advanced practice nurses, social nurses, and one patient representative from a national cancer care organisation. For detailed information about the participants, see Table 3. This allowed new barriers and intervention components to emerge, enabling prioritization of the most clinically relevant elements. Using a rapid-cycle refinement

approach [61], the intervention was continuously adjusted, resulting in the development of the model's prototype.

During Phase II, four workshops were conducted with a total of 34 participants representing a broad range of perspectives (see Table 3). These workshops aimed to refine the Phase I prototype through a structured co-production process. Video recordings and field notes were analysed to extract key themes, including successful patient trajectories, psychosocial aspects, and cross-sector collaboration. Using a rapid-cycle approach, the research group refined and finalized the prototype for pilot testing [61].

In Phase III, the prototype was tested among 13 patients with head and neck, breast, or lung cancer and SMDs at two outpatient clinics at a Danish University Hospital. Patients tested the intervention in two stages: first, five patients tested selected intervention components, and subsequently, eight patients tested the complete prototype. Patient perspectives were gathered through focused observations and informal interviews, while healthcare professionals provided feedback on the interventions' sustainability, meaningfulness, and clinical relevance through informal interviews. Field notes and observations were analysed to identify key uncertainties and impacts, which informed refinements and the final version of the prototype.

Table 3: Involved participants in the development phases

Phase	Data type	Participants					
		Department of Oncology	**Department of Psychiatry**	**General practice**	**Other healthcare professionals**	**Patients and patient representatives**	**Total number of participants**
I	Informal interviews	24 physicians from two outpatient clinics 27 nurses from two outpatient clinics	35 physicians from three departments	Two general practitioners	10 health and social care professionals from the Specialised Palliative Care Unit One psychologist from the Department of Oncology One Advanced Practice Nurse from the municipality One social nurse from a University Hospital	One representative from a cancer care organisation	102
II	Workshop I	Four oncologists	Three psychiatrists One research assistant	Two general practitioners			10
	Workshop II	Four nurses	One nurse		One psychologist from the Department of Oncology One social nurse from Aarhus University Hospital	Two representatives from a cancer care organisation	9
	Workshop III					Eight patient representatives from a national psychiatric care organisation	8
	Workshop IV					Six patient representatives from a national psychiatric care organisation	6
III	Pilot	Two oncologists Two nurses	One psychiatrist	Three general practitioners		Thirteen patients with cancer and SMDs, and the relatives of six of them.	27

4.5 Study IV

To assess the acceptability and feasibility of the intervention, a mixed-methods feasibility study was conducted, guided by the MRC's framework for developing and evaluating complex interventions [41].

Inclusion

Patients were identified through the hospital's electronic system, which screened new referrals for lung, breast, or head and neck cancer and a prior hospital contact for SMD within the past ten years. The first author (LEF) thereafter notified the oncologists in person about the patient. Recruitment occurred during the patient's first oncology visit from April 1, 2023, to June 1, 2024. Exclusion criteria were the absence of planned oncological treatment or less than 5 days of planned oncological treatment. If patients were not currently under psychiatric care, one of two hospital-based project psychiatrists participated in the online opMDT.

Data collection and analysis

Inspired by the implementation outcomes suggested by Proctor et al. [62], the quantitative and qualitative feasibility outcomes included intervention delivery, acceptability, burden, other negative consequences, and mechanisms of change. See Table 4.

Quantitative data were obtained from patient questionnaires and patient hospital records. At baseline, patients completed questionnaires covering demographics and patient-centered concerns related to cancer treatment, together with validated scales assessing health-related quality of life (EORTCQLQ-C15-PAL) [52] and psychiatric symptoms (SCL-92) [53], totalling 110 items. Three months after treatment initiation, patient records were reviewed to assess patient characteristics, scheduled consultations, hospital admissions, and continuity of oncological healthcare professionals.

Qualitative data were collected through semi-structured interviews with 10 patients and 18 healthcare professionals, including five oncologists, four oncology nurses, two project psychiatrists, one palliative care specialist, three GPs who had participated in opMDTs, and three who had not (Appendix S2). Recruitment aimed to capture diverse perspectives on the intervention, its context, and cross-sector collaboration. Interview guides, developed by the multidisciplinary research team, explored acceptability, operational feasibility, negative consequences, and mechanisms of change (Appendix S3). Field notes during recruitment, opMDTs, follow-up calls, and interviews were conducted by the first author (LEF). Hospital healthcare professionals were interviewed near the end of the study, while GPs and patients were interviewed approximately three months post-inclusion.

Table 4: Operationalization of outcomes

Central concept	Operationalization	Quantitative measures	Qualitative measures
Delivery*	Reach (Reaching the target group).	Percentages of recruited patients out of the eligible group. Patient characteristics.	Which experience did the HCPs have regarding the recruited patients and the patients' reasons for nonparticipation?
	Fidelity (Did we deliver the intervention as intended?).	HCP participation in opMDT Number of patients who filled out the questionnaires	
Acceptability+	Was the intervention acceptable for the patient to participate in, for the HCP to use, and in what way?		How did the HCPs perceive the intervention? Which reflections did the patients have about participation?
Burden+	Did the HCPs or the patients find the intervention burdensome?	Average time for the opMDT and the follow-up calls to the patients informing them of clinical actions.	Did the HCPs find participation in the intervention burdensome, and how much time did they spend on preparation for the opMDT?
Negative consequences#			Did the HCPs or patients experience any adverse consequences of the intervention, and in what way?
Mechanisms of change*	1) Identification of psychiatric comorbidity.	Number of patients where the psychiatric diagnosis was noted after the opMDT.	How did the patients experience the focus on their psychiatric disease?
	2) Patient-centered approach.	Percentage of patients receiving the planned oncological treatment.	Which experiences did the HCPs have regarding patient relationships? In what way did the patients experience the HCPs' approach to them? Did the patients miss any supportive initiatives during treatment?
	3) Engagement of significant caregivers.		In what way were the private and professional caregivers engaged, and what thoughts did the patients have about support from them?
	4) Enhanced collaboration between sectors.	Number and kind of supportive clinical actions suggested at the opMDT Number and kind of clinical actions accepted or declined by the patients	What experiences did the HCPs have regarding changes in inter-sectoral collaboration due to the opMDT? What did the patients think about the collaboration between sectors?
	5) Education of the oncological HCPs.	Number of education sessions.	Which reflections did the oncological HCPs have about the education?
	6) Continuity among HCPs.	How many HCPs did the patient engage with during treatment? Did a senior consultant see them at the first visit?	Which reflections did the HCPs and patients have regarding continuity? Did the patients experience continuity and why?

* Inspired by Moores et al [63]

+ Inspired by TFA framework [64]

Inspired by Bonell [65]

5 Ethical considerations

This Dissertation was conducted in accordance with the highest ethical and scientific standards, emphasizing transparency in methodology, unbiased data selection, and full disclosure of potential conflicts of interest, funding sources, and the use of AI tools. Ethical principles were followed in accordance with the Declaration of Helsinki [66]. Data handling complied with the General Data Protection Regulation (GDPR) of the European Union [67], and data storage was approved by the Central Denmark Region (Act No. 1-10-72-1-22). The study was not subject to formal ethical approval according to the Danish Act on Research Ethics Review of Health Research Projects (Act No. 1-16-02-249-22) [68].

All participants received both oral and written information about the study and provided written informed consent before participation, with the option to withdraw at any time. The study used inclusive, person-centered, and non-stigmatizing language to ensure that patients' perspectives on SMDs were represented respectfully and authentically.

Including patients with SMDs in cancer research raises important ethical considerations. Although persons with mental illness may be considered a vulnerable group, systematically excluding them from research would perpetuate inequity and limit the generalizability of findings, as has been the case for many years [69]. Ethically, it is therefore essential to ensure that research reflects the diversity of real-world patient populations, including those living with SMDs [33]. This Dissertation also demonstrates that it is both feasible and ethically necessary to include this population, provided that consent participation was supported through clear communication, adapted information materials, and opportunities for participants to involve caregivers or relatives when needed.

Conducting research in one’s own clinical department also requires careful ethical reflection. The researcher (LEF), an MD and oncology registrar with training in qualitative research, had no prior relationship with the participating patients or GPs but was a professional colleague of some of the oncologists, psychiatric professionals, and oncology nurses involved in the studies. To minimize potential bias or undue influence, transparency and reflexivity were continuously maintained through documentation, regular supervision, and discussion within the supervisor group. This approach aimed to balance scientific rigor with empathy and respect for participants, ensuring that the study both protects vulnerable persons and helps reduce research inequity for patients with SMDs.

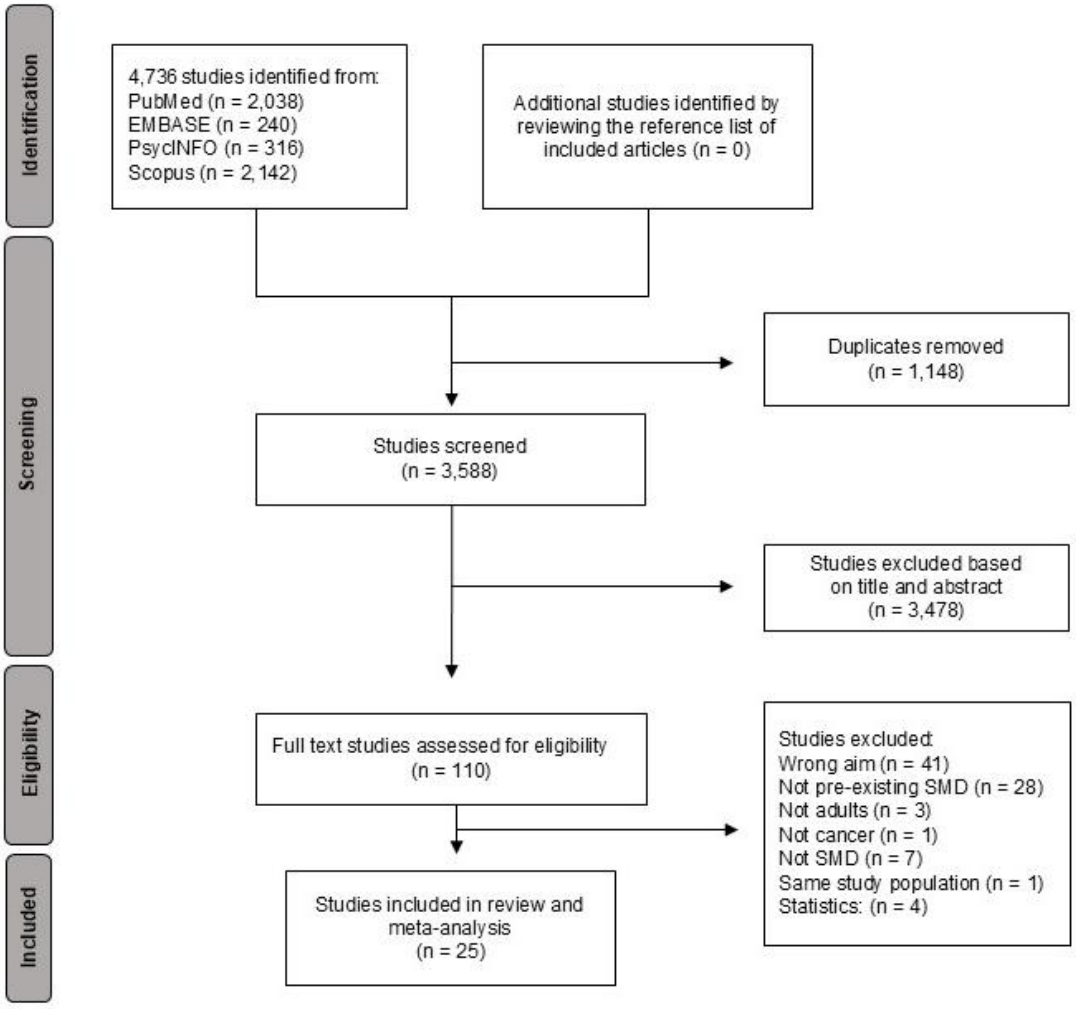
6 Results

In the following sections, the main results from Study I-IV are outlined. Full results sections are described in the individual papers included at the end of this Dissertation.

6.1 Study I

In all, 25 studies were included in the systematic review. Figure 2 presents the PRISMA flowchart outlining the selection process.

Figure 2: PRISMA flow diagram



The included studies were heterogeneous in terms of sample size, study design, and psychiatric diagnosis inclusion. The total number of participants with cancer and SMDs included ranged from 145 to 107,481, with a mean of 17,621 [1].

Patients with cancer and SMDs showed a markedly increased cancer-specific mortality, with an overall cancer-specific mortality of 1.37. The excess risk was most significant among those

diagnosed with schizophrenia or other psychotic disorders, who had up to a 1.47-fold higher cancer mortality. Patients with affective disorders also demonstrated an enhanced relative mortality risk of 1.25 compared to patients with cancer without SMDs.

This pattern was consistent across cancer types. For lung and breast cancer, patients with SMDs had elevated mortality risks of 1.33 and 1.49, respectively. The most pronounced disparity emerged among patients with breast cancer and comorbid schizophrenia or other psychotic disorders, who experienced nearly double the cancer-specific mortality risk compared with their counterparts without SMDs.

A further important observation from the meta-analysis was the divergence between all-cause mortality (ACM) and cancer-specific mortality (CSM). In cancer cohorts, ACM only slightly exceeded CSM, whereas the difference was substantially larger in general population cohorts. The higher ACM suggests that persons with SMDs face a broad spectrum of other challenges beyond cancer, e.g., somatic comorbidity.

When it came to identifying the most critical gap, the largest effect sizes in cancer cohorts were seen in studies where the SMD diagnosis occurred within the first six years preceding the cancer diagnosis, when follow-up spanned approximately 2.5 to 9.5 years, and when study samples reflected the general adult population rather than selected subgroups such as older adults in Medicare populations.

6.2 Study II

Patient characteristics

Forty patients with cancer and SMDs were enrolled between January 2023 and June 2024, and 80 matched controls were enrolled between November 2023 and June 2025. Due to matching, the groups were comparable with respect to sex, cancer type, and treatment intent.

Patients with SMDs differed markedly in several sociodemographic and health-related characteristics, as they were less often in full-time employment (7.7% vs. 46.8%) and more commonly lived alone (43.6% vs. 17.1%). Alcohol misuse was also more prevalent in the SMD group (34.2%) compared to the control group (6.3%). Patterns of next-of-kin designation also differed. Patients with SMDs more frequently named friends, colleagues, or non-relatives as next of kin (35.9% vs. 3.9%) and were less likely to designate a partner (51.3% vs. 80.3%). Conversely, patients with SMDs more often listed their children as next of kin (25.9% vs. 15.8%).

Regarding relationships with healthcare professionals, patients with SMDs more often reported having an established and positive relationship with their GP (78.9% vs. 50.0%). In comparison, nearly half of the control group indicated having no personal relationship with any healthcare professional (48.6%). A complete overview of patient characteristics is provided in Table 5.

Health-related quality of life

Patients with cancer and SMDs consistently demonstrated poorer HRQoL across all assessed domains. Overall HRQoL was markedly reduced in the SMD group, with a mean score of 56.67 (95% CI 48.75–64.58) compared to 69.01 (95% CI 65.20–72.90) in the control group, yielding a mean ratio of 0.82 (95% CI 0.71–0.95). Comparable reductions were observed in both physical and emotional functioning, indicating a broad and clinically meaningful impairment in HRQoL among patients with SMDs at the beginning of cancer treatment. Symptom scales in the HRQoL-assessment tool similarly revealed a higher symptom burden in the SMD group, particularly for dyspnoea, insomnia, fatigue, and pain. Although constipation, loss of appetite, and nausea were also more frequently reported, these differences were not statistically significant.

Table 5: Patient characteristics

Characteristics	Patients with SMD n = 40	Control group n = 80
Female, n (%)	26 (65.0)	54 (65.0)
Age, median (IQR)	59 (51.0-68.0)	62 (52.0-68.0)
Cancer type, n (%)		
Breast	20 (50.0)	40 (50.0)
Head and neck	11 (28.0)	22 (28.0)
Lung	9 (22.0)	18 (22.0)
Curative intended treatment, n (%)	34 (85.0)	68 (85.0)
Severe mental disorder, n (%)		
Moderate to severe depression	23 (57.5)	-
Bipolar disorder	10 (25.0)	-
Schizophrenia and other psychoses	7 (17.5)	-
Educational level, n (%)		
No higher education	12 (32.4)	9 (11.8)
Low/Middle	22 (59.4)	58 (76.3)
Higher	3 (8.1)	9 (11.8)
Uses online healthcare applications n (%)		
Yes	26 (65.0)	79 (98.9)
No	8 (20.0)	1 (0.1)
Lives alone, n (%)		
Yes	17 (43.6)	13 (17.1)
No	22 (55.0)	64 (80.0)
Job situation, n (%)		
Fulltime work	3 (7.7)	36 (46.8)
Parttime work	5 (12.8)	8 (10.4)
Age pensioner	13 (33.3)	25 (32.5)
Disability pensioner	15 (38.5)	0 (0.0)
Social benefits	3 (7.7)	2 (2.6)
Other	0 (0.0)	6 (7.8))
Abuse of alcohol, n (%)		
Current	6 (15.8)	2 (2.5)
Former	7 (18.4)	3 (3.8)
No current or former abuse	25 (65.8)	7 (93.8)
Smoking status, n (%)		
Current	15 (39.5)	10 (12.5)
Former	16 (42.1)	24 (30.0)
No current or former smoking	7 (18.4)	46 (57.5)
Designation of next of kin, n (%)*		
Partner	20 (51.3)	61 (80.3)
Child	10 (25.6)	12 (15.8)
Friend	5 (12.8)	1 (1.3)
College	1 (2.6)	0 (0.0)
Other	8 (20.5)	2 (2.6)
No next of kin	2 (5.1)	0 (0.0)
Good relationship with HCP, n (%)*		
General practitioner	30 (78.9)	35 (50.0)
Home nurse	2 (5.3)	1 (1.4)
Public navigator (E.g., from patients' organisations)	4 (10.5)	0 (0.0)
Psychologist	1 (2.6)	2 (2.9)
Psychiatrist	3 (7.9)	0 (0.0)
Not a good relationship with any HCPs	4 (10.5)	34 (48.6)

*Possible to choose more than one

Not all variables were available for all included patients; the Table is modified from Paper II [2]

Table 6: EORTC QLQ-C15-PAL scores at the beginning of cancer treatment

	Patients with SMDs n=40 Mean (95% CI)	**Control group** n=80 Mean (95% CI)	**Mean ratio** (95% CI)	**Numbers from the Danish norm population study [70]** Mean (95% CI)
Health-related-QoL (High score: good)	56.67(48.75-64.58)	69.01 (65.20-72.90)	0.82 (0.71-0.95)	73 (71.95-74.05)
Functional scale (High score: good)				
Physical functioning	69.15 (61.67-76.63)	88.12 (85.65-90.62)	0.78 (0.70-0.88)	86 (85.10-86.90)
Emotional functioning	69.17 (60.59-77.75)	90.73 (87.29-94.16)	0.76 (0.67-0.87)	84 (83.13-84.87)
Symptom scale (Low score: good)				
Fatigue	44.44 (36.18-52.71)	27.22 (22.23-32.26)	1.63 (1.26-2.11)	24 (22.94-25.06)
Nausea	9.59 (2.45-6.30)	4.38 (2.45-6.30)	2.19 (0.10-4.82)	3 (2.54-3.46)
Pain	27.92 (19.53-36.30)	17.71 (12.48-22.94)	1.58 (1.04-2.39)	20 (18.80-21.20)
Dyspnoea	16.67 (10.41-22.92)	3.96 (2.17-5.74)	4.2 (2.36-7.52)	11 (10.04-11.96)
Insomnia	47.50 (36.70-58.30)	27.08 (20.75-33.42)	1.75 (1.27-2.42)	21 (19.77-22.23)
Appetite loss	19.00 (11.74- 26.60)	16.25 (11.55-20.95)	1.18 (0.73-1.90)	7 (6.22-7.78)
Constipation	20.00 (10.31-29.69)	10.42 (5.22-15.61)	1.92 (0.96-3.82)	6 (5.18-6.82)

The table is modified from Paper II [2]

Psychiatric symptoms

Across all psychiatric symptom domains, patients with SMDs reported markedly higher symptom levels than controls (Table 7). The Global Severity Index was substantially elevated in the SMD group, with a mean of 0.74 (95% CI 0.56-0.91) compared with 0.25 (95% CI 0.20-0.30) in the control group, corresponding to a mean ratio of 2.95 (95% CI 2.19-3.98). The most significant differences were seen in the domain's phobic anxiety and hostility, followed by depression and anxiety, the last showing mean ratios of approximately 2.5, indicating more than a twofold higher psychiatric symptom burden in patients with SMDs. These findings demonstrate a markedly elevated psychiatric symptom burden across multiple domains among patients with SMDs at the time they enter cancer treatment.

Table 7: SCL-92 scores at the beginning of cancer treatment

	Patients with SMDs n = 36 Mean (95% CI)	**Control group** n = 80 Mean (95% CI)	**Mean ratio** (95% CL)	**Numbers from a Danish norm population study** Mean (SD) [71]
Global Severity Index	0.74 (0.56-0.91)	0.25 (0.20-0.30)	2.95 (2.19-3.98)	0.45 (0.43-0.48)
Somatization	0.71 (0.54-0.87)	0.35 (0.27-0.43)	2.05 (1.48-2.84)	0.49 (0.46-0.52)
Anxiety	0.73 (0.53-0.94)	0.30 (0.23-0.38)	2.42 (1.69-3.49)	0.44 (0.41-0.47)
Interpersonal sensitivity	0.73 (0.50-0.95)	0.14 (0.10-0.18)	5.24 (3.45-7.97)	0.54 (0.51-0.57)
Phobic Anxiety	0.48 (0.26-0.71)	0.03 (0.01-0.05)	14.27 (6.85-29.72)	0.13 (0.11-0.15)
Obsessive-Compulsive	1.02 (0.27-0.43)	0.35 (0.27-0.43)	2.92 (2.11-4.03)	0.63 (0.59-0.66)
Depression	0.99 (0.75-1.23)	0.36 (0.30-0.46)	2.58 (1.88-3.54)	0.59 (0.55-0.63)
Anger	0.50 (0.29-0.70)	0.11 (1.88-3.54)	4.57 (2.69-7.77)	0.34 (0.32-0.36)
Hostility	0.39 (0.23-0.56)	0.05 (0.02-0.08)	7.56 (3.64-15.69)	0.46 (0.43-0.49)
Psychoticism	0.40 (0.27-0.52)	0.10 (0.07-0.13)	3.92 (2.54-6.05)	0.22 (0.20-0.24)

The table is modified from Paper II [2]

6.3 Study III

Based on the three developmental phases, which involved 163 stakeholders, the prototype of the CASEMED Model was developed. The model consisted of the following six elements: 1) Identification of psychiatric comorbidity, 2) Patient-centered approach, 3) Engagement of significant caregivers, 4) Enhanced collaboration between sectors, including the opMDT, 5) Education of the oncological HCPs, and 6) Continuity among HCPs. The development of the six intervention components is described below.

Phase I: Development of the prototype
In this phase, key *patient-, provider-, and system-level barriers* to optimal cancer care were identified, along with potential intervention components as described below. Stakeholders agreed that patient-level barriers should be met by system adaptations rather than placing responsibility on patients. Stakeholders further emphasized that any model must be feasible in routine clinical workflows and not introduce significant burdens to the clinic, if it should be sustainable.

At the *patient-level*, stakeholders identified unstable psychiatric and physical symptoms, stigma, insufficient identification of psychiatric comorbidity, and poor self-care as central barriers to optimal cancer care. Although some healthcare professionals expressed concern that documenting mental illness might reinforce stigma, patient representatives emphasized that failing to acknowledge these conditions is more stigmatizing and may undermine trust. Across discussions, the most feasible and impactful intervention elements were: *1) systematic identification of psychiatric comorbidity*, and a *2) patient-centred approach* aimed at stabilizing both somatic and psychiatric symptoms early in the cancer trajectory.

At the *provider-level*, healthcare professionals described difficulties in assessing decision-making capacity, particularly when patients lacked reliable caregivers, a concern amplified by the risks associated with cancer treatment if side effects are not addressed promptly. Consequently, two intervention elements were identified as essential: 3) *identification and involvement of caregivers* and relevant healthcare professionals (e.g., GPs, psychiatric services or home-care nurses) during the first oncology visit, and *5) education of oncological healthcare professionals* in communication and supportive strategies for patients with SMDs. These components were viewed as critical to improving safety, continuity, and decision-making support during cancer treatment.

At the *system-level*, stakeholders highlighted inconsistent clinical practices and the absence of structured approaches, leading to inequal care and, in some cases, treatment delays. Fragmentation between sectors further complicated coordination and information exchange. To address these issues, stakeholders emphasized the need for a simple, acceptable, and efficient collaboration model capable of bringing all relevant professionals together to support rapid, well-informed decisions.

This led to the development of the online 4) opMDT, involving general practice, psychiatry, oncology, and other relevant specialties. Building on the existing multidisciplinary team (MDT) conferences, which are familiar collaborations among disciplines for the oncologist when deciding on treatment strategies, the opMDT was designed to be easy to implement while strengthening cross-sector collaboration at the time of cancer diagnosis. Both patients and healthcare professionals also highlighted continuity as an essential factor for enhancing treatment alliances. Therefore, 6) *continuity* with the same healthcare professionals was identified as a critical component to support patient-centered assessment and promote adherence.

Phase II: Refinement of the prototype

In the workshops, healthcare professionals found the prototype feasible to integrate into their daily workflow, and all intervention components were viewed as relevant and clinically meaningful. Patient representatives particularly emphasized the value of the patient-centred elements, including patient-centered care planning and strengthened collaboration within and across sectors. Consequently, no components were added or removed in phase II; instead, targeted refinements were made to improve practicality and implementation. These refinements included:

- Introducing electronic screening for psychiatric comorbidity.
- Adding screening for psychiatric symptoms and HRQoL through two questionnaires and three supplementary questions.
- Developing electronic guidelines and a learning module to support oncology healthcare professionals' education.
- Enhancing electronic booking notifications to strengthen continuity of care.

Phase III: The final CASEMED model

The prototype from Phase II was generally well-received. Healthcare professionals found it feasible to use in daily practice, and both clinicians and patients valued the improved continuity of care. The interdisciplinary discussions during the opMDT were viewed as particularly helpful, especially when GPs participated, as they contributed essential contextual knowledge about the patients. A nurse from the radiotherapy department elaborated:

"I think that it (the opMDT) will facilitate our work, by getting a good start and making it more appropriate from the start. Patients are so different, so it is important to get all the way around."

The GPs themself appreciated gaining a clearer understanding of oncological treatment, which improved their ability to support their patients. Patients described feeling safer knowing that multiple professionals were involved in their care planning. Of the 21 eligible participants, 13 were included. Non-participation was primarily due to patients not

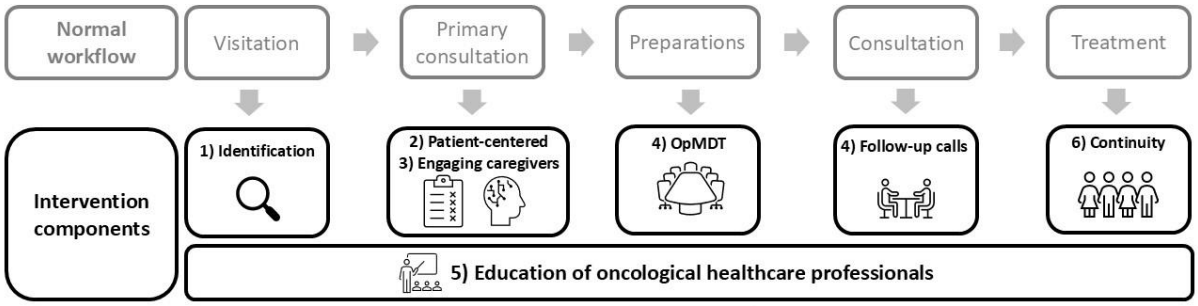
perceiving a need for additional support. GPs expressed support for the model but had difficulty attending on short notice.

Changes implemented in the final model included:

- Minimum one-week notice to the GPs before opMDT.
- Weekly scheduled opMDTs and the possibility to convene extra opMDTs if needed.
- Standardized list of discussion points sent to GPs.
- Post-opMDT summary letter sent to all GPs.

These revisions informed the development of the CASEMED Model presented in Figure 3.

Figure 3: The CASEMED Model



Intervention component	Description of the intervention component
1) Identification of psychiatric comorbidity	Systematic electronic identification of patients with pre-existing SMDs recorded in the hospital journal within the last 10 years, and enunciation the psychiatric comorbidity at the first visit at the Department of Oncology.
2) Patient-centered approach	Questionnaires to screen for psychiatric symptoms and health-related quality of life were distributed to patients at their first encounter in the Department of Oncology, along with screening for alcohol or drug abuse, preferred communication form, and three open-ended patient-centered questions about barriers and facilitators to optimal cancer care.
3) Engagement of significant caregivers	The oncologist assesses the patient's private and professional networks during the first visit.
4) Enhanced collaboration between sectors	An online opMDT conference between the oncologist from the patients' initial consult, the patient's general practitioner, and a psychiatrist, discussing the patients' resources, medication, housing conditions, nutrition, possible substance abuse, need for follow-up, and the need for referral to the psychiatric ward.
5) Education of the oncological HCPs	An online document available to HCPs, concerning supportive offers for patients with SMDs, together with an educational programme featuring a visit from a patient with SMD, focusing on lived experiences and communication.
6) Continuity among HCPs	Prioritising continuity among HCPs by highlighting the name and the HCP in the secretary's notes and the electronic booking system.

Table 8: Barriers for optimal cancer care for patients with pre-existing SMDs and corresponding intervention component

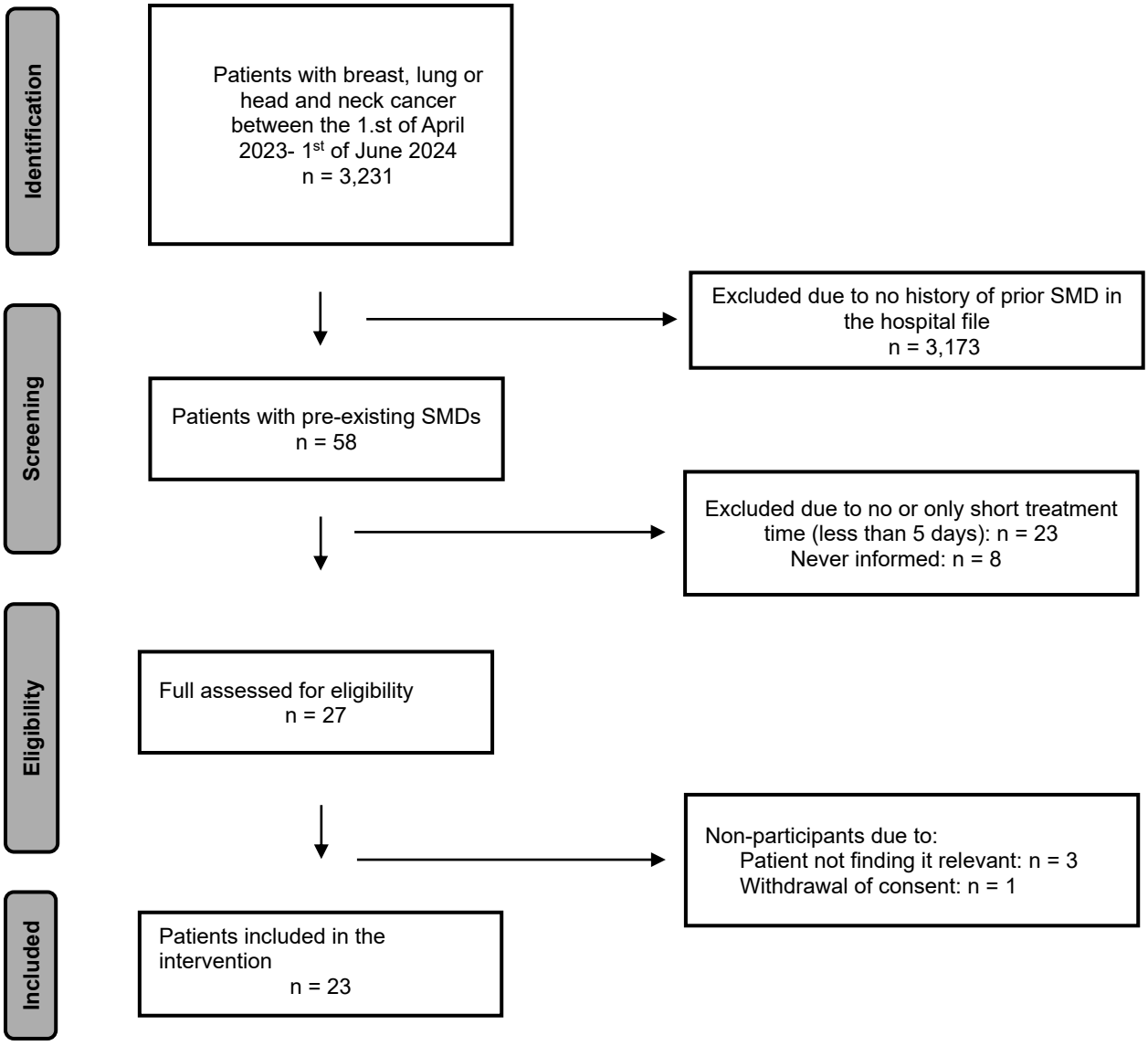
Level	Barriers	Possible intervention components			Final intervention components
		Phase I	**Phase II**	**Phase III**	
Patient level	Lack of systematic identification	Identification of psychiatric comorbidity	Addressing psychiatric comorbidity Electronic screening for SMD		**Identification of psychiatric comorbidity** Electronic screening for SMD in the journal Addressing psychiatric comorbidity at the first visit
	Unstable psychiatric symptoms	Initial screening of symptoms	Screening through SCL-92 and EORTC QLQ-C15-PAL questionnaires		**Patient-centred approach** Screening of psychiatric symptoms and quality of life through SCL-92 and EORTC QLQ-C15-PAL questionnaires
	Social isolation	Identification and engaging private and professional caregivers	Individual treatment plans instead of a fixed intervention		**Engagement of significant caregivers** Identification and engagement of caregivers **Patient-centred approach** Individual treatment plans
	Difficulties comprehending information about the diagnosis and treatment plan				
	Lack of social or economic resources				
	Neglect of self-care needs				
	Mistrust towards the healthcare system and HCPs	Continuity among HCPs	Enhanced notifications in the booking system and prioritising of the group		**Continuity among HCPs** Through notifications in the booking system and prioritising the group
	Rejection of supportive initiatives from the HCPs				
	Difficulties in noticing physical symptoms				
	Lack of compliance and treatment adherence				
	Abuse of alcohol or drugs		Screening for alcohol or drug abuse		**Patient-centred approach** Screening for alcohol or drug abuse
	Lack of use of electronic solutions to get in touch with the patient		Screening for the preferred communication form up front		**Patient-centred approach** Screen for preferred communication form up front
Provider level	Limited resources and time in the clinic to inform and coordinate treatment	Enhancing collaboration through opMDT	opMDT visitation checklist	A list of fixed subjects for GPs as preparation for opMDT Correspondence letter afterwards to the GPs*	**Enhanced collaboration between sectors** Through opMDTs, checklists, and a correspondence letter to the GPs afterwards.
	Fear of doing more harm than good				
	Confusion about who is responsible for the treatment				
	Difficulties in prioritizing cancer or mental illness				
	Lack of assessing a patient's decision-making capacity	Education of HCPs opMDT Continuity among HCPs	Learning event with patients with severe mental disorders		**Education of the oncological HCPs** Through learning events with patients with SMDs and the development of electronic guidelines **Continuity among HCPs**
	Stigma towards patients with psychiatric diseases				
	HCPs feel ill-equipped to deal with mental health.				
	Diagnostic overshadowing				
System level	Fragmentation of cancer and mental health services and a lack of coordination between sectors	Enhancing collaboration through an opMDT		opMDT with the possibility of a repeated opMDT Prolonged notice of opMDT to GPs	**Enhancing collaboration between sectors** Through opMDTs every week, and with the possibility of a repeated opMDT
	Prioritising patients with pre-existing SMDs				
	Lack of knowledge of medical interactions				
	Limited access or long waiting list to psychiatry				
	Lack of continuity among HCPs	Enhancing continuity			**Continuity among HCPs**

The whole table is available in Paper III [3]

6.4 Study IV

The inclusion process is shown in Figure 4, and in total, 23 of 27 eligible patients (85%) participated. Three non-participants cited minor or asymptomatic SMD as their reason, and one patient withdrew consent due to fear of stigma in a community setting if the hospital file at the cancer department mentioned her SMD in the electronic record.

Figure 4: Inclusion process in the feasibility study of the CASEMED Model



The included patients ranged in age from 37 to 80 years, with a median of 58 years (Interquartile range (IQR) 50-66 years). The majority were female (74%), 65% with depression, 26% with affective bipolar disorders, and 9% with schizophrenia. They were in good performance status (87% were PS 0-1), 43% lived alone, and 65% were on public support. 30% had a current, and 17% a former, misuse of alcohol or drugs. For detailed patient characteristics, see Table 9.

Table 9: Patient characteristics

Female gender, n (%)	17 (74)
Age, median (IQR)	58 (50-66)
WHO performance scale (PS), n (%)	
PS 0	11 (48)
PS 1	9 (39)
PS 2	3 (13)
Cancer type, n (%)	
Breast	11 (48)
Head and neck	6 (26)
Lung	6 (26)
Severe mental disorder, n (%)	
Moderate to severe depression	15 (65)
Affective bipolar disorder	6 (26)
Schizophrenia and other psychoses	2 (9)
Currently treated at the Department of Psychiatry n (%)	2 (9)
Lives alone, n (%)	10 (43)
On public support, n (%)	15 (65)
Uses online health applications (yes), n (%)	18 (78)
Abuse of alcohol or drugs	
Current abuse	7 (30)
Former abuse	4 (17)
No current or former abuse	12 (52)
SCL-92 global score*, median (IQR)	0.72 (0.58-1.08)
EORTC health-related-QOL measure*, mean (IQR)	59.3 (50.0-83.3)
Physical functioning, mean (IQR)	67.4 (46.7-93.3)
Emotional functioning, mean (IQR)	68.14 (41.7-91.7)
Unscheduled consultations[+], n, median (IQR)	
With an oncological physician	19, 1 (0.0-1.5)
Unscheduled telephone consultations [+], n, median (IQR)	60, 1 (0.0-3.0)
Hospital admissions[+], n, median (IQR)	13, 0 (0.0-5.0)
Hospital admission in days[+], n, median (IQR)	88, 0 (0.0-39.0)

*Five missing data because of the lack of completed questionnaires

[+]During the first three months of treatment

Overall, Study IV showed that a collaborative, patient-centered cancer care model for patients with SMD was acceptable and feasible in routine practice, see Table 10. The intervention was integrated smoothly into clinical workflows and achieved high patient participation (85%) with minimal burden for patients and healthcare professionals. An oncologist elaborated.

”*It (using the intervention) also means that we start off better, both we, and I think the patient too, because it opens up the conversation, and we set things up early. (…) Because otherwise, they aren't always so receptive to our good ideas. I mean, when things have gone sideways*”.

The structured focus on psychiatric symptoms, combined with educational elements and incorporation of patient perspectives, appeared to reduce stigma. The opMDT strengthened cross-sector collaboration and led to clinical actions in 87% of cases. Clinicians reported that the opMDT enhanced decision-making and coordination of supportive measures.

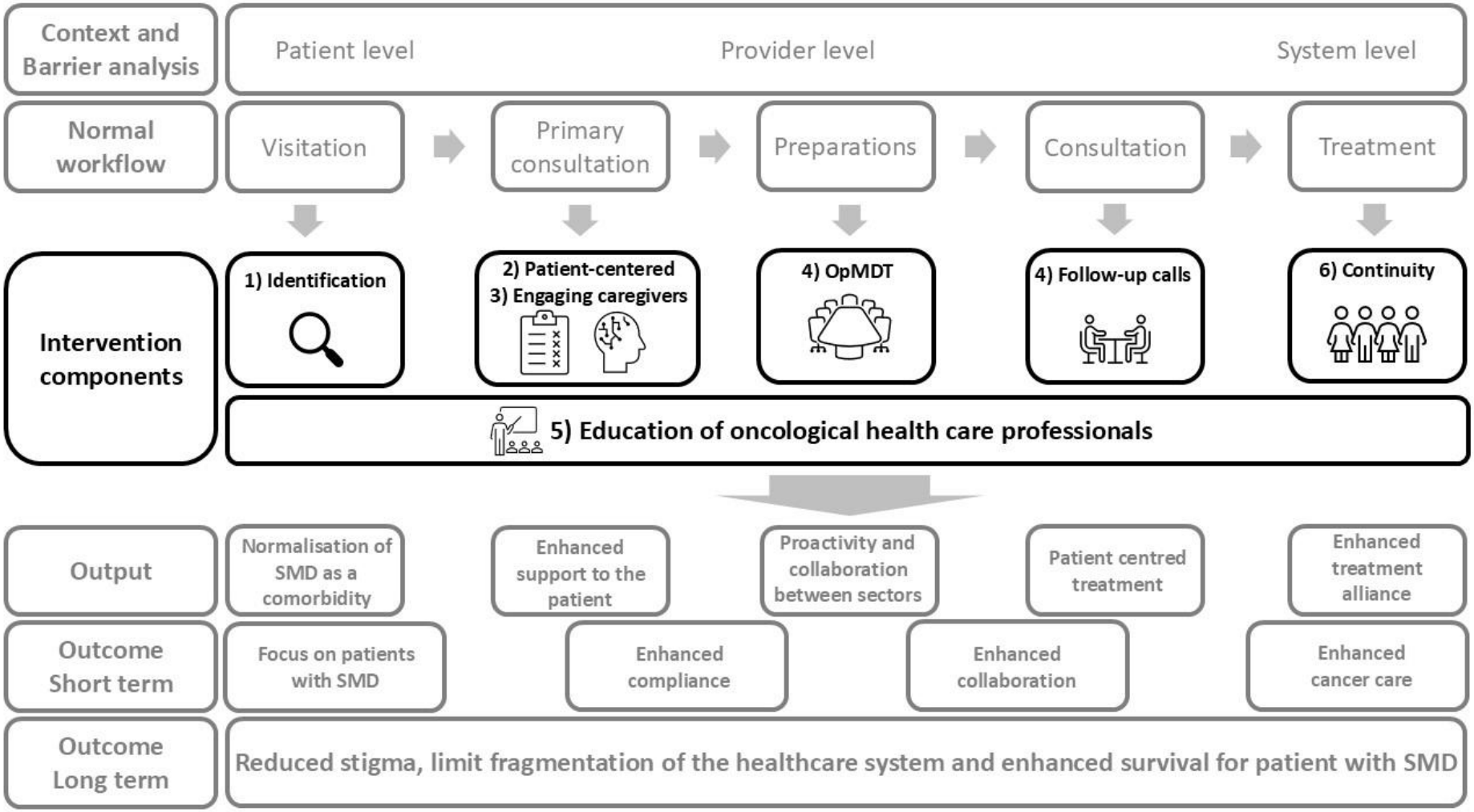
Despite a high indication of acceptability and feasibility several challenges towards successful implementation were identified. Identifying the right target population, overly lengthy questionnaires, maintaining continuity among oncological healthcare professionals and ensuring consistent GP participation in opMDTs proved challenging. Despite these limitations, the intervention facilitated a multidisciplinary and patient-centered approach and enhanced the healthcare professionals' decision-making.

Table 10: Combined analysis of the CASEMED Model feasibility study

Quantitative analysis	**Integrated analysis**	**Qualitative analysis**
Participation in intervention of eligible patients asked: **23/27** (85%) Completed questionnaires: **18/23** (78%) Number of opMDTs: **23/23** (100%) <u>Participation in opMDT:</u> Known oncologist present: **12/23** (52%) GP present: **4/23** (17%) GP intended to participate: **14/23** (61%) Psychiatrist present: **23/23** (100%) Palliative specialist present: **7/11** (64%)	**Delivery** The main parts of the intervention were delivered as intended. The participation percentage were high and non-participation were mainly due to patients not feeling the need for extra support. The participation of GPs at the opMDT were low, the GPs expressed that they found it relevant to participate but were prevented due to structural barriers.	• Patients were easily enrolled. • Non-participation was primarily due to "no need" by patients or oncologists. • Absences due to leave and conferences further reduced oncologists' involvement in opMDTs. • GP participation was hindered by understaffing, acute care duties, and leave. • Some HCPS where in doubt if the inclusion criteria accurately captured the intended target population.
	Acceptability Overall, the intervention was perceived acceptable for both patients and HCPs. The different intervention components fitted well into the daily clinic.	• The patients found the intervention acceptable and meaningful. • The HCPs found the intervention fitted well into the clinical workflow.
Time spent on each opMDT in minutes: Median (IQR): **12** (8-15) Time spent on each follow-up call after opMDT in minutes: Median (IQR): **11** (8-14)	**Burden** The form of the opMDT were acceptable and feasible, and the burden for the HCPs to participate in the intervention were minimal. Some GPs found it hard to find time to participate and the lack of future remuneration were a barrier for implementation. Some patients argued that the questionnaires were too long.	• All HCPs found the timing and format of the opMDT appropriate. • No HCPs reported difficulties preparing for the opMDT. • Some GPs reported difficulty integrating the opMDT into their clinical schedule. • GPs noted a lack of future remuneration under current Danish welfare agreements.
	Negative consequences Only minor negative unintended consequences were detected.	• Oncology nurses felt excluded from opMDTs but found documentation (notes and checklists) useful.

The psychiatric diagnosis was mentioned in the electronic journal after the opMDT: **16/23** (70%)	**Mechanisms of change** **1) Identification of psychiatric comorbidity** The identification of psychiatric comorbidity and its enunciation were possible and found meaningful for both patients and HCPs, as it helped to reduce stigma towards patients with pre-existing SMDs.	• Patients found it meaningful when HCPs acknowledged their psychiatric comorbidity, and positively received when they raised the comorbidity themselves • HCPs felt the intervention legitimized discussing psychiatric comorbidity.
Patients receiving the planned oncological treatment: **19/23** (82%) Patients treated after guidelines**: 23/23** (100%)	**2) Patient-centered approach** In general, the patients received the planned treatment and found that their needs and personal preferences were considered during their cancer treatment.	• Patients felt that HCPs generally considered their personal preferences. Some patients still experienced the system as very rigid at times.
	3) Engagement of significant caregivers The opMDT helped integrate caregivers and other supportive measures into the cancer trajectory. Professional caregiver support was crucial to private caregivers, allowing them to focus on emotional support for patients.	• The patients found the caregivers well integrated into the cancer treatment • HCPs elaborated that opMDT initiated focus on supportive measures. • The patients were grateful for the professional support, which they felt eased the work of their caregivers.
<u>opMDT clinical actions:</u> Number of patients receiving any intervention **20/23** (87%) Adding a resource person: **3/23** (13%) Chancing in medicine: **8/23** (35%) Extra appointments: **13/23** (57%) Referred to the psychiatry: **3/23** (13%)	**4) Enhanced collaboration between sectors** The opMDT was found helpful by all HCPs, especially when the GPs attended. It made patients feel safer and made treatment decisions easier for oncologists. Medical adjustments and extra appointments were the most common clinical actions.	• GPs valued the collaboration and input from specialists; some noted reduced workload with maintained care quality. • Hospital HCPs found interdisciplinary input reassuring and valued GP attendance for deeper patient insight. • Patients in contact with their GP found them well-informed.
	5) Education of the oncological HCPs The education program was easily implemented into the clinical workflow. It lowered stigma and inspired the nurses to use distraction techniques and environmental adjustments.	• The education program enhanced the HCPs' understanding of challenges faced by patients with pre-existing SMDs. • The program contributed to reduced stigma and improved communication.
Seen by the same HCPs in minimum 50% of the scheduled consultations: Physicians: **10/22**, (45%) Nurses: **11/22** (50%) Seen by the same HCP in > 50% of the scheduled consultations Physicians: **6/22**, (27%) Nurses: **9/22** (41%)	**6) Continuity among HCPs** The patients and the HCPs found continuity crucial as it enhanced the depth of the relationship, the compliance, and made treatment decisions easier for the HCPs. The criteria for continuity were not fulfilled, but were enhanced when consultants saw the patients.	• Patients valued continuity, as it enhanced their sense of safety and reduced the need to explain their situation repeatedly. • Even when continuity was lacking, patients generally found new HCPs to be kind and engaging. • HCPs noted that continuity supported decision-making.

Figure 5: The CASEMED Model in relation to context



7 Discussion of Methods

A significant strength of this Dissertation is its comprehensive, multimethod design. Cancer-specific mortality was examined through a systematic meta-analysis, while health-related quality of life and psychiatric symptom burden were investigated using a matched case-control study. In addition, the Dissertation includes the systematic development of interventions with extensive involvement of multiple stakeholders, followed by feasibility testing to support future implementation. Together, these complementary methodological approaches provide a broad and nuanced understanding of cancer trajectories among patients with SMDs and strengthen the validity and clinical relevance of the findings.

7.1 Study I

A significant strength of Study I is its explicit focus on cancer-specific mortality among patients with pre-existing SMDs, addressing a critical gap in the literature that has previously been dominated mainly by analysis on all-cause mortality. By including only studies in which SMDs were diagnosed before cancer onset, the risk of reverse causality was minimized, strengthening the validity of the findings. Subgroup analyses by psychiatric and cancer diagnosis further enabled a nuanced assessment of disparities.

Key limitations include substantial heterogeneity across studies in definitions of SMDs, cancer types investigated, study designs, and covariate adjustment. Differences in healthcare systems and diagnostic practices across regions may also limit comparability across studies, as residual confounding is likely, given inconsistent reporting of information on psychiatric treatment, cancer treatment, and time since psychiatric diagnosis. In addition, some subgroup analyses were based on relatively few studies, which could also reflect unknown study-specific factors. Collectively, these limitations underscore the need for future studies using standardized definitions of SMDs and detailed clinical data, and longitudinal designs.

7.2 Study II

A key strength of Study II is the close matching of cases and controls by sex, age, cancer type, and treatment intent, which enhanced comparability between groups and reduced confounding from major clinical determinants. In addition, the use of validated and widely applied instruments further strengthens the internal validity of the group comparisons.

The study also has limitations. The sample size was modest, and although matching reduced confounding related to age and cancer characteristics, residual differences persisted in socioeconomic and health-related factors, including social support, educational level, and

tobacco and alcohol use. Furthermore, symptom assessment relied on patient-reported outcomes, which may be influenced by psychiatric symptom expression and level of insight into illness.

7.3 Study III

A primary strength of Study III lies in its methodological rigor, particularly in the use of the internationally recognized and highly validated MRC framework for developing complex interventions. The method included a multimethod, participatory design approach that combined barrier analyses, individual interviews, group discussions, and co-creation workshops involving patients, patient representatives, and healthcare professionals. The iterative co-production process enabled continuous refinement of the intervention. It facilitated early identification of practical and organizational barriers, thereby strengthening both feasibility and long-term sustainability of the CASEMED Model. Inclusion of stakeholders across multiple healthcare sectors provided complementary perspectives and improved understanding of existing workflows, resources, and cross-sectoral coordination capacities. Addressing implementation challenges during the development phase further enhanced the model's clinical relevance.

Thus, several limitations must be acknowledged. The pilot sample size was small, which limited generalizability, and healthcare professionals were more heavily represented than patients in the early development phases. In addition, the model was tested in only two oncology clinics, limiting broader insights across institutional contexts. These factors underscore the need for larger, multi-site evaluations in future studies.

7.4 Study IV

Overall, the model provides robust evidence that well-designed complex interventions can meaningfully enhance cancer care for patients with severe mental disorders. When it comes to limitations, the patient sample size was modest, and the observed prevalence of pre-existing SMD was lower than anticipated, likely reflecting the selection of patients with relatively good performance status who were eligible for active cancer treatment. Consequently, the most vulnerable persons, those who never reached oncology services or received only short-term palliative care, were not represented. The intervention was tested in only two oncology clinics within a single Danish university hospital, which may limit generalizability to other settings. In addition, certain logistical elements, including coordination of the opMDTs, were handled by the research team and were not thoroughly evaluated under routine clinical conditions.

8 Discussion of results

8.1 Main findings

This Dissertation examined cancer trajectories among patients with SMDs. It addressed critical gaps in understanding how psychiatric comorbidity influences mortality, health-related quality of life, symptom burden, and the need for tailored supportive cancer care. Patients with SMDs consistently entered cancer care in a more vulnerable state compared to patients without SMDs, reporting significantly poorer HRQoL and higher psychiatric symptom burden. As to that, they also have a considerably higher cancer-specific mortality compared to patients without SMDs. These findings reinforce a growing body of knowledge showing that cancer patients with SMDs experience complex, multifactorial barriers throughout the cancer pathway, from diagnosis and treatment initiation to survivorship and end-of-life care. These inequalities can be addressed by patient-centered, multidisciplinary, collaborative care models, which Paper IV demonstrated to be feasible in a real-world clinical setting.

8.2 Patients with cancer and SMDs

The patients included in Study II and IV were younger than the general Danish cancer population, with a median age of 59 years (IQR 51-68) [43]. Patients with pre-existing SMDs differed markedly from controls in several health-related and socioeconomic characteristics, including a higher prevalence of current and former misuse of alcohol, drugs, and tobacco compared to the control group [2,4]. All of which are well-established factors that adversely affect both cancer incidence and survival [43]. In addition, patients with SMDs were less likely to have higher education, less likely to use digital health applications, which are often used in an illness trajectory in Denmark, and more frequently received disability pension [2].

Together with reduced social support, these social and clinical vulnerabilities constitute substantial challenges in navigating cancer care and are likely to contribute to inequalities in outcomes [26,73]. Patients with SMDs were also less likely to designate a partner as next of kin and more often relied on friends, colleagues, or adult children [2]. The absence of a cohabitating partner may complicate care coordination, shared decision-making, and symptom monitoring [74]. Social isolation itself has also been associated with increased cancer mortality in a study by Kroenke CH et al., likely reflecting reduced access to practical and emotional support during treatment [75]. Conversely, patients with SMDs more frequently reported stable relationships with GP, indicating that primary care serves as a key anchor for continuity across sectors [2,76].

All this demonstrates that patients with SMDs live with a cumulative complexity, in which mental illness is closely intertwined with social adversity, physical comorbidity, impaired

treatment capacity, and fragmented care systems. As complexity increases, patients' ability to manage treatment demands tends to decline [77]. This aligns with the multilevel model proposed by Grassi et al., conceptualizing inequalities across patient, healthcare, and societal levels [71]. Standardized cancer pathways, therefore, often fail to meet the needs of patients with mental illness [78], underscoring the necessity of integrated, patient-centered, and context-sensitive care aligned with patients' capacity.

The findings of this Dissertation thereby underscore the necessity for integrated cancer care interventions, in which the level of support is tailored to the patient's individual capacity and life circumstances. This aligns with the concept of contextualizing care described by Weiner and Schwartz, which emphasizes the systematic identification of contextual factors, such as financial strain, limited social resources, and challenges in self-care, and their active integration into clinical decision-making through targeted communication strategies [78]. Such an approach allows clinicians to adapt treatment plans to real-world patient circumstances, thereby improving equity in care delivery [78].

8.3 Mortality

In Study I, patients with cancer and SMDs had a 1.37 (95% 1.30-1.44) higher relative risk of cancer-specific mortality than patients without SMDs. The most significant excess risk was observed among patients with schizophrenia or other psychotic disorders, where a relative mortality risk of 1.47 (95% Cl 1.33-1.63) was seen, but even patients with affective disorders had an elevated relative mortality risk at 1.25 (CL 95% 1.18-1.32) [1]. These findings are consistent with other studies [79], and mechanisms contributing to this high mortality are likely to include reduced cancer screening participation, advanced stage at diagnosis, comorbidity, and a lower likelihood of receiving guideline-based cancer treatment [13,14,15,16,17,18,19,20].

Another key finding was that all-cause mortality exceeded cancer-specific mortality, particularly in population-based cohorts. One explanation could be that all-cause mortality includes deaths from both accidental and intentional injuries, which are overrepresented among persons with mental illness [80]. In addition, the elevated all-cause mortality also likely reflects the substantial burden of somatic comorbidity in people with SMD, who have a higher prevalence of smoking, obesity, and metabolic disturbances [8].

The high all-cause mortality was further supported by Study II, in which patients with SMDs demonstrated a markedly higher prevalence of current and former smoking as well as alcohol and substance use [2]. These factors are strongly associated with cardiovascular disease and are also well-established risk factors for the development of cancer [8,72].

When looking at mortality effect sizes and time from SMD diagnosis until cancer diagnosis in Study I, the highest relative mortality risk was found among patients whose SMDs had been diagnosed within 0–6 years before the cancer diagnosis, suggesting a time-dependent

impact of mental illness on cancer outcomes [1]. The time-dependent finding aligns with existing knowledge that mental illness may remit over time and, consequently, may exert a diminishing effect on specific barriers to optimal cancer care. These results further underscore the importance of a patient-centered approach, as some patients may be profoundly affected by active SMD at the time of cancer diagnosis. In contrast, others may have limited or no functional impairment related to their prior psychiatric condition as shown in Study III and IV [3,4].

8.4 Health-related quality of life and psychiatric symptom burden

To our knowledge, Study II is the first to directly compare HRQoL and psychiatric symptom burden between patients with cancer and SMDs and matched controls. The findings reinforce existing evidence that patients with SMDs face substantial structural and psychosocial disadvantages that shape their cancer trajectory and outcomes [26,27]. In Study II, patients with SMDs reported significantly poorer HRQoL across physical and emotional functional domains and higher symptom burden, particularly when it came to fatigue, pain, dyspnoea, and insomnia. This indicated a generally more compromised state when entering cancer treatment [2]. Pre-treatment somatic symptom burden is strongly associated with poorer tolerance of cancer treatment, which may increase the risk of early discontinuation and lower survival [81].

As expected, psychiatric symptom burden was markedly higher in the SMD group, not only for depression and anxiety, but with particularly elevated scores in phobic anxiety, hostility, and interpersonal sensitivity, domains that may negatively influence communication, adherence, and help-seeking behaviour. The nearly threefold higher Global Severity Index highlights profound psychological distress at treatment onset and supports the need for routine, structured psychiatric assessments integrated systematically into oncology care. Significantly, the differences in HRQoL between patients with and without SMDs exceeded the threshold for clinical relevance (>10 points) across several domains [82].

The EORTC-QLQ-C15-PAL and European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core-30 (EORTC- QLQ-C30) instruments are considered sufficiently comparable for use in this context; however, it remains unclear whether the observed differences in symptom burden reflect a difference in impact of a newly diagnosed cancer on the two groups, or represent an underlying, general difference between the groups. Interestingly, patients with newly diagnosed cancer in the control group in Study II scored higher on the physical and emotional functioning scales of the EORTC QLQ C30 than the Danish reference population, and only slightly lower on global health status [2,70]. A similar pattern was observed for psychiatric symptoms, as the control group here reported a lower symptom burden on the SCL-92 scale than the general Danish population [71]. The reason for this finding remains unclear, but it is most likely related to the relatively small sample size. It may also reflect differences in case definitions, as patients with SMDs were

included in the population-based reference data but explicitly excluded from the control group in Study II. Another possible explanation is the relatively low median age of the participants in Study II, as age-stratified analyses in the Danish reference population have shown lower scores among younger persons [70], although a higher symptom burden would still be expected among patients with newly diagnosed cancer than in the reference population [83].

8.3 The CASEMED Model

Despite growing international recognition that psychosocial care is fundamental to high-quality cancer treatment and increasing awareness of the inequities faced by patients with SMDs, evidence-based healthcare interventions remain limited, particularly in European healthcare systems [3,65]. Cancer treatment depends on timely delivery, high treatment adherence, and proactive symptom management. Yet, patients with SMDs are at increased risk of delayed initiation, missed appointments, and treatment discontinuation due to cognitive burden, psychiatric symptoms, and limited social support [27,73,84]. At the same time, oncology teams often expressed a need for more time to create effective, sustainable treatment plans and lack structured guidance and resources for integrating psychiatric and psychosocial care into routine practice [26,32,33].

To address this gap, the CASEMED supportive cancer care model was developed in Denmark as the first systematically developed, stakeholder-informed intervention in Europe targeting cancer trajectories, patients with cancer, and SMDs. The model was co-produced with patients, oncologists, psychiatric professionals, nurses, and GPs and comprises six core components: (1) early identification of psychiatric comorbidity, (2) systematic symptom screening, (3) engagement of significant caregivers, (4) enhanced continuity, (5) education of oncology healthcare professionals, and (6) cross-sector and multi-disciplinary collaboration through an online opMDT [4].

The model was shown to align well with existing clinical workflows and was perceived as meaningful by both patients and healthcare professionals. Feasibility testing demonstrated high acceptability, successful integration into daily practice, and strong support for addressing psychiatric issues openly [4]. While effectiveness was not formally evaluated, the mechanisms underpinning the model, patient-centeredness, continuity, and structured cross-sector collaboration, are well established as key drivers of high-quality cancer care [37,73,74,84].

A systematic approach to patient-centeredness

Patients with SMDs are often at risk of being primarily defined by their psychiatric diagnosis rather than being recognized as whole persons with complex somatic needs [26,28]. When this occurs, physical symptoms may be under-recognized or misattributed to mental illness, potentially leading to delayed diagnosis, insufficient symptom management, or

inappropriate limitation of treatment options. Such diagnostic overshadowing causes inequity in care and may directly compromise clinical outcomes. Open, explicit, and respectful inquiry into patients' psychiatric history is therefore essential to establish a trusting patient–clinician relationship and to ensure comprehensive, patient-centered care [4]. Together with the educational components and the systematic inclusion of the patient perspective, the CASEMED Model appeared to reduce stigma by addressing SMDs as any other comorbidity and to improve mutual understanding between patients and healthcare professionals [4].

Although previous studies report divergent trajectories, some describing worsening psychiatric symptoms during cancer treatment, while others note improved mental resilience and even symptom reduction as patients mobilize coping resources. Study II demonstrates that patients with SMDs, overall, enter cancer treatment with a substantial burden of impaired HRQoL and elevated psychiatric symptom burden [2,85]. This finding underscores the importance of early and systematic identification of symptom burden to enable timely supportive interventions. Many healthcare professionals experience treatment dilemmas when managing patients with cancer and SMDs, partly due to concerns that oncological treatment may exacerbate psychiatric symptoms, a fear also shared by the patients [28,32]. These complexities highlight the need to optimize symptom management and ensure balanced, patient-centered care and continuity throughout the cancer trajectory [32].

Across the cancer trajectory, strong and supportive relationships with both HCPs and caregivers are essential for patients with SMDs [23,32,85]. Due to mental health challenges, many patients struggle to advocate for themselves and may hesitate to disclose their psychiatric illness to oncology clinicians [23,32]. While willingness to discuss mental health varies, patients value being asked respectfully and with permission [23,32,85]. Study II also demonstrated that patients with SMDs had markedly different social networks than controls, with greater social isolation and fewer stable caregivers. As social isolation complicates practical support, early assessment of both private and professional care networks is crucial to ensure adequate support during cancer treatment [3,4].

Enhancing cancer care through collaboration and continuity

Fragmentation and siloed organization within healthcare systems remain significant barriers to coherent care for patients with SMDs [26]. Cancer care and mental health services often operate in parallel rather than in coordination, leading to complex transitions, unclarified responsibilities, and gaps in care, particularly at discharge or during treatment changes [26]. Patients with SMDs frequently present with cumulative complexity across psychiatric, physical, and social domains, a level of need that standardized cancer care pathways are poorly equipped to address [73]. The online opMDT directly addresses silo formation by bringing oncologists, psychiatrists, GPs, and supportive services together [3,4]. The healthcare professionals in Study III and IV elaborated that the opMDT structure supported

shared decision-making, reduced treatment dilemmas, and strengthened clinical confidence when managing concurrent psychiatric and oncological conditions [3,4].

Continuity of care is another central element of high-quality cancer treatment and is valued by both patients and healthcare professionals [28,32]. Studies III and IV further demonstrated that continuity is essential for patients with SMDs, which is consistent with existing evidence showing that continuity improves patients' sense of safety and reduces mortality [3,4,76]. In the CASEMED Model, continuity was addressed through several mechanisms and different types of continuity [3,4,86,87]. *Relational continuity* aimed to foster trust and psychological safety for patients throughout the cancer trajectory, enabling patients to discuss mental health concerns more openly [3,4,28]. *Informational continuity* was supported through the opMDT, which integrates the patient's psychiatric history and insights from general practitioners [3,4]. *Management continuity* was likewise strengthened through opMDT with care coordination across sectors [3, 4,86,87]. However, achieving complete relational continuity remained difficult due to complex treatment pathways, structural barriers, and reliance on standardized cancer care structures [4,26]. These barriers highlight the system-level challenges in delivering flexible, patient-centered care to patients with SMDs, despite the well-documented survival benefits associated with relational continuity [4,76].

Comparison to other healthcare interventions

As noted earlier, targeted healthcare interventions have demonstrated effectiveness in improving outcomes for patients with SMDs, including increased participation in cancer screening programs [39,40]. Building on this evidence, it is essential to adapt proven strategies to the specific healthcare context in which they are implemented.

The CASEMED Model is closely informed by the BRIDGE intervention, adapted to the Danish healthcare system. The feasibility and acceptability of the CASEMED Model among both patients and healthcare professionals were consistent with findings from the American BRIDGE intervention [4,37,38]. Collaborative care principles inspire BRIDGE, which comprises five core components that are also reflected in the CASEMED Model: (1) identification of patients with SMDs, (2) assessment of psychiatric symptoms and resources, (3) interdisciplinary team meetings, (4) patient-centered care and continuity, and (5) involvement of caregivers or community navigators [37,88]. While BRIDGE applies a structured, case-manager-led approach with regular assessments, the more flexible, adaptive design of CASEMED was perceived as feasible and supportive of patient-centered care, with low perceived burden, which contributes to the interventions' sustainability [3,4]. The overall value of integrated cancer care interventions is further supported by the preliminary results from the BRIDGE randomized trial, which indicate fewer cancer care disruptions and significant improvements in psychiatric symptom severity and anxiety among the participants. [37,38]. Before any conclusions can be drawn about whether similar

effects apply to the CASEMED Model, the intervention needs to be evaluated in a broader context.

8.4 Sustainability of the CASEMED Model

Ensuring sustainability is a fundamental requirement in the development of healthcare interventions, particularly for vulnerable populations such as patients with cancer and SMDs. Interventions that demonstrate feasibility or short-term benefit in pilot settings have limited value if they cannot be embedded into routine practice and maintained over time. Sustainability entails not only continued delivery of intervention components after project funding but also preservation of patient benefits and the capacity for adaptation to changing organizational contexts. Shelton et al. emphasize that sustainability includes ongoing use of core intervention elements, maintenance of behavioural change, and dynamic adaptation within healthcare systems [89]. Likewise, Shelton et al. stress that sustainability must be considered from the earliest phases of intervention development rather than as a post hoc concern [89]. In the CASEMED intervention, sustainability was prioritized through alignment with existing clinical workflows, reliance on established collaboration formats (e.g., the MDT structure), and shared responsibility across sectors, reflecting that meaningful system improvement does not necessarily require resource-intensive interventions, but instead structured collaboration and recognition of patients' lived experiences [4].

Two key components were discussed during the development of the CASEMED Model, but were not implemented. The first was the inclusion of a designated case manager, as in the BRIDGE intervention [37]. Although both patients and healthcare professionals emphasized the need for continuity, and that nurse navigation in other studies has been shown to improve psychological outcomes, patient knowledge, and treatment adherence in other vulnerable cancer populations [90,91], this role was excluded due to concerns regarding cost and limited sustainability and scalability within the Danish healthcare system. Notably, Study IV also demonstrated that even modest structural adaptations, such as clear points of contact, proactive communication, and enhanced continuity in oncology consultations, can substantially improve patient security and support more stable cancer trajectories [4].

The second issue of discussions before the study concerned possible patient participation in the opMDT. While patient participation could potentially strengthen patient-centeredness and transparency, healthcare professionals expressed several concerns. In particular, they feared that the presence of patients might restrict open professional discussion, as opMDTs often involve navigation of clinical uncertainty, differing professional perspectives, and preliminary deliberations about sensitive psychiatric and oncological issues. The psychiatrists especially emphasized that some of these discussions could be distressing for patients and of limited direct benefit to the patients. The patient’s representatives in the workshop supported this conclusion. Furthermore, it was considered unrealistic to conduct respectful, meaningful, patient-inclusive discussions within the short 12-minute time frame allocated for each opMDT [4]. Including patients would likely require substantially more time and

resources, thereby reducing the model's feasibility and sustainability. Given that the GP participation was already challenged by short notice and time constraints, adding patient participation was considered an additional structural barrier. To preserve both professional dialogue, patient protection, and long-term sustainability, patient involvement in the opMDTs was therefore not implemented [3,4].

At the same time, attention to potential unintended consequences is essential. Bonell et al.'s concept of "dark logic" highlights how well-intended public health interventions may inadvertently produce harm if contextual mechanisms are overlooked [65]. This principle guided the cautious design of the CASEMED Model, particularly in avoiding overburdening patients and clinicians or introducing parallel systems that might undermine existing care structures [65].

8.5 Barriers towards full implementation of the CASEMED Model

Despite thorough stakeholder involvement, several barriers to full implementation were identified. First, the inclusion criteria did not consistently capture the intended target population. Some patients with limited psychiatric burden were included, while socially marginalized patients with substantial needs but no formally documented psychiatric diagnosis were excluded [4]. Clinicians noted that the latter group might have benefited most from the intervention, suggesting that future models may need to allow extra clinician-driven inclusion based on clinical judgment and social vulnerability [4].

Second, although the questionnaires were acceptable to most patients, some found them burdensome due to the length, and clinicians perceived limited clinical utility of the full SCL-92 [53]. Future implementation may benefit from refining the screening instruments, for example, by using the relevant subscales of the SCL-92, e.g., SCL-28, which assess interpersonal sensitivity, neurasthenia, anxiety, and depression, domains that showed a high symptom burden in the present study [4,92].

Thirdly, relational continuity of care in the oncology setting remained difficult to secure, and despite being a core component of the model, it was not consistently achievable within standardized oncology workflows. However, continuity improved substantially when the patient was assigned to a consultant at the Department of Oncology [4].

Fourth, GP participation in the opMDTs was limited due to structural and logistical barriers. To address this, a follow-up coordination meeting was proposed 2-4 weeks after the initial opMDT to strengthen cross-sector communication [4].

Despite these barriers, the intervention promoted multidisciplinary, patient-centered care and improved clinical decision-making. Future large-scale implementation will require refined targeting, sustainable continuity strategies, and strengthened institutional support for cross-sector collaboration to ensure long-term sustainability and impact.

9 Perspectives

9.1 Clinical perspectives

The increased cancer-specific mortality observed in Study I and the pronounced disparities in HRQoL and psychiatric symptom burden at the time of entering cancer treatment in Study II underscore a clear need for structured supportive cancer care models tailored to patients with SMDs. Early identification of patients with SMDs is essential, as timely stratification enables the provision of targeted supportive interventions, which have been shown to reduce cancer care disruptions and improve psychiatric symptom severity and anxiety [76]. Proactive assessment and management of symptom burden, particularly fatigue, sleep disturbance, and pain, are likely to mitigate declines in HRQoL and treatment tolerance, especially in patients with concurrent psychiatric conditions [2]. In line with recent recommendations by Grassi et al., these findings highlight the importance of increasing clinical awareness and providing clear guidance on how to optimally support patients with SMDs throughout the cancer trajectory [73].

Findings from Studies III and IV indicate that the CASEMED Model can be implemented in routine clinical practice with only minor refinements and without substantial additional resource requirements [3,4]. Preparation time for the opMDT was limited, and most intervention components were easily integrated into existing workflows [3,4]. However, a prosperous and sustainable implementation requires prioritizing staff education, continuity of care, and formal remuneration for GPs' participation in opMDTs [4].

Furthermore, responsibilities initially held by the research project leader must be transferred to routine clinical staff [4]. Prioritizing education and actively reducing stigma are key leadership responsibilities in healthcare. Interventions such as this require clear managerial support and an explicit organizational commitment that inequalities in health care for patients with SMDs are unacceptable. This includes recognizing that patients with SMDs often need more flexible and differentiated approaches than standard care to achieve equitable access to effective cancer treatment and support. As the intervention is not tailored to a specific cancer diagnosis, cancer treatment, or mental illness, the model appears transferable to other clinical settings when context-sensitive adaptation is taken into consideration [93]. Given that patients with SMDs often present with multiple chronic comorbidities, the model may also be adapted to support this population during hospital admissions for conditions beyond oncology, thereby addressing broader psychiatric and social care needs, of course, with appropriate contextual adaptation.

9.2 Research perspectives

The present findings highlight several important directions for future research. A significant challenge in the current literature is the heterogeneity in definitions of SMD, as shown in Study I; this hampers comparisons across studies and limits the cumulative knowledge base. Future studies should apply clear, standardized diagnostic definitions to improve comparability and external validity. Ethical inclusion of patients with SMDs in cancer research is also essential, as their historical underrepresentation both limits evidence-based care and perpetuates stigma. Importantly, participation in research and systematic identification of psychiatric comorbidity have been shown to reduce stigma and improve clinical recognition of mental illness [4].

The present findings underscore the need for future randomized and feasibility studies to determine whether systematic psychiatric and psychosocial screening at cancer diagnosis, within integrated oncology-psychiatry-primary care models, improves clinical and patient-reported outcomes [46]. In parallel, longitudinal studies are warranted to clarify how psychiatric symptoms and HRQoL develop across the entire cancer trajectory, including survivorship and end-of-life care. While randomized controlled trials are essential to establish causal effects, feasibility and implementation studies remain equally important to ensure real-world applicability. In this context, the CASEMED Model offers a strong foundation for future large-scale evaluations of effectiveness and implementation across diverse clinical settings.

10 References

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11 Paper I-IV

Acta Psychiatrica Scandinavica

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Acta Psychiatrica Scandinavica

SYSTEMATIC REVIEW

The Impact of Preexisting Severe Mental Disorders on Cancer Mortality: A Systematic Review and Meta-Analysis

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ABSTRACT

Purpose: People with severe mental disorders (SMD) face a significantly lower life expectancy compared to people without SMD. Studies have reported divergent results concerning cancer-specific mortality. Therefore this systematic review and meta-analysis aimed to assess the cancer-specific mortality for people with preexisting SMD.

Methods: A comprehensive literature search was conducted across PubMed, Embase, Psycinfo, and Scopus for studies published since January 2003. Inclusion criteria targeted adult cancer patients with a known SMD diagnosis prior to their cancer diagnosis. Two authors independently screened records based on predefined criteria, resolving discrepancies through discussion. Data extraction and quality assessment were conducted using the Newcastle-Ottawa Scale. A random effects model was employed to conduct the analysis, with heterogeneity across the studies quantified using the I^2 statistic.

Results: The search yielded 4736 records, of which 25 studies met the eligibility criteria. Findings consistently indicated higher cancer-specific mortality among patients with preexisting SMD, with a 1.37 (95% CI: 1.30–1.44) higher relative risk of cancer-specific mortality for patients with preexisting SMD. The highest mortality rates were found among patients with schizophrenia and other psychosis with a relative cancer mortality risk at 1.47 (95% CI: 1.33–1.63).

Conclusion: This review and meta-analysis highlighted a concerning higher relative cancer-specific mortality risk for patients with preexisting SMD. These findings underscore the need for integrated healthcare approaches addressing both cancer treatment and mental health to improve outcomes for this vulnerable population.

1 | Introduction

People diagnosed with severe mental disorders (SMD) are reported to have shorter life expectancy than the general population with reported gaps up to 15 and 20 years compared to people without SMD [1–3]. SMD are, in this study, defined as moderate to severe depression, bipolar affective disorders, schizophrenia and other psychosis in line with the WHO ICD-10 definition [1]. The reason for the shorter life expectancy is multifactorial but the majority of years of life lost in people with SMD relate to poor physical health with cardiometabolic diseases being the leading cause [4, 5]. Smoking,

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Summary

Summations

- People with preexisting severe mental disorders faces a higher cancer specific mortality than people without.
- The highest mortality is found among patients with schizophrenia and other psychosis.

Limitations

- The heterogeneity of the included studies, including inconsistencies in the definition of SMD, an uneven distribution of cancer types, and substantial variation in the covariates used for adjustments are all limitations to the comparability between the included studies.

excessive alcohol consumption, and obesity among others are more prevalent across a broad range of mental disorders and represent established risk factors for cancer development [4]. However, when directing attention to cancer-specific mortality for patients with preexisting SMD, notable inconsistencies are emerging across the existing studies [5–8]. This may suggest that the risk of cancer mortality associated with SMD might vary concerning sex, competing risk factors, cancer or study types.

2 | Aims of the Study

Thus, we hypothesize that patients with preexisting SMD have increased cancer-specific mortality compared to patients without SMD, and the aim of this systematic review and meta-analysis is to investigate the evidence on the cancer-specific mortality among patients with preexisting SMD compared to those without.

3 | Material and Methods

3.1 | Search Strategy and Selection Criteria

The systematic review and meta-analysis were performed according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines [9] and were reported to the International Prospective Register of Systematic Reviews (PROSPERO) with ID: CRD42023475227 [10]. A comprehensive search in the PubMed, Embase, Psycinfo and Scopus databases was conducted to identify relevant articles published from January 1, 2003 up until the search was executed on October 19, 2024. This time frame was selected to reflect contemporary cancer treatment and was updated prior to submission, encompassing more than two decades of data. The PubMed search was performed using a combination of MeSH terms and keywords related to cancer, severe mental disorders, and survival/mortality, and the search string was modeled by a professional research librarian. Depression was included only as a MeSH term, thereby excluding articles focusing on only milder forms of depression, which were not relevant to this review. Only English studies were included due to limited translation resources. The final search string was constructed for PubMed and subsequently converted to Embase, Psycinfo and Scopus (Table S1).

3.1.1 | Selections Process

Records eligible for inclusion met the following criteria: (1) participants: adult cancer patients (18 years or older) with preexisting SMD; (2) outcome: Only studies that reported cancer-specific mortality, defined as deaths directly attributable to cancer, were included.

Studies were excluded if they met any of the following criteria: (1) studies in which psychiatric disorder were diagnosed after the cancer diagnosis; (2) studies reporting other association measurements than mortality rate ratio (MRR), standardized mortality ratio (SMR) and hazard rate ratio (HR) incl. subdistribution hazard rate ratio (SHR); (3) studies not available in English; (4) study types: systematic reviews, meta-analyses, and reviews; (5) statistical issues as assumed typographical errors or only reporting CI's when the results were significant. This is further explained in Supplementary Document 1, (6) studies only including mortality estimates adjusted for aspects of cancer treatment.

The records identified from the initial search were independently screened by the authors NR and MV on titles and subsequent abstracts. Later, full-text records were obtained for potentially eligible records and were screened independently using the inclusion and exclusion criteria. Disagreements were settled through discussion with the remaining group of authors.

3.1.2 | Data Extraction

The following data were extracted from each of the included records: title, authors, publication year, location, study duration and type/design, sex, cancer and psychiatric diagnosis, adjustment information, cancer-specific mortality and if included in the study also all-cause mortality. Data extractions were independently conducted by the authors (NR, MV and LEF).

3.1.3 | Risk of bias Assessment

Study quality was assessed using the Newcastle-Ottawa Scala (NOS, scores of 0–9) for the included studies [11]. Quality assessment was independently conducted by the authors (NR, MV and LEF) and disagreements were settled by consensus. Consensus was achieved in all cases. The studies with a total NOS-score ≥ 7 were considered a low risk of bias, whereas a total score of 0–3 indicated a high risk, and 4–6 indicated a moderate risk of bias.

3.2 | Data Analysis

The detailed methodology for the data analysis in the meta-analysis is provided in Supplementary Document 1. In summary, a random effects model was employed to conduct the

analysis, with heterogeneity across the studies quantified using the I^2 statistic. To investigate potential sources of heterogeneity, subgroup analyses were performed based for cancer types, if five or more studies were identified, and three psychiatric diagnosis categories; affective disorders (encompassing moderate to severe depression, mood disorders, mania and bipolar disorders), schizophrenia and other psychotic disorders including Nonaffective psychotic disorders (NAPD) and SMD representing a mix of the two combined.

Exploratory analyses were undertaken to assess the hypothesized associations between severe mental disorders (SMD) and cancer-specific mortality, considering the potential influence of the interval between psychiatric and cancer diagnoses, duration of follow-up after cancer diagnosis, and patient age. Three study designs were evaluated across both the primary endpoint (cancer-specific mortality, CSM) and the secondary endpoint (all-cause mortality, ACM): cancer cohorts, defined as cohorts comprising patients with cancer, generally smaller and hospital-based, reporting hazard ratios (HRs) or mortality rate ratios (MRRs); and two types of population-based cohorts derived from the general population, one reporting HRs or MRRs and the other standardized mortality ratios (SMRs). This approach enabled comparison of effect estimates across study designs differing in sampling frame and analytical metric.

Each study accounted for various confounding factors, and for the purpose of meta-analysis, we utilized the simplest models, which for all studies controlled for at least age and sex. All statistical analyses were performed in Stata version 18.0 (Stata Corp LLC, Texas, USA).

4 | Results

The database searches yielded 4736 records: 2038 from PubMed, 240 from Embase, 316 from PsycINFO, and 2142 from Scopus. After removing 1148 duplicates, 3588 records remained for screening. Titles and abstracts were assessed, leading to the exclusion of 3478 records, primarily due to irrelevant study aims or absence of data on the association between preexisting SMD and cancer mortality. A total of 110 records were reviewed in full text for eligibility. Of these, 85 were excluded for not meeting the inclusion criteria, and an additional four were excluded during data analysis (see Supplementary Document 1). Thus, 25 records were included in this review. Figure 1 presents the PRISMA flowchart outlining the selection process.

The included studies were heterogeneous in terms of study design, sample sizes, and the inclusion of psychiatric diagnosis. The total number of participants included in each study ranged from 145 [12] to 107,481 [13], including patients with preexisting SMD (mean 17,621). The main characteristics of the 25 studies are summarized in Table 1.

A total of 15 studies [7, 8, 14, 15, 17, 19–21, 24, 25, 28, 32, 33] were conducted in Europe with eight originating from the Scandinavian countries (Finland, Denmark and Sweeden). Six

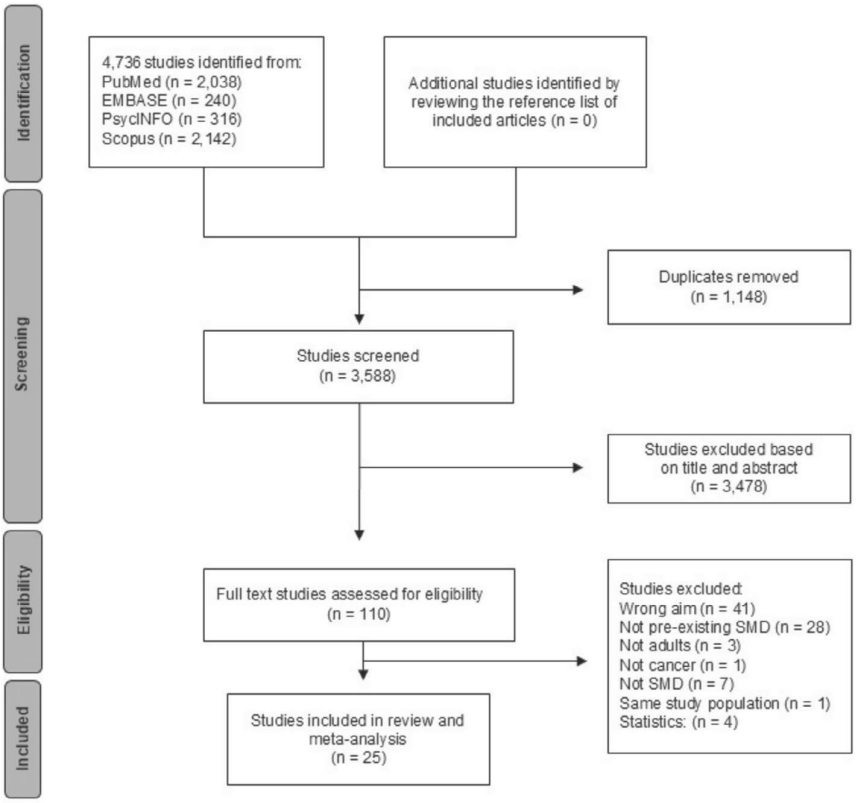

FIGURE 1 | PRISMA flow diagram.

TABLE 1 | Characteristics and quality assessment from the studies included in the meta-analysis.

Author, year of publication	Country of origin	Study duration	Psychiatric diagnosis	Cancer types	Sex	Population size (cases/comparison group)	Effect size and confidence limits	Quality assessment risk of bias
Ahlgrén-Rimpiläinen et al. [14]	Finland	1990–2013	Mood disorders	Breast	Women	1855/80,671	HR (CSM): 1.15 (1.03–1.30)	Low
			NAPD			2245/80,671	HR (CSM): 1.70 (1.56–1.87)	
Arffmann et al. [15]	Finland	1990–2013	Mood disorder, Including bipolar disorder, depression, and mania	Lung, SCC	Men	108/27,557	HR (CSM): 1.06 (0.85–1.32)	Low
					Women	45/10,295	HR (CSM): 0.93 (0.70–1.25)	
				Lung, SCLC	Men	59/27,557	HR (CSM): 1.12 (0.87–1.43)	
					Women	45/10,295	HR (CSM): 1.01 (0.76–1.35)	
				Lung, adenocarcinoma	Men	63/27,557	HR (CSM): 0.89 (0.66–1.22)	
					Women	67/10,295	HR (CSM): 1.42 (1.12–1.80)	
			NAPD, including schizophrenia, delusional disorder among others	Lung, SCC	Men	248/27,557	HR (CSM): 1.49 (1.29–1.71)	
					Women	49/10,295	HR (CSM): 1.69 (1.23–2.33)	
				Lung, SCLC	Men	96/27,557	HR (CSM): 1.26 (0.98–1.61)	
					Women	81/10,295	HR (CSM): 1.82 (1.43–2.31)	
				Lung, adenocarcinoma	Men	115/27,557	HR (CSM): 1.13 (0.90–1.42)	
					Women	69/10,295	HR (CSM): 1.19 (0.88–1.60)	
Baillargeon et al. [16]	USA	1993–2005	Mood disorder	Colon	Both	8261/80,670	HR (ACM): 1.11 (1.08–1.15)	Low
						8261/80,670	HR (CSM): 1.03 (0.99–1.08)	
			Psychotic disorder			3576/80,670	HR (ACM): 1.30 (1.24–1.36)	
						3576/80,670	HR (CSM): 1.19 (1.11–1.27)	
Batty et al. [17]	Sweden	1952–1976	Bipolar	All cancer	Men	36/16,498	HR (CSM): 0.95 (0.43–2.12)	Moderate
			Depression			230/16,498	HR (CSM): 1.59 (1.23–2.06)	
			NAPD			99/16,498	HR (CSM): 1.39 (0.91–2.12)	
			Schizophrenia			111/16,498	HR (CSM): 1.49 (1.00–2.23)	
Bergamo et al. [18]	USA	1992–2007	Schizophrenia	Lung	Both	1303/96,702	HR (ACM): 1.07 (1.01–1.13)	Low

(Continues)

TABLE 1 | (Continued)

Author, year of publication	Country of origin	Study duration	Psychiatric diagnosis	Cancer types	Sex	Population size (cases/comparison group)	Effect size and confidence limits	Quality assessment risk of bias
Cheng et al. [13]	Taiwan	2000–2019	Schizophrenia	All cancer	Both	107,481/429,924	SMR (CSM): 1.30 (1.24–1.37)	Low
				Pancreas		107,481/429,924	SMR (CSM): 1.25 (1.00–1.57)	
				CRC		107,481/429,924	SMR (CSM): 1.28 (1.12–1.47)	
				Lung		107,481/429,924	SMR (CSM): 1.06 (0.95–1.19)	
				Breast	Women	48,743/243,715	SMR (CSM): 2.40 (1.97–2.93)	
				Prostate	Men	58,738/293,690	SMR (CSM): 0.58 (0.37–0.91)	
Crump et al. [19]	Sweden	2003–2009	Schizophrenia	All cancer	Men	4787/2,970,850	HR (ACM): 3.35 (3.09–3.63)	Low
				All cancer	Men	4787/2,970,850	HR (CSM): 1.47 (1.18–1.84)	
				All cancer	Women	3490/3,126,984	HR (ACM): 3.19 (2.92–3.47)	
				All cancer	Women	3490/3,126,984	HR (CSM): 1.95 (1.59–2.41)	
				Breast	Women	3490/3,126,984	HR (CSM): 2.87 (1.83–4.51)	
				Colon	Men	4787/2,970,850	HR (CSM): 1.84 (0.87–3.86)	
				Colon	Women	3490/3,126,984	HR (CSM): 2.53 (1.31–4.86)	
				Lung	Men	4787/2,970,850	HR (CSM): 2.61 (1.74–3.94)	
				Lung	Women	3490/3,126,984	HR (CSM): 2.70 (1.70–4.29)	
				Prostate	Men	4787/2,970,850	HR (CSM): 0.84 (0.42–1.67)	
Cunningham et al. [12]	New Zealand	2006–2010	SMD	Breast	Women	112/8772	HR (CSM): 2.55 (1.49–4.35)	Low
			SMD	CRC	Both	33/4022	HR (CSM): 2.92 (1.75–4.87)	
Dalton et al. [20]	Denmark	1995–2011	Schizophrenia	Breast	Women	499/56,152	HR (ACM): 1.78 (1.52–2.08)	Low
						499/56,152	HR (CSM): 1.50 (1.18–1.90)	
Drevinskaite et al. [21]	Lithiuan	1992–2020	Schizophrenia	All cancers	Women	391/4234	SMR (ACM): 1.28 (1.11–1.48)	Low
				All cancers	Men	282/4319	SMR (ACM): 0.82 (0.70–0.96)	
				Breast	Women	107/4234	SMR (ACM): 1.90 (1.44–2.51)	
				Prostate	Men	73/4319	SMR (ACM): 0.89 (0.51–1.57)	
				Lung	Women	15/4234	SMR (ACM): 1.34 (0.78–2.30)	
				Lung	Men	48/4319	SMR (ACM): 0.85 (0.63–1.15)	

(Continues)

TABLE 1 | (Continued)

Author, year of publication	Country of origin	Study duration	Psychiatric diagnosis	Cancer types	Sex	Population size (cases/comparison group)	Effect size and confidence limits	Quality assessment risk of bias
Fried et al. [22]	USA	2006–2013	SMD	Prostate	Men	523/49,985	HR (CSM): 1.39 (1.04–1.84)	Low
						523/49,985	HR (CSM): 1.41 (1.06–1.89)	
Girardi et al. [23]	Italy	2008–2018	Affective disorder	All cancer	Men	18,248/22,827	SMR (ACM): 1.90 (1.80–2.00)	Moderate
							SMR (CSM): 1.20 (1.00–1.30)	
					Women	18,248/31,523	SMR (ACM): 1.80 (1.70–1.90)	
							SMR (CSM): 1.20 (1.10–1.30)	
				Breast	Women	18,248/31,523	SMR (CSM): 1.40 (1.10–1.70)	
				Lung	Men	18,248/22,827	SMR (CSM): 1.20 (0.90–1.50)	
					Women	18,248/31,523	SMR (CSM): 1.10 (0.80–1.40)	
			Schizophrenia and related disorder	All cancer	Men	12,996/22,827	SMR (ACM): 2.80 (2.60–3.00)	
							SMR (CSM): 1.50 (1.40–1.70)	
					Women	12,996/31,523	SMR (ACM): 2.60 (2.40–2.80)	
							SMR (CSM): 1.50 (1.30–1.70)	
				Breast	Women	12,996/31,523	SMR (CSM): 2.20 (1.70–2.80)	
				Lung	Men	12,996/22,827	SMR (CSM): 2.00 (1.60–2.40)	
					Women	12,996/31,523	SMR (CSM): 1.10 (0.70–1.60)	
Goodwin et al. [6]	USA	1993–1996	Depression	Breast	Women	1841/24,696	HR (ACM): 1.39 (1.23–1.55)	Low
						1841/24,696	HR (CSM): 1.42 (1.13–1.79)	

(Continues)

TABLE 1 | (Continued)

Author, year of publication	Country of origin	Study duration	Psychiatric diagnosis	Cancer types	Sex	Population size (cases/comparison group)	Effect size and confidence limits	Quality assessment risk of bias
Grassi et al. [24]	Italy	2008–2017	Mania and bipolar disorder	All cancer	Men	1910/[a]	SMR (ACM): 2.12 (1.18–2.46)	Moderate
						1910/[a]	SMR (CSM): 1.41 (1.03–1.88)	
					Women	2535/[a]	SMR (ACM): 1.82 (1.57–2.11)	
						2535/[a]	SMR (CSM): 1.58 (1.19–2.06)	
					Both	4445/[a]	SMR (ACM): 1.96 (1.76–2.17)	
						4445/[a]	SMR (CSM): 1.50 (1.22–1.82)	
				Breast	Women	2535/[a]	SMR (CSM): 1.80 (0.86–3.31)	
				CRC	Men	1910/[a]	SMR (CSM): 1.25 (0.34–3.20)	
					Women	2535/[a]	SMR (CSM): 2.01 (0.81–4.15)	
					Both	4445/[a]	SMR (CSM): 1.65 (0.82–2.95)	
				Lung	Men	1910/[a]	SMR (CSM): 1.63 (0.89–2.73)	
					Both	4445/[a]	SMR (CSM): 1.73 (1.11–2.58)	
				Pancreas	Both	4445/[a]	SMR (CSM): 0.83 (0.22–2.13)	
			SMD	All cancer	Men	5861/[a]	SMR (ACM): 2.35 (2.15–2.57)	
						5861/[a]	SMR (CSM): 1.34 (1.10–1.62)	
					Women	6524/[a]	SMR (ACM): 1.97 (1.81–2.13)	
						6524/[a]	SMR (CSM): 1.62 (1.37–1.90)	
					Both	12,385/[a]	SMR (ACM): 2.13 (2.00–2.25)	
						12,385/[a]	SMR (CSM): 1.49 (1.31–1.68)	
				Breast	Women	6524/[a]	SMR (CSM): 1.52 (0.95–2.30)	
				CRC	Men	5861/[a]	SMR (CSM): 1.26 (0.60–2.31)	
					Women	6524/[a]	SMR (CSM): 1.55 (0.87–2.55)	
					Both	12,385/[a]	SMR (CSM): 1.42 (0.92–2.09)	

(Continues)

TABLE 1 | (Continued)

Author, year of publication	Country of origin	Study duration	Psychiatric diagnosis	Cancer types	Sex	Population size (cases/comparison group)	Effect size and confidence limits	Quality assessment risk of bias
				Lung	Men	5861/[a]	SMR (CSM): 1.31 (0.86–1.90)	
					Women	6524/[a]	SMR (CSM): 1.85 (1.20–2.73)	
					Both	12,385/[a]	SMR (CSM): 1.52 (1.14–2.00)	
				Pancreas	Men	5861/[a]	SMR (CSM): 0.99 (0.32–2.30)	
					Women	6524/[a]	SMR (CSM): 1.64 (0.85–2.86)	
					Both	12,385/[a]	SMR (CSM): 1.37 (0.80–2.20)	
				Prostate	Men	5861/[a]	SMR (CSM): 1.46 (0.59–3.00)	
			Schizophrenia	All cancer	Men	3951/[a]	SMR (ACM): 2.49 (2.23–2.78)	
						3952/[a]	SMR (CSM): 1.29 (0.99–1.66)	
					Women	3989/[a]	SMR (ACM): 2.04 (1.85–2.42)	
					Both	7940/[a]	SMR (ACM): 2.22 (2.06–2.38)	
						7940/[a]	SMR (CSM): 1.49 (1.27–1.74)	
				Breast	Women	3989/[a]	SMR (CSM): 1.35 (0.70–2.36)	
				CRC	Men	3951/[a]	SMR (CSM): 1.26 (0.46–2.74)	
					Women	3989/[a]	SMR (CSM): 1.29 (0.56–2.54)	
					Both	7940/[a]	SMR (CSM): 1.28 (0.70–2.14)	
				Lung	Men	3951/[a]	SMR (CSM): 1.08 (0.57–1.85)	
					Women	3989/[a]	SMR (CSM): 1.82 (1.02–3.01)	
					Both	7940/[a]	SMR (CSM): 1.38 (0.92–1.99)	
				Pancreas	Women	3989/[a]	SMR (CSM): 2.38 (1.19–4.26)	
					Both	7940/[a]	SMR (CSM): 1.72 (0.91–2.93)	
				Prostate	Men	3951/[a]	SMR (CSM): 1.68 (0.54–3.91)	

(Continues)

TABLE 1 | (Continued)

Author, year of publication	Country of origin	Study duration	Psychiatric diagnosis	Cancer types	Sex	Population size (cases/comparison group)	Effect size and confidence limits	Quality assessment risk of bias
Herweijer et al. [25]	Sweden	1978–2018	Depression	Cervical	Women	392/6725	HR (ACM): 1.26 (1.06–1.50)	Low
						392/6725	HR (CSM): 1.13 (0.91–1.40)	
			Schizophrenia, NAPD and psychotic disorders			92/6725	HR (ACM): 1.74 (1.34–2.27)	
						92/6725	HR (CSM): 1.64 (1.18–2.30)	
Iglay et al. [26]	USA	2005–2007	Depression	Breast	Women	1465/19,028	HR (ACM): 1.39 (1.22–1.58)	Low
						1465/19,028	HR (CSM): 1.09 (0.86–1.39)	
			SMD, including bipolar disorder, schizophrenia, or other psychotic disorders			496/19,028	HR (ACM): 2.19 (1.84–2.60)	
						496/19,028	HR (CSM): 1.20 (0.82–1.74)	
Kisely et al. [27]	Western Australia	1988–2007	Depression	All cancer	Men	423/135,442	MMR (ACM): 1.48 (1.29–1.69)	Moderate
						423/135,442	MMR (CSM): 1.23 (1.04–1.46)	
					Women	538/135,442	MMR (ACM): 1.29 (1.12–1.48)	
						538/135,442	MMR (CSM): 1.12 (0.94–1.32)	
			Schizophrenia		Men	129/135,442	MMR (ACM): 2.21 (1.75–2.78)	
						129/135,442	MMR (CSM): 2.00 (1.51–2.64)	
					Women	146/135,442	MMR (ACM): 1.77 (1.41–2.22)	
						146/135,442	MMR (CSM): 1.68 (1.29–2.18)	
Launders et al. [28]	United Kingdom	2000–2018	Bipolar disorder	All cancer	Both	24,601/278,528	HR (ACM): 1.23 (1.14–1.34)	Low
						24,601/278,528	HR (CSM): 1.00 (0.86–1.17)	
			Schizophrenia			15,271/278,528	HR (ACM): 1.64 (1.45–1.86)	
						15,271/278,528	HR (CSM): 1.96 (1.57–2.44)	

(Continues)

TABLE 1 | (Continued)

Author, year of publication	Country of origin	Study duration	Psychiatric diagnosis	Cancer types	Sex	Population size (cases/comparison group)	Effect size and confidence limits	Quality assessment risk of bias
Mahar et al. [29]	Canada	2007–2012	SMD, inpatient	CRC	Both	258/24,507	HR (ACM): 1.91 (1.63–2.25)	Low
						258/24,507	HR (CSM): 1.69 (1.36–2.09)	
			SMD, outpatient			482/24,507	HR (ACM): 1.40 (1.22–1.59)	
						482/24,507	HR (CSM): 1.24 (1.04–1.48)	
Mandabacka et al. [7]	Finland	1990–2013	Mood disorder	All cancer	Men	4367/295,364	HR (ACM): 1.09 (1.04–1.15)	Low
					Women	7793/333,071	HR (ACM): 1.11 (1.07–1.16)	
			Schizophrenia		Men	5325/295,364	HR (ACM): 1.59 (1.53–1.65)	
					Women	7988/333,071	HR (ACM): 1.64 (1.58–1.70)	
Osborn et al. [8]	United Kingdom	June 1987–April 2002	SMD	Seven most common cancer, age 18–49	Both	46,136/346,382	HR (ACM): 1.10 (0.63–1.90)	Low
				Seven most common cancer, age > 75		46,136/346,382	HR (ACM): 0.90 (0.75–1.09)	
				Seven most common cancer, age 50–75		46,136/346,382	HR (ACM): 1.16 (0.99–1.36)	
				Respiratory cancer, age 18–49	Both	46,136/346,382	HR (ACM): 1.38 (0.47–4.07)	
				Respiratory cancer, age 50–75		46,136/346,382	HR (ACM): 1.32 (1.04–1.68)	
				Respiratory cancer, age > 75		46,136/346,382	HR (ACM): 0.74 (0.51–1.06)	
Paredes et al. [30]	USA	2004–2016	SMD	Pancreas	Both	764/54,234	HR (ACM): 1.20 (1.01–1.40)	Moderate
						764/54,234	HR (CSM): 1.27 (1.17–1.37)	

(Continues)

TABLE 1 | (Continued)

Author, year of publication	Country of origin	Study duration	Psychiatric diagnosis	Cancer types	Sex	Population size (cases/comparison group)	Effect size and confidence limits	Quality assessment risk of bias
Perini et al. [31]	Italy	1982–2006	Affective disorder	All cancer	Both	3376/9931	SMR (CSM): 1.14 (0.96–1.34)	Moderate
				Breast	Women	3376/5647	SMR (CSM): 0.65 (0.36–1.10)	
				CRC	Both	3376/9931	SMR (CSM): 0.88 (0.46–1.57)	
				Pancreas	Both	3376/9931	SMR (CSM): 0.89 (0.44–1.63)	
				Prostate	Men	3376/4284	SMR (CSM): 0.86 (0.29–2.05)	
				Respiratory cancer	Both	3376/9931	SMR (CSM): 1.36 (0.96–1.89)	
			Schizophrenia	All cancer	Both	695/9931	SMR (CSM): 0.83 (0.50–1.30)	
				Breast	Women	695/5647	SMR (CSM): 0.31 (0.03–1.47)	
				CRC	Both	695/9931	SMR (CSM): 0.53 (0.05–2.51)	
				Pancreas	Both	695/9931	SMR (CSM): 1.19 (0.24–3.84)	
				Prostate	Men	695/9931	SMR (CSM): 3.23 (0.64–10.34)	
				Respiratory cancer	Both	695/9931	SMR (CSM): 0.24 (0.02–1.14)	
Seppänen et al. [32]	France	2013–2017	SMD	Breast	Women	1346/5384	HR (CSM): 1.39 (1.03–1.87)	Low
Suppli et al. [33]	Denmark	1998–2011	Depression, antidepressiva	Breast	Women	6068/45,325	HR (ACM): 1.33 (1.25–1.41)	Low
						6068/45,325	HR (CSM): 1.13 (1.05–1.22)	
			Depression, hospital contact			744/45,325	HR (ACM): 1.19 (0.99–1.44)	
						744/45,325	HR (CSM): 1.01 (0.79–1.29)	

Abbreviations: ACM, all-cause mortality; CRC, colorectal cancer; CSM, cancer-specific mortality; HR, hazard ratio; NAPD, nonaffective psychotic disorders; SCC, squamous-cell carcinoma; SCLC, small-cell lung carcinoma; SMD, severe mental disorders; SMR, standardized mortality ratios.
[a]Only supplied as person years.

vstudies were conducted in the United States [6, 16, 18, 22, 26, 30], one in Taiwan [13], one in Canada [29], one in New Zealand [12], and one in Australia [27].

Among the included studies, eight encompassed all cancer types [7, 17, 19, 21, 24, 27, 28, 31]. The remaining studies focused on one or more specific cancer types. Ten studies investigated breast cancer [6, 8, 12–14, 20, 23, 26, 32, 33], five studies examined lung cancer [8, 13, 15, 18, 23], four studies focused on colorectal cancer [12, 13, 16, 29], two studies each focused on prostate cancer [13, 22] and pancreatic cancer [13, 30], and one study investigated cervical cancer [25].

A total of 16 studies primarily investigated cancer-specific mortality among patients with schizophrenia and other psychotic disorders, either as their main objective or as a component of their main research aim and reported specific mortality rates for these patients [7, 13–21, 23–25, 27, 28, 31]. Additionally, 13 studies exclusively examined mortality among patients with affective disorders [6, 7, 14–25, 27, 33]. Furthermore, eight studies reported results for SMD as a group [8, 12, 22, 24, 26, 27, 30, 32].

The 25 studies encompassed three distinct overall study designs. The first design, employed in 17 studies, investigated the association between preexisting SMD and survival outcomes in cancer patients [6, 7, 12, 14–18, 20, 25, 27, 32, 33]. These studies reported changes in survival using HRs or MRRs, with follow-up commencing at the time of cancer diagnosis. The second design, utilized in three studies [8, 19, 28], compared survival between cohorts of individuals with and without SMD. Similar to the first design, these studies report HRs or MRRs, but with follow-up starting at the time of cohort collection. The third design, applied in five studies [13, 21, 23, 24, 31], also compared survival between cohorts of individuals with and without SMD but employed Standardized Mortality Ratios (SMRs) for analysis.

The quality assessment for each study is shown in Table 1, for detailed analysis see Table S2. The quality of the included studies varied, but the majority of the studies (19 in all) showed a low risk of bias. The most frequently observed bias was the insufficient length of follow-up time from cancer diagnosis to the occurrence of death. Additionally, there was a selection bias, with several studies not receiving any stars for the representativeness of their study populations for example, Friet et al. and Baillargeon et al. only including SEER-Medicare patients of the age of 67 or older, a population not comparable to the general population in the US as only 18.7% of the population were covered by Medicare in 2022 [16, 33, 34].

When examining the cancer-based cohort studies, significant heterogeneity was observed across three parameters. First, the period of exposure varied, with some studies excluding patients diagnosed with SMD within the first year before the cancer diagnosis, and with differences in the maximum duration of exposure ranging from just before the cancer diagnosis to more than 20 years before the cancer diagnosis. Second, the length of follow-up time after cancer diagnosis differed among the studies ranging from 2.5 years to more than 10 years of follow-up time. Lastly, the studies could be categorized into two groups based on the age of the cancer patients included: those aged 18 and older, and those aged 65 and older.

These three parameters—period of exposure, length of follow-up, and age of patients—are depicted in Figure S1. The highest effect-size measures in the cancer cohort studies were observed when the SMD were diagnosed within 0–6 years prior to the cancer diagnosis, when the follow-up period was between 2.5 to 9.5 years, and when the patient population was considered representative of the general population (e.g., not only +65 years).

A proposal for the hypothesized association between SMD and cancer-specific mortality are shown in Figure 2. The plot includes potential confounding factors used in at least one of the included studies, as well as their mutual relationship. The analysis indicates that cancer treatment acts as a mediator, and therefore, studies where all models included aspects of cancer treatment were excluded (Supplementary Document 1).

For studies reporting HRs, Cox proportional hazards regression was used for all-cause mortality (ACM) analysis. Cancer-specific mortality (CSM) was analyzed using cause-specific Cox proportional hazards regression, or the Fine-Gray subdistribution hazard model. The purpose of subdistribution hazard rate ratios (SHR) is to quantify the difference in cumulative risk, while cause-specific HRs quantify the difference in rate. These two quantities are interchangeable without the presence of competing risks. However, for an etiological interpretation under competing risks, differences in rates are preferred over differences in risk [35]. Four papers reported SHRs [11, 14, 23, 25]. However, cause-specific Cox regression analysis was conducted as sensitivity in one of these studies, and reported no significant difference between the cause-specific HRs and the corresponding SHRs [14]. Thus, for the purposes of the meta-analysis, SHRs and cause-specific HRs were considered equivalent and MRRs were considered equivalent to HRs. Thirteen of the original studies provided data on both CSM and ACM across various subgroups, enabling a direct comparison of effect sizes [6, 16, 19, 20, 23–30, 33]. In the subset of data that included both ACM and CSM estimates, mortality rates increased following SMD, with the strongest associations observed in patients with schizophrenia and other psychotic disorders and the weakest associations noted in patients with affective disorders (Figure S2A–C). In cancer cohorts, ACM rates were consistently higher than CSM rates, though the differences were marginal with a relative increase of 15% (95% CI: −13%, +50%) (Figure S2D). Conversely, in population cohorts, ACM rates were substantially higher than CSM rates with a relative increase of +49% (95% CI: +14%, +95%) (Figure S2D).

The six studies from the United States based on the SEER database [12, 16, 18, 22, 26, 30] were characterized by short exposure periods, limited follow-up durations, and cohorts restricted to cancer patients aged 65 years and older. As these study characteristics were consistently associated with smaller effect estimates (Figure S1), the SEER studies were analyzed separately (Figure S3). Although these studies indicated increased mortality among cancer patients with preexisting SMD, the observed effect sizes were modest, with no clear association between the

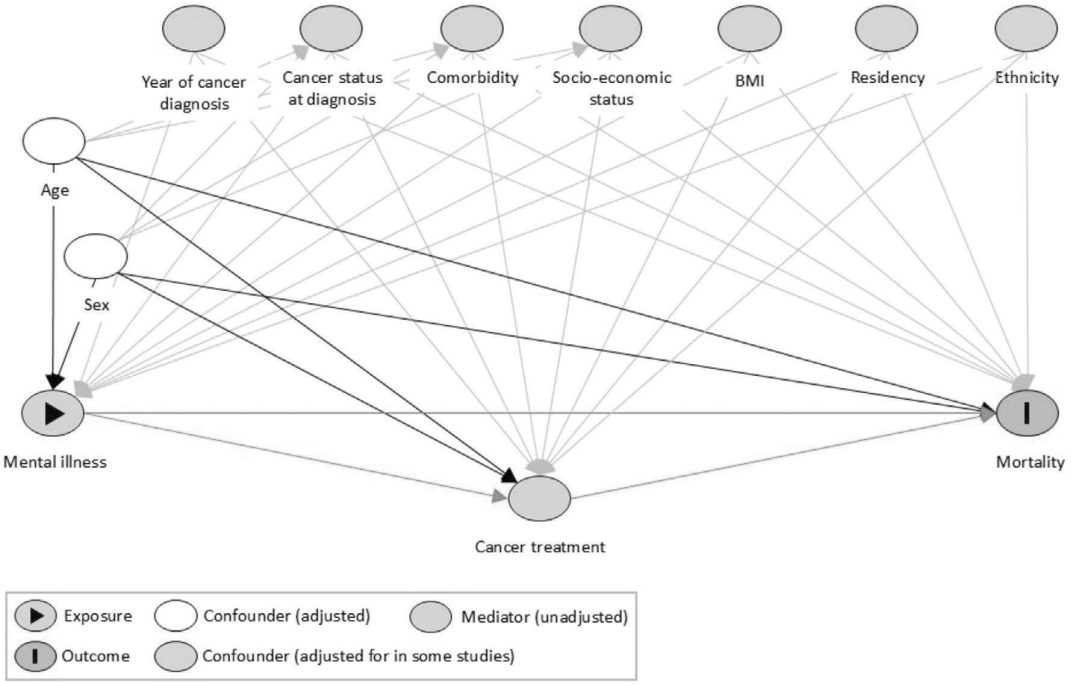

FIGURE 2 | Proposal for hypothesized association between severe mental disorder and cancer survival.

severity of psychiatric diagnosis and mortality, and no significant differences between cancer-specific (CSM) and all-cause mortality (ACM). Consequently, the SEER studies were excluded from the pooled analyses, leaving 19 studies for subsequent meta-analytic evaluation [6–8, 13–15, 17, 19–21, 23–25, 27–29, 31–33].

Three exploratory meta-analyses were then conducted to evaluate the three study designs—cancer cohorts (HR or MRR), population cohorts (HR or MRR), and population cohorts (SMR)-across the two survival endpoints, CSM and ACM. These exploratory analyses included all reported data and were not limited to data where CSM and ACM were reported concurrently for the same patients with the same psychiatric diagnosis and cancer type (as in Figure S2).

In the first exploratory analysis, HR and MRR data from studies on cancer cohorts were divided into two subgroups, ACM and CSM [6, 7, 14, 15, 17, 20, 25, 27, 29, 32, 33] (Figure S4). Consistent with previous findings (Figure S2), this analysis suggested that different SMD groups had distinct effects, with studies on ACM reporting slightly higher effect sizes resulting in an overall HR of 1.46 (95% CI: 1.33–1.61) versus 1.31 (95% CI: 1.22–1.41) for CSM ($p = 0.08$).

In the second exploratory analysis, HR and MRR data from studies on population cohorts were similarly divided into ACM and CSM subgroups [8, 19, 28] (Figure S5). As observed in the cancer cohort studies (Figure S4), different SMD groups appeared to have distinct effects sizes, though no significant difference between ACM and CSM was detected ($p = 0.27$).

The third exploratory meta-analysis examined SMR data from studies on population cohorts, again dividing the results into ACM and CSM subgroups [13, 23, 24, 31] (Figure S6). With SMR as the endpoint, ACM was higher than CSM resulting in overall HRs of 2.15 (1.99–2.33) versus 1.38 (1.29–1.47), ($p < 0.001$).

Based on these exploratory analyses, the final analyses included studies based on either cancer cohorts or population cohorts that reported HR, MRR, or SMR, and specifically reported cancer-specific mortality. Two studies that only reported all-cause mortality were excluded [7, 8], leaving 17 studies for the final analyses [6, 13–15, 17, 19–21, 23–25, 27–29, 31–33].

Firstly, as presented in Figure 3, the presence of a preexisting SMD was associated with significantly elevated cancer mortality across several cancer types, as demonstrated by a pooled effect size (HR, MRR, or SMR) of 1.37 (1.30–1.44, $p < 0.001$). Preexisting schizophrenia and other psychotic disorders were associated with the largest effect size of 1.47 (1.33–1.63, $p < 0.001$), while affective disorders were associated with the smallest effect size of 1.25 (1.18–1.32, $p < 0.001$).

Secondly, for lung (Figure 4) and breast cancer (Figure 5) there were enough studies to make subgroup analyses, which showed similar magnitudes of effect sizes and associations with preexisting SMD. The overall effect sizes for lung cancer and breast cancer were 1.33 (1.20–1.47, $p < 0.001$) and 1.49 (1.27–1.75, $p < 0.001$); see Figures 4 and 5 respectively. For lung cancer, there was a difference in effect sizes between the psychiatric diagnosis categories, even though it was not significant ($p < 0.17$), Figure 4.

In the subgroup analysis, the highest cancer-specific mortality was observed in the breast cancer population, where patients with schizophrenia or other psychotic disorders had significantly higher mortality compared to those without preexisting

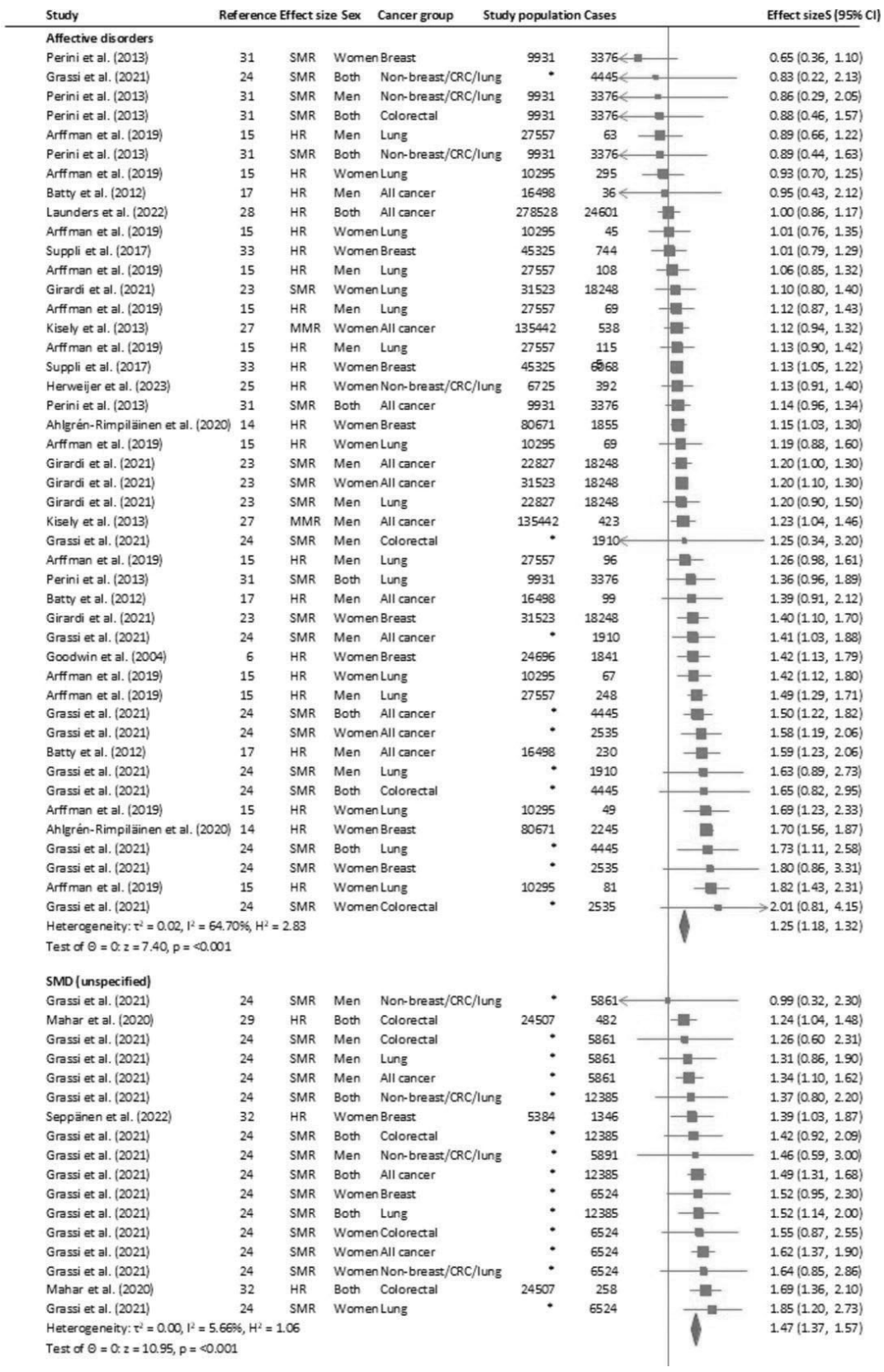

FIGURE 3 | Meta-analysis of cancer-specific mortality for people with SMD compared to people without SMD measured as HR, MRR, or SMR, by prior psychiatric diagnosis categories.

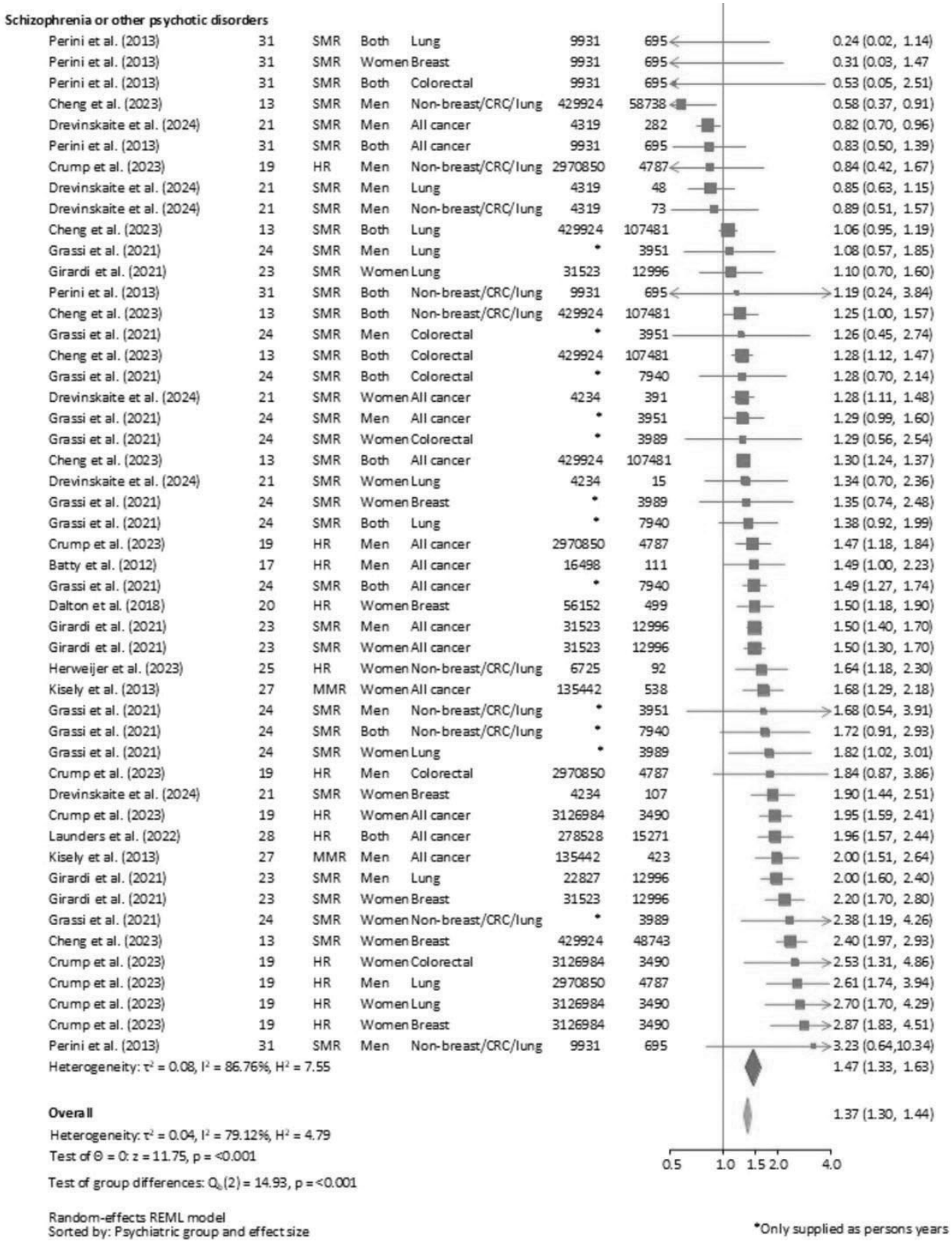

FIGURE 3 | (Continued)

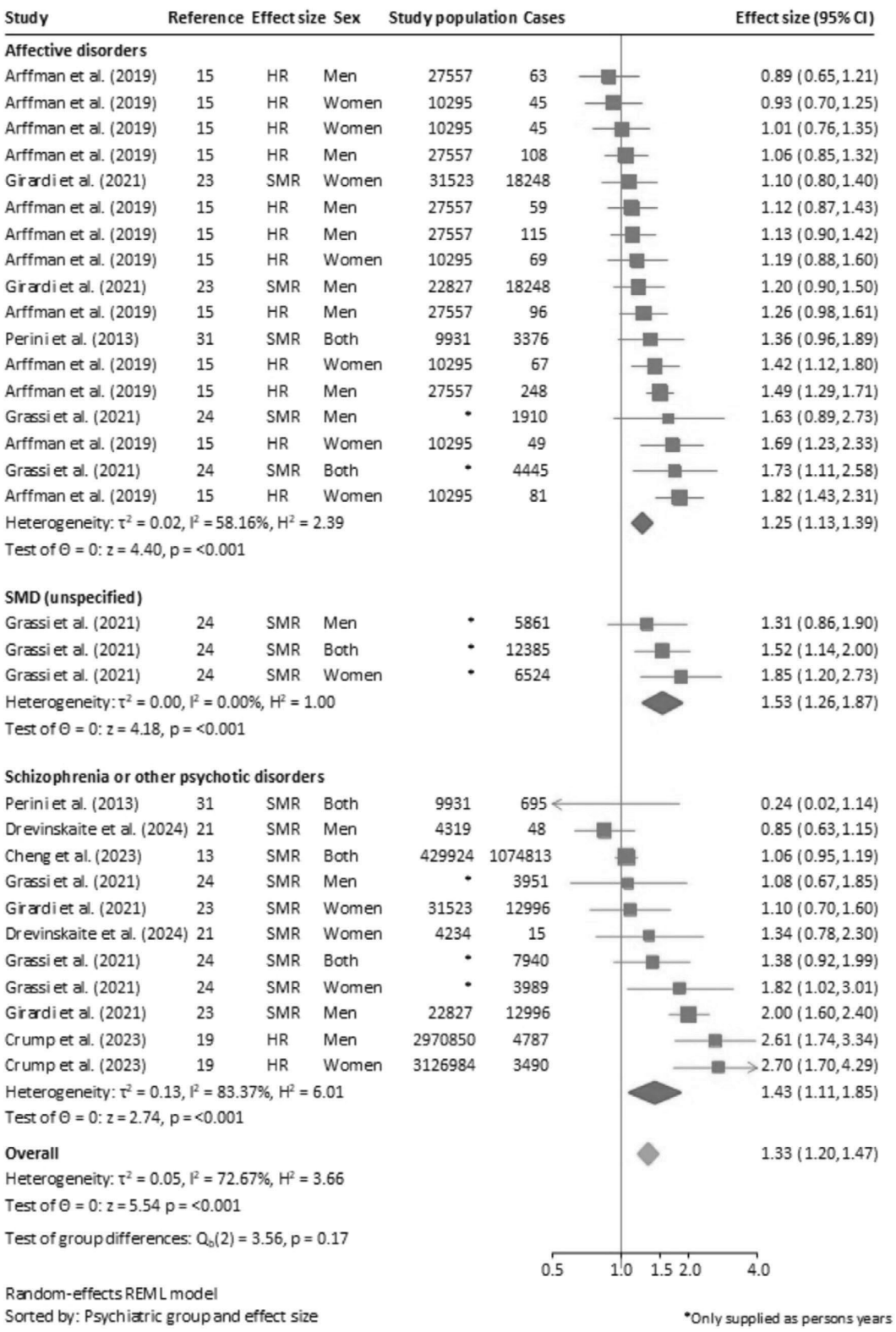

FIGURE 4 | Subgroup meta-analysis on studies reporting cancer-specific mortality of people with lung cancer and SMD compared to people without SMD. Studies are divided into subgroups based on psychiatric diagnosis categories and sorted by effect size.

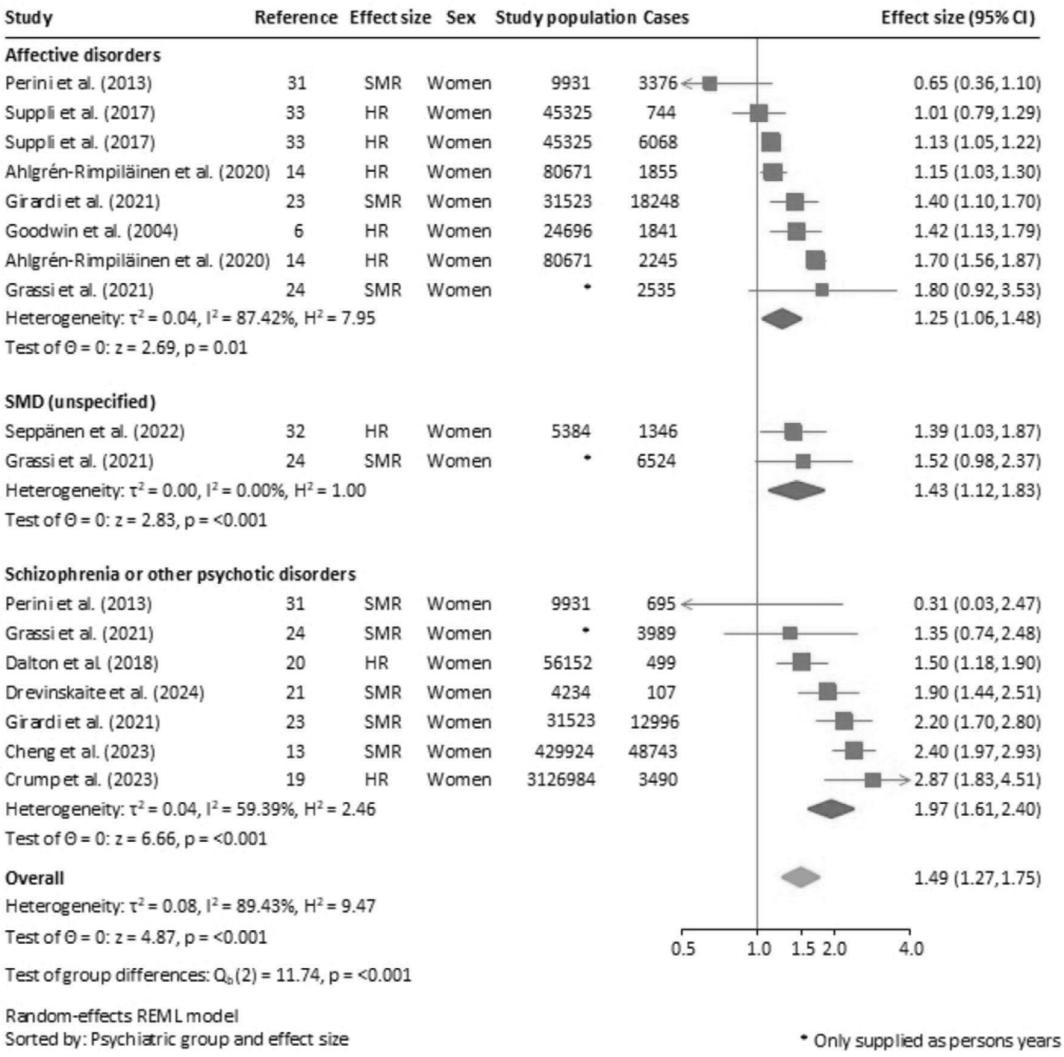

FIGURE 5 | Subgroup meta-analysis on studies reporting cancer-specific mortality of people with breast cancer and SMD compared to without SMD. Studies are divided into subgroups based on psychiatric diagnosis categories and sorted by effect size.

SMD with an effect size of 1.97 (95% CI: 1.61–2.40, $p < 0.001$), see Figure 5.

5 | Discussion

In this study, we found that patients with cancer and preexisting SMD have a significantly higher relative risk of cancer-specific mortality at 1.37 compared to patients without preexisting SMD. The main burden was carried by the patients with preexisting schizophrenia or other psychotic disorders with an up to 1.47 higher relative cancer mortality risk compared to patients without preexisting SMD, but even patients with affective disorders faced an increased relative mortality risk at 1.25. These findings were sustainable across the investigated cancer types with a combined elevated relative cancer-specific mortality risk at 1.33 and 1.49 among patients with lung and breast cancer and preexisting SMD compared to patients without preexisting SMD. The highest mortality rates were found among patients with breast cancer and preexisting schizophrenia or other psychotic disorders, with an elevated relative mortality risk of 1.97 compared to patients without preexisting SMD.

Another key finding was the difference between ACM and CSM. In cancer cohorts, ACM was only slightly higher than CSM, whereas in population cohorts, ACM rates were sustainedly higher. Some of the explanation for the elevated ACM among patients with preexisting SMD, is probably due to the great burden of comorbidity within this group with higher smoking, obesity, and metabolic disturbance, leading to significant cardiovascular diseases [36]. Factors who are also known to increase cancer incidences [37].

The highest effect-size measures in the cancer cohort studies were also observed when the SMD were diagnosed within 0–6 years prior to the cancer diagnosis, an indication that the time of onset of the psychiatric diagnosis is important, since many psychiatric diagnoses indeed can remit over time, and there by not having the same impact on some of the barriers towards optimal cancer care. No meta-analysis on cancer mortality

among patients with preexisting SMD has been conducted before, but similar results for patients with preexisting schizophrenia have been found by Zhuo et al. reporting a pooled HR at 1.51 (1.13–2.03) and by Davis et al. reporting a pooled HR at 1.59 (1.41–1.81) [38, 39]. The elevated relative risk for cancer-specific mortality among patients with preexisting affective disorders at 1.23 found in our study is also supported by the meta-analysis by Davis et al., in which they reported a pooled HR at 1.17 (95% CI: 1.05–1.30) in a subgroup consisting of patients with preexisting depression and mood disorders [39]. Our subgroup analysis showing a high cancer-specific mortality risk ratio for patients with breast cancer and schizophrenia is further supported by Ni et al. presenting a mortality risk ratio of 1.97 (95% CI: 1.38–2.83) in this group [40].

The results of this review and meta-analysis reveal significant disparities in cancer mortality among patients with preexisting SMD compared to patients without SMD. This disparity may, in part, stem from a reduced tendency towards screening participation, as evidenced by the meta-analysis by Solmi et al., who reported a 24% lower participation rate in cancer screening among individuals with a mental disease compared to the general population [41]. Similar results were found in a new, large population-based cohort study by Thomsen et al. examining the screening participation for colorectal cancer [42]. This discrepancy could result in a higher likelihood of advanced cancer stages at the time of diagnosis. The meta-analysis by Davis et al. supports this notion, implying that patients with preexisting mental disorders are at greater risk of advanced cancer stage at the time of diagnosis [39]. Another explanation for the increased mortality and advanced cancer stage could be that patients with preexisting SMD more often are diagnosed through emergency hospital admissions, which are also associated with poor prognosis [43].

Finally, the increased cancer mortality could further be explained by individuals with preexisting SMD not receiving treatment according to current guidelines. For instance, approximately 5.5% of the adult population in the United States has a mental, behavioral, or emotional disorder that impacts their daily functioning and thereby, presents a substantial challenge in navigating healthcare systems [43, 44]. This is supported by Baillargeon et al. who found that patients with colon cancer and preexisting psychotic disorders have a 42% greater risk of not receiving any cancer treatment compared to patients without SMD [16]. The same seems to apply to patients with lung and breast cancer, with fewer receiving surgery and radiotherapy treatment [27, 45, 46].

5.1 | Strengths and Limitations

This systematic review and meta-analysis offer a novel contribution by focusing explicitly on CSM among patients with preexisting SMD, a dimension often overlooked in previous literature dominated by all-cause mortality metrics. By isolating CSM, we address a key knowledge gap and provide more accurate insights into cancer outcomes within this vulnerable group. Our review stands out by including only studies that diagnosed SMD prior to cancer onset, thereby strengthening the validity of the conclusions by reducing bias from reverse causality. Covering four major databases and spanning over two decades of research, our methodology ensures comprehensive coverage and global representation. The scope of this review includes exploratory and subgroup analyses by psychiatric diagnosis and cancer type. These in-depth analyses allow for a more nuanced understanding of disparities and support evidence-based discussions on intervention.

Several important limitations should be acknowledged. While the inclusion of studies from diverse global regions increases the generalizability of the findings, it may also complicate interpretation. Differences in healthcare systems, access to cancer treatment, availability of psychiatric care, and the reporting of diagnoses and causes of death may limit comparability across studies. Unmeasured confounding further remains a considerable challenge, as information on undiagnosed psychiatric disorders, treatment status for both psychiatric and oncological conditions, and time since diagnosis was inconsistently reported. Nevertheless, synthesizing results from different regions provides a broader overview of the evidence base and may reveal patterns that would not be apparent in individual settings. Some limitations also pertain to the search strategy and analyses. Only English-language literature was included due to limited translation resources and the risk of translational bias, and relevant studies published in other languages may have been overlooked, although this risk is considered minor. Furthermore, the meta-analyses were not stratified by sex, which would have provided additional insights and nuance to the findings and interpretations. Other limitations also affected comparability between the included studies. These include inconsistencies in the definition of SMD, an uneven distribution of cancer types, heterogeneity in study designs, and substantial variation in the covariates used for adjustment. In addition, some subgroup analyses were based on relatively few studies, meaning that the results could also reflect unknown study-specific factors. Collectively, these limitations pose challenges to the direct application of findings to real-world settings. All this calls for a more comprehensive approach with clear definition of SMD, time of onset of psychiatric diagnosis and follow-up and for further studies.

5.2 | Clinical Implications

The reasons behind the above mentioned disparities are situated at both patient-, provider- and system levels [47]. These factors include for example, evasion of responsibility between sectors, stigma towards the patient group, diagnostic overshadowing, restricted social support network, reduced awareness of physical symptoms, lack of identification of psychiatric comorbidity, lack of continuity by healthcare professionals, fragmentation of the healthcare system and limited time and resources in the oncological clinic [47].

Despite these disparities, only few studies have developed interventions to improving cancer care for this population. This is in spite of the fact that interventions in other healthcare areas show that sufficient support enables patients with schizophrenia to participate in colorectal cancer screening at rates comparable to the general population [48].

Currently, only two known interventions to support patients with preexisting SMD through out their cancer care appear to

exist, namely the Bridge intervention and the CASEMED Model [49, 50]. The interventions are developed in different healthcare systems, namely the United States and Denmark, but both focus on a patient-centered, cross-sectorial, interdisciplinary approach with the integration of psychiatry into the oncology clinics to ensure optimal cancer care for patients with preexisting SMD. There is a need for increased focus on the development of sustainable cancer care interventions to address mortality inequalities among patients with cancer and preexisting SMD.

6 | Conclusion

The presence of a preexisting SMD was associated with a significantly elevated cancer-specific mortality across diverse cancer types at 1.37. Preexisting schizophrenia or other psychotic disorders were associated with the largest elevated mortality at 1.47, while affective disorders are associated with the smallest at 1.25. Similar effect sizes and associations with preexisting SMD were observed across the major reported cancer groups, including lung and breast cancer. However, the heterogeneity in study designs, statistical approaches, definitions of SMD, and the unrepresentative distribution of cancer types in the studies, together highlights the need for more comprehensive and methodologically consistent research in the future. In all, this review and meta-analysis demonstrate a more nuanced understanding of cancer specific mortality for patients with preexisting SMD, and the findings emphasize the urgent need for integrated psychiatric–oncologic care models and greater awareness among both mental health and general health professionals to address disparities in cancer outcomes for patients with preexisting SMD.

Author Contributions

Nikoline Riis: investigation, validation, writing – original draft. **Malene Vestergaard:** investigation, validation, writing – original draft. **Mette Asbjoern Neergaard:** conceptualization, resources, validation, supervision, funding acquisition, reviewing and editing. **Jan Alsner:** methodology, formal analysis, visualization and data curation. **Jesper Grau Eriksen:** reviewing and editing. **Poul Videbech:** reviewing and editing. **Anna Mygind:** reviewing and editing. **Søren Paaske Johnsen:** reviewing and editing. **Jan Brink Valentin:** methodology, reviewing and editing. **Louise Elkjær Fløe:** conceptualization, investigation, resources, validation, project administration, funding acquisition, writing – reviewing and editing.

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Ethics Statement

This review and meta-analysis have been conducted with adhere to high ethical standards, including transparent in methodology, unbiased data selection, and full disclosure of conflicts of interest, funding and use of AI, to ensure the integrity and reliability of evidence. The article has focus on reflecting an inclusive and nonstigmatizing language.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section. **Data S1:** Supporting Information.

11.2 Paper II

Symptom burden and quality of life in patients with severe mental disorders initiating cancer treatment

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Abstract

Background

Patients with pre-existing severe mental disorders (SMDs), defined as moderate to severe depression, bipolar disorder, or schizophrenia, face barriers to optimal cancer care and may experience elevated mental and physical symptom burden and reduced quality of life.

Aim

To assess health-related quality of life (HRQoL) and psychiatric symptom burden among patients with SMD before initiating cancer treatment.

Methods

In this case-control study patients with lung, breast, or head and neck cancer and a documented hospital contact for SMD within the past ten years were included. The patients were matched 1:2 with controls without SMD, using sex, age (±5 years), cancer type, and treatment intent. Recruitment occurred at the first oncology visit (January 2023-June 2025). HRQoL and psychiatric symptoms were measured using validated instruments on patient reported outcomes. Patient characteristics were extracted from medical electronic medical journals. Means with confidence intervals (CI) and mean ratios were calculated to compare the two groups.

Results

Patients with cancer and pre-existing SMD reported significantly poorer HRQoL than matched controls, with a mean of 56.67 (95% CI 48.75-64.58), compared to patients without SMD (mean: 69.01 (95% CI: 65.20-72.90)). Similarly, both physical and emotional functioning were lower in the SMD group, and the psychiatric symptom burden was substantially higher among patients with SMD.

Conclusion

Patients with cancer and pre-existing SMD initiate cancer treatment with substantially poorer HRQoL, higher emotional and physical symptom burden, and markedly elevated psychiatric symptom burden compared with controls. These findings highlight the need for early, integrated psychiatric and supportive care to improve outcomes in this high-risk group.

Introduction

Individuals with severe mental disorders (SMD), such as moderate to severe depression, bipolar disorders, schizophrenia, or other psychotic disorders, comprise a vulnerable patient population with higher cancer mortality and poorer cancer prognosis [1,2]. At a population level, they face more challenges when diagnosed with cancer and experience a higher burden of mental and psychical symptoms and lower quality of life [3]. Patient-reported outcome measures (PROMs) are widely used by healthcare professionals to guide symptom management, inform shared decision-making, and monitor treatment-related toxicity [4,5]. Even though a growing body of research with several qualitative studies have investigated the different cancer experiences and barriers towards optimal cancer trajectories [3,6,7], patients with pre-existing SMDs have historically been underrepresented in research, and little is known about how their psychiatric comorbidity may be associated with the perception and reporting of cancer-related symptoms and quality of life [8].

Receiving a cancer diagnosis is psychologically challenging for many patients [9]. Even among individuals without pre-existing SMD, a substantial burden of distress is common, driven by confrontation with a potentially life-threatening illness, fear of the unknown, and practical and social disruptions [9,10]. Evidence regarding psychological responses at the time of diagnosis is, however, heterogeneous. A systematic review has shown that patients who report greater internal resources and resilience at treatment initiation often experience lower distress, more adaptive coping strategies, and better quality of life [9]. Coping strategies at the time of diagnosis have also been linked to psychological growth and the ability to find meaning in life despite of the cancer diagnosis [9]. Whether similar adaptive processes apply to patients with pre-existing SMD is unknown, but a qualitative study suggests that responses to a terminal cancer diagnosis among patients with cancer and pre-existing SMD also vary, with some individuals experiencing worsening depression, while others show improved emotional stability and adaptive coping [11]. To address the above-mentioned knowledge gaps, this study aimed to examine health-related quality of life (HRQoL) and psychiatric symptom burden among patients with SMD facing cancer treatment.

Methods

This case-control study was conducted at Aarhus University Hospital. Patients were enrolled at their first consultation at the Department of Oncology and completed questionnaires and demographics within the first two weeks of initiating cancer treatment.

Setting

The Danish healthcare system is tax-funded and provides free-of-charge access to somatic and mental health care [12]. Cancer treatment is centralized at large hospitals and primarily delivered as outpatient treatment [13]. Patients with SMD are treated in hospital-based psychiatric services, while milder or uncomplicated conditions are typically managed by general practitioners, private psychiatrists, or, in some cases, psychologists [14]. All professionals work in close collaboration with community nurses and social services.

Participants

Patients included in this study were newly referred to the Department of Oncology with a diagnosis of lung, breast, or head and neck cancer. Cases were identified as patients with a documented hospital contact related to a prior diagnosis of SMD recorded in the electronic medical record within the past ten years. SMDs were defined according to ICD-10 codes as moderate to severe depressive episodes (F32.1-F32.9, F33.1-F33.9), bipolar affective disorders (F30-F31), schizophrenia, and other psychotic disorders (F20-F25, F28-F29). Patient identification was performed automatically at the time of referral to the Department of Oncology via an electronic algorithm. Patients with a history of SMD were matched in a 1:2 ratio with control patients without any hospital contact related to SMD within the past ten years, as documented in the electronic medical record. Matching criteria included sex, age (±5 years), cancer type, and treatment intent (curative vs. palliative). Patients attending their initial oncology consultation between 1st January 2023, and 1st June 2025, were recruited.

Data

The data were collected at entrance into the study from electronic medical records and patient questionnaires including demographics, HRQoL and psychiatric symptoms.
HRQoL was assessed using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core-15 Palliative (EORTC QLQ-C15-PAL), which is a 15-item questionnaire including a quality of life item, two functional scales (physical and emotional) and seven symptom items (fatigue, nausea & vomiting, pain, dyspnoea, insomnia, appetite loss and constipation) [15].

Psychiatric symptom burden was evaluated using the Symptom Checklist-92 (SCL-92), which is a 92-item questionnaire which can be converted into ten predefined themes including a

Global Severity Index, somatization, anxiety, interpersonal sensitivity, phobic anxiety, obsessive-compulsive disorder, depression, anger, hostility and psychoticism [16].

Questionnaires were completed either in paper format or electronically, according to patient preference. The electronic study data were collected and managed using The Research Electronic Data Capture (REDCap) tool hosted at Central Danmark Region [17,18]. REDCap is a secure, web-based software platform designed to support data capture for research studies. Patient characteristics were retrieved through the electronic medical record.

Data analysis

Descriptive statistics comparing patients with and without pre-existing SMD concerning patient characteristics, along with the questionnaires, were sampled. All EORTC-QLQ-C15-PAL items were converted to a 0 to 100 scale according to the scoring manual with a higher score representing better functional status, higher QoL or, for symptom scales, a higher level of symptoms [15,19,20]. The SCL-92 scales were converted into the 10 predefined themes according to the scoring manual [16].

For continuous outcomes (EORTC-QLQ-C15-PAL and SCL-92 scores) we calculated mean values and corresponding 95% confidence intervals (CIs) to allow visual comparisons with normative data for EORTC QLQ-C30 and SCL-92. Between-group comparisons were expressed as mean ratios with 95% CIs, calculated as the mean value of the SMD group divided by that of the control group. Confidence limits derived from the standard error of the log-transformed mean ratio and subsequently back-transformed to the original scale. All statistical analyses were performed in Stata version 18.0 (Stata Corp LLC, Texas, USA).

Ethics

This study has been conducted in accordance with the hospital's ethical standards, including transparency in methodology, unbiased data selection, and full disclosure of conflicts of interest, funding, and the use of AI. This to ensure the integrity and reliability of evidence as in line with the Declaration of Helsinki [21]. Data storage and access complied with the General Data Protection Regulation (GDPR) of the European Union [22]. The data were stored after permission of The Central Region of Denmark act number 1-10-72-1-22. The study was not subject to ethical clearance according to The Danish Act on Research Ethics Review of Health Research Projects recording act number 1-16-02-249-22 [23]. All participants were informed orally and in writing and subsequently signed consent forms with the possibility to always draw consent. The paper has a focus on reflecting an inclusive and non-stigmatising language.

Results

Patient characteristics

Forty patients with cancer and pre-existing SMD were enrolled from January 2023 to June 2024, and 80 matched controls were enrolled from November 2023 to June 2025. The distribution of sex (65% female), cancer type (breast 50%, lung 28%, and head and neck 22%), and treatment intent (85% receiving curative treatment) was comparable between the two groups due to matching (Table 1). The group with pre-existing SMD was slightly younger (median 59 years vs. 62 years).

Patients with pre-existing SMD were more frequently characterized by lower educational level (no formal education: 32.4% vs. 11.8%), lower likelihood of full-time employment (7.7% vs. 46.8%), and a higher proportion living alone (43.6% vs. 17.1%). One out of five didn't use online healthcare applications (e.g. for booking blood samples and keeping trac of hospital appointments) and current or active alcohol abuse was also more common among patients with SMD (34.2% vs. 6.3%).

Regarding designation of next of kin, patients with SMD were more likely to identify colleagues, friends, or other non-family members (35.9% vs. 3.9%), and less likely to appoint a partner (51.3% vs. 80.3%). Instead, they more often designated their children as next of kin (25.9% vs. 15.8%).

In relation to healthcare professionals, patients with SMD more frequently reported having a good relationship with their general practitioner (78.9% vs. 50.0%). In contrast, nearly half of the patients without SMD reported not having a personal relationship with any healthcare professional (48.6%). A detailed overview of patient characteristics is presented in Table 1.

Table 1: Patient characteristics

Characteristics	Patients with SMD n = 40	Control group n = 80
Female, n (%)	26 (65.0)	54 (65.0)
Age, median (IQR)	59 (51.0-68.0)	62 (52.0-68.0)
Cancer type, n (%)		
Breast	20 (50.0)	40 (50.0)
Head and neck	11 (28.0)	22 (28.0)
Lung	9 (22.0)	18 (22.0)
Curative intended treatment, n (%)	34 (85.0)	68 (85.0)
Severe mental disorder, n (%)		
Moderate to severe depression	23 (57.5)	-
Bipolar disorder	10 (25.0)	-
Schizophrenia and other psychosis	7 (17.5)	-

Educational level, n (%)		
No higher education	12 (32.4)	9 (11.8)
Low/Middle	22 (59.4)	58 (76.3)
Higher	3 (8.1)	9 (11.8)
No provided information	3 (7.5)	4 (5.0)
Uses online healthcare applications n (%)		
Yes	26 (65.0)	79 (98.9)
No	8 (20.0)	1 (0.1)
No provided information	6 (15.0)	0 (0.0)
Lives alone, n (%)		
Yes	17 (43.6)	13 (17.1)
No	22 (55.0)	64 (80.0)
No provided information	1 (2.5)	3 (3.75)
Job situation, n (%)		
Fulltime work	3 (7.7)	36 (46.8)
Parttime work	5 (12.8)	8 (10.4)
Age pensioner	13 (33.3)	25 (32.5)
Disability pensioner	15 (38.5)	0 (0.0)
Social benefits	3 (7.7)	2 (2.6)
Other	0 (0.0)	6 (7.8)
No provided information	1 (2.5)	3 (3.75)
Abuse of alcohol, n (%)		
Current	6 (15.8)	2 (2.5)
Former	7 (18.4)	3 (3.8)
No current or former abuse	25 (65.8)	7 (93.8)
No provided information	2 (5.0)	0 (0.0)
Smoking status, n (%)		
Current	15 (39.5)	10 (12.5)
Former	16 (42.1)	24 (30.0)
No current or former smoking	7 (18.4)	46 (57.5)
No provide information	2 (5.0)	0 (0.0)
Designation of next of kin, n (%)*		
Partner	20 (51.3)	61 (80.3)
Child	10 (25.6)	12 (15.8)
Friend	5 (12.8)	1 (1.3)
College	1 (2.6)	0 (0.0)
Other	8 (20.5)	2 (2.6)
No next of kin	2 (5.1)	0 (0.0)
No provided information	1 (2.5)	4 (5.0)
Good relationship with healthcare professionals, n (%)*		
General practitioner	30 (78.9)	35 (50.0)
Home nurse	2 (5.3)	1 (1.4)
Public navigator (E.g. from patients' organisations)	4 (10.5)	0 (0.0)
Psychologist	1 (2.6)	2 (2.9)
Psychiatrist	3 (7.9)	0 (0.0)
Not a good relationship with any healthcare professional	4 (10.5)	34 (48.6)
No provided information	2 (5.0)	8 (10.0)

Not all variables were available for all included patients.

IQR: Inter Quartile Range

*Possible to choose more than one

Health-related quality of life

Regarding HRQoL, patients with cancer and pre-existing SMD consistently reported lower scores across all measured domains (Table 2). The mean overall HRQoL score was significantly lower among patients with pre-existing SMD at 56.67 (95% CI 48.7564.58), compared with 69.01 (95% CI: 65.2072.90) in patients without SMD, corresponding to a mean ratio of 0.82 (95% CI 0.71-0.95). A similar pattern was observed for physical functioning, with mean scores of 69.15 (95% CI: 61.67-76.63) in the SMD group versus 88.12 (95% CI: 85.65-90.62) in the control group, and for emotional functioning, with mean scores of 69.17 (95% CI: 60.59-77.75) versus 90.73 (95% CI: 87.29-94.16), respectively.

The symptom scales likewise demonstrated higher symptom burden among patients with pre-existing SMD. Fatigue was reported at a mean score of 44.44 (95% CI: 36.18-52.71) compared with 27.22 (95% CI: 22.23-32.26) in the control group. Pain was 27.92 (95% CI: 19.53-36.30) versus 17.71 (95% CI: 12.48-22.94). Dyspnoea was reported at 16.67 (95% CI: 10.41-22.92) versus 3.96 (95% CI: 2.17-5.74), and insomnia at 47.50 (95% CI: 36.70-58.30) versus 27.08 (95% CI: 20.75-33.42).

The patients with pre-existing SMD also tended to report higher levels of constipation, appetite loss, nausea and vomiting, but these differences did not reach statistical significance.

Table 2: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core-15 Palliative (EORTC QLQ-C15-PAL) scores at beginning of cancer treatment

	Items*	**Patients with SMD** n=40 Mean (95% CI)	**Control group** n=80 Mean (95% CI)	**Mean ratio** (95% CI)
EORTC health-related-QOL measure (High score: good)	15	56.67(48.75-64.58)	69.01 (65.20-72.90)	0.82 (0.71-0.95)
Functional scale (High score: good)				
Physical functioning	1-3	69.15 (61.67-76.63)	88.12 (85.65-90.62)	0.78 (0.70-0.88)
Emotional functioning	13,14	69.17 (60.59-77.75)	90.73 (87.29-94.16)	0.76 (0.67-0.87)
Symptom scale (Low score: good)				
Fatigue	7,11	44.44 (36.18-52.71)	27.22 (22.23-32.26)	1.63 (1.26-2.11)
Nausea and vomiting	9	9.59 (2.45-6.30)	4.38 (2.45-6.30)	2.19 (0.10-4.82)
Pain	5,12	27.92 (19.53-36.30)	17.71 (12.48-22.94)	1.58 (1.04-2.39)
Dyspnoea	4	16.67 (10.41-22.92)	3.96 (2.17-5.74)	4.2 (2.36-7.52)
Insomnia	6	47.50 (36.70-58.30)	27.08 (20.75-33.42)	1.75 (1.27-2.42)
Appetite loss	8	19.00 (11.74-26.60)	16.25 (11.55-20.95)	1.18 (0.73-1.90)
Constipation	10	20.00 (10.31-29.69)	10.42 (5.22-15.61)	1.92 (0.96-3.82)

*Item number(s) in EORTC QLQ C15-PAL

Psychiatric symptoms

As expected, across all psychiatric symptom domains, patients with pre-existing SMD reported significantly higher mean SCL-90 scores compared with patients without SMD (Table 3). The Global Severity Index was markedly elevated in the SMD group, with a mean score of 0.74 (95% CI: 0.56-0.91), compared with 0.25 (95% CI: 0.20-0.30) in the control group. This difference corresponds to a mean ratio of 2.95 (95% CI: 2.19-3.98), indicating that patients with pre-existing SMD experienced nearly threefold higher overall psychiatric symptom burden.

The largest differences in mean ratio were observed in the domains of phobic anxiety and hostility. For phobic anxiety, patients with pre-existing SMD had a mean score of 0.48 (95% CI: 0.26-0.71), compared with 0.03 (95% CI 0.01-0.05) among patients without SMD, corresponding to a mean ratio of 14.27 (95% CI 6.85-29.71). Similarly, hostility was substantially higher in the SMD group, with a mean score of 0.38 (95% CI: 0.23-0.56) compared to 0.05 (95% CI: 0.02-0.08) in the control group.

In the domains of depression and anxiety, patients with pre-existing SMD likewise reported higher symptom levels. For depression, the mean score was 0.99 (95% CI 0.75-1.23) in the SMD group compared with 0.36 (95% CI 0.300.46) in the control group. For anxiety, the mean score was 0.73 (95% CI: 0.530.94) among patients with SMD compared to 0.30 (95% CI: 0.23-0.38) among those without SMD. Both domains corresponded to mean ratios of approximately two and a half, indicating more than a twofold higher symptom burden among patients with pre-existing SMD.

Patients with pre-existing SMD scored higher symptom burden than the control group in the domains of anger, interpersonal sensitivity, and psychoticism, with mean ratios of 4.57 (95% CI: 2.69-7.77), 5.24 (95% CI: 3.45-7.97), and 3.92 (95% CI: 2.54-6.05), respectively. These findings indicate substantially elevated symptom levels across multiple affective and interpersonal domains among patients with pre-existing SMD when entering cancer treatment.

Table 3: Symptom Checklist-92 (SCL-92) scores at beginning of cancer treatment

	Items*	Patients with SMD n = 36+ Mean (95% CI)	Control group n = 80 Mean (95% CI)	Mean ratio (95% CI)
SCL-92 global score	All 92 items	0.74 (0.56-0.91)	0.25 (0.20-0.30)	2.95 (2.19-3.98)
Somatization	1,4,12,27,40,42, 48,49,52,53,56,58	0.71 (0.54-0.87)	0.35 (0.27-0.43)	2.05 (1.48-2.84)
Anxiety	2,17,23,33,39, 57,72,78,80,86	0.73 (0.53-0.94)	0.30 (0.23-0.38)	2.42 (1.69-3.49)
Interpersonal sensitivity	6,21,34,36, 37,41,61,69,73	0.73 (0.50-0.95)	0.14 (0.10-0.18)	5.24 (3.45-7.97)
Phobic Anxiety	13,25,47, 50,70,75,82	0.48 (0.26-0.71)	0.03 (0.01-0.05)	14.27 (6.85-29.72)
Obsessive-Compulsive	3,9,10,28,38, 45,46,51,55,65	1.02 (0.27-0.43)	0.35 (0.27-0.43)	2.92 (2.11-4.03)
Depression	5,14,15,20,22,26, 29,30,31,32,54,71,79	0.99 (0.75-1.23)	0.36 (0.30-0.46)	2.58 (1.88-3.54)
Anger	11,24,63, 67,74,81	0.50 (0.29-0.70)	0.11 (1.88-3.54)	4.57 (2.69-7.77)
Hostility	8,18,43, 68,76,83	0.39 (0.23-0.56)	0.05 (0.02-0.08)	7.56 (3.64-15.69)
Psychoticism	7,16,35,62,77, 84,85,87,88,90	0.40 (0.27-0.52)	0.10 (0.07-0.13)	3.92 (2.54-6.05)

* Item number(s) in SCL-92

+ Only 36 out of 40 patients completed the questionnaire

Discussion

Main findings

In this study, patients with cancer and pre-existing SMD demonstrated substantially poorer HRQoL and higher physical and psychiatric symptom burden compared with matched patients without SMD when entering cancer treatment. Although the groups were comparable in cancer type and treatment intent, patients with SMD differed significantly from controls in sociodemographic characteristics and patterns of social support. Especially when it came to pain, phobic anxiety and hostility, patients with pre-existing SMD had a significantly higher symptom burden than the control group. These findings indicate that patients with cancer and pre-existing SMD enter cancer treatment with a more vulnerable psychosocial profile, lower quality of life, and markedly higher physical and psychiatric symptom burden than patients with cancer without SMD at the beginning of cancer treatment.

The present study is to the best of our knowledge the first to compare HRQoL and psychiatric symptoms between patients with cancer and with and without SMD, thereby reinforce existing evidence that individuals with SMD experience structural disadvantages and psychosocial challenges that may shape their cancer care experiences and treatment outcomes [6,24].

The lower HRQoL observed among patients with SMD across physical and emotional domains, combined with higher levels of symptom burden, e.g. fatigue, pain, dyspnoea, and insomnia, suggests that patients with SMD may enter cancer treatment with a compromised physical and emotional state. Previous research has shown that pre-treatment symptom burden is strongly associated with lower tolerance of treatment, which may increase the risk of early discontinuation and lower survival [25]. The presence of both physical and psychiatric symptom complexity may therefore place this patient group at particular risk of unmet supportive care needs during the cancer trajectory.

As expected, patients with cancer and SMD showed a higher overall psychiatric symptom burden on the SCL-92 scale compared to patients without SMD. The psychiatric symptom patterns were notable not only for depression and anxiety, but also enlightened disproportionate high scores in phobic anxiety, hostility, and interpersonal sensitivity. These domains may influence communication, adherence, and help-seeking behaviour during oncology care. The nearly threefold higher Global Severity Index score among patients with SMD underscores the extent of psychological distress at cancer treatment onset and suggests the need for routine, structured psychiatric assessment or psychological intervention integrated into oncology care. However, it remains unclear whether the observed differences in symptom burden reflect the difference in impact of a newly diagnosed cancer on the two groups or represent an underlying difference between the two groups.

Differences in social support structures also appeared clinically relevant. Patients with SMD were less likely to designate a partner as next of kin and more often relied on friends, colleagues, or adult children. The absence of a cohabitating partner has previously been associated with increased caregiver burden placed on alternative contacts and may complicate coordination of appointments, shared decision-making, and symptom monitoring [26]. Moreover, social isolation has been linked to higher mortality among breast cancer patients, likely reflecting reduced access to practical support and the absence of close relational caregiving during treatment [27]. Conversely, patients with SMD more frequently reported a stable relationship with their general practitioner, suggesting that primary care serves as a key continuity anchor in their care network. Leveraging this existing therapeutic relationship could be beneficial in care coordination, particularly during transitions between psychiatric, oncology, and community services.

A British study has attempted to quantify a clinically meaningful change in EORTC scores [28]. Hammelid et al. reported that a change of 10–20 points correspond to a “moderate” perceived change, whereas changes greater than 20 points reflect a “very much” perceived change. In the present study, score differences between groups of moderate to very high clinical relevance was observed for overall quality of life, physical and emotional functioning, fatigue, pain, and dyspnoea. This substantial difference in HRQoL scores between patients with cancer and pre-existing SMD and controls is consistent with findings from a Danish normative population study [29]. In the Danish reference population, the mean Global Health Status score was 73, compared with 56.67 among patients with cancer and pre-existing SMD. Similar differences were observed across physical functioning, emotional functioning, and symptom scales.

Interestingly, the control group without pre-existing SMD in this study scored higher than the Danish reference population on both the physical and emotional functioning scales, and only slightly lower on Global Health Status (69.01 vs. 73) [29]. The same were observed for the SCL scale where patients without SMD reported a lower psychiatric symptom burden than the general Danish population [16]. The reason for this remains unclear but it is probably mainly due to the relative low number of participants. Though the Danish reference population completed the EORTC QLQ-C30 questionnaire while the control group in the present study completed the EORTC QLQ-C15-PAL, the two instruments are considered sufficiently comparable for use in this context [30]. A plausible explanation for the observed differences could also be the relatively low median age in the present sample. Age-stratified analyses in the Danish reference population show smaller between-group differences in younger individuals, although one would still expect a higher symptom burden among patients with cancer [30].

Implications

Clinical implications

The findings from the present study have important clinical implications and reinforce existing evidence that patients with cancer and pre-existing SMD encounter challenges already in the beginning of their cancer trajectory [6,24].

First, systematic identification of psychiatric symptom severity and psychosocial vulnerability at the time of cancer diagnosis is essential, as early stratification can guide the provision of tailored supportive care which have shown to lower cancer treatment disruptions and improved psychiatric illness severity and anxiety [31].

Secondly, integrating psychiatry or psycho-oncology services directly within cancer care pathways has been shown to enhance continuity, improve communication across disciplines, and support emotional regulation and treatment adherence [31,32]. Therefore, consideration should be given to integrating differential monitoring strategies, liaison psychiatry involvement, and psychosocial support interventions into cancer care pathways.

Thirdly, proactive management of key symptoms, particularly targeting fatigue, sleep disturbance, and pain, is likely to mitigate declines in HRQoL and improve treatment tolerance, especially among patients with co-occurring psychiatric conditions. Therefore, as highlighted by Grassi et al., there is a need to increase clinical awareness and provide clear guidance on how to optimally support patients with pre-existing SMD throughout their cancer care [33].

Research implications

The inequality and barriers for patients with cancer and pre-existing SMD have been known for a long time; however, this is the first study to investigate HRQoL and psychiatric symptoms when entering cancer treatment between patients with and without SMD. These findings thereby indicate several important directions for future research.

First, studies should evaluate how systematic screening for psychiatric symptoms and psychosocial vulnerability at the time of cancer diagnosis can be integrated into routine oncology workflows and whether this improves outcomes for patients with pre-existing SMD. The SCL-92 questionnaire has previously been described as long and burdensome in clinical settings, and in this study not all participants with pre-existing SMD were able to complete it in full [32]. Given that patients with SMD reported particularly high symptom levels in the domains of phobic anxiety, hostility, depression, and anxiety, the shorter SCL-28 may represent a more pragmatic alternative in routine clinical practice. The SCL-28 captures these core symptom dimensions while substantially reducing respondent burden, thereby potentially improving completion rates and feasibility in vulnerable patient populations [34].

Secondly, there is a need for intervention studies testing models of integrated or collaborative care that strengthen coordination between oncology, psychiatry, and primary

care and if these interventions, can mitigate the observed deficits in HRQoL and reduce psychiatric symptom burden.

Finally, longitudinal research is needed to clarify how psychiatric symptoms and HRQoL evolve over the cancer trajectory for patients with SMD, including into survivorship and end-of-life care.

Limitations

This study has several limitations. First, the sample size was modest, and although matching reduced confounding related to age and disease characteristics, the patient characteristics indicated residual differences in socioeconomic and health-related factors such as social support, educational level, and smoking and alcohol use. Additionally, the SMD group represented a highly heterogeneous group, ranging from moderate depression to schizophrenia with varying levels of psychiatric severity, and unmeasured factors may also have contributed to the observed group differences. Secondly, symptom assessment relied on patient-reported outcomes, which may be influenced by psychiatric symptom expression and level of illness insight. However, the use of validated and widely applied instruments strengthens the internal validity of the comparisons.

Conclusion

Patients with cancer and pre-existing SMD enter cancer treatment with significantly lower HRQoL, higher physical symptom burden, and substantially elevated psychiatric distress compared with matched controls. Further, patients with SMD enter cancer treatment in lower socioeconomic positions and with poorer social networks, yet more trustful, existing relations to healthcare professionals. These findings underscore the importance of proactive, integrated psychiatric and psychosocial supportive care approaches at the time of cancer diagnosis. Future research should evaluate targeted interventions aimed at strengthening care coordination, optimizing symptom management, and improving social support structures in this high-risk patient population.

Statements and Declarations

Data Availability Statement

The data that support the findings of this study are available in the supplementary material and from the corresponding author upon reasonable request.

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Competing Interests

All authors declare no conflict of interest.

AI statement

During the preparation of this work the authors used ChatGPT in order to improve the readability and language of the work and have not replaced researcher tasks such as producing scientific insights, analysing and interpreting data, or drawing scientific conclusions. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

Author Contributions (CRediT)

Louise Elkjær Fløe: Conceptualization, Investigation, Resources, Validation, Project administration, Funding acquisition, Writing- Reviewing and Editing. **Jesper Grau Eriksen:** Reviewing and Editing. **Poul Videbech**: Reviewing and Editing. **Anna Mygind**: Reviewing and Editing. **Kirstine Bundsbæk Bøndergaard**: Reviewing and Editing. **Mette Asbjoern Neergaard**: Conceptualization, Resources, Validation, Supervision, Funding acquisition, Reviewing and Editing.

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Development of a supportive cancer care model for patients with CAncer and pre-existing SEvere MEntal Disorders

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ABSTRACT

Purpose: Cancer patients with pre-existing severe mental disorders (SMD), including moderate to severe depression, bipolar disorder and schizophrenia, have reduced life expectancy and are less likely to receive optimal cancer treatment. The aim of this study is to develop and pilot test a supportive care model, to enhance cancer care in this population.

Methods: The model was developed through three phases. In phase I, a barrier analysis and prototype of the model were conducted from reviewing the literature and through 162 informal interviews with healthcare professionals, patients and patient representatives. In phase II, the prototype was refined through four workshops with a total of five cancer nurses, four clinical oncologists, three psychiatrists, two general practitioners, one psychologist, and 16 patient representatives. Thereafter, a pilot test with 13 patients was carried out, where continuous adaptations to the prototype from phase II, were made. The quantitative and qualitative data were analysed focusing on components which were prominent and able to fit into the clinical setting.

Results: The final CASEMED supportive cancer care model included: Early identification of psychiatric comorbidity, engagement of significant caregivers, education of the oncological HCPs, securing continuity among staff and enhanced collaboration between sectors. The latter was achieved through an online psychiatric multidisciplinary team conference where the patient's general practitioner, a psychiatrist and the patient's oncologist participated.

Conclusion: This study indicates that the model can be implemented in practice and has the potential to optimize cancer care for patients with cancer and pre-existing SMD. A larger feasibility study is currently being conducted.

1. Introduction

People with severe mental disorders (SMD) (i.e. moderate to severe depression, bipolar disorder, schizophrenia or other psychotic disorders) comprise a vulnerable group of patients with a 2–3 times higher mortality than the general population (WHO guidelines, 2018). The higher mortality also applies to patients with cancer and pre-existing SMD (Manderbacka et al., 2017). The reasons for the high mortality are multifactorial, but patients with SMD are more likely not to receive optimal cancer treatment (Kurashige et al., 2021; Lachina et al., 2017) and are more often diagnosed with more advanced cancer disease (Nordentoft et al., 2021; Bhattacharya et al., 2023). Furthermore, they are less likely to participate in screening programs (Jensen et al., 2016; Kaerlev et al., 2018) and are often not diagnosed through regular cancer patient pathways from primary care (Virgilsen et al., 2022). Thus, they have a higher probability of being diagnosed through unplanned admissions (Virgilsen et al., 2022), which is associated with a poorer cancer prognosis (Danckert et al., 2021). Studies estimate that approximately 5% of the adult population in the world have a mental, behavioural, or emotional disorder that impacts their daily living (National Institute of Mental Health). However, limited knowledge exists concerning healthcare utilisation among cancer patients with pre-existing

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SMD (Humphreys et al., 2015; Howard et al., 2010; Kisely et al., 2013).

Several barriers at patient-, provider- and system levels have been identified towards optimal cancer care, see Appendix 1 for definition (Bentson et al., 2023; Glasdam et al., 2023; Leahy et al., 2021). At the patient level, unstable psychiatric symptoms, cognitive deficits, suboptimal selfcare, and challenges with consent and adherence to treatment have been identified as prominent barriers. At the provider level, lack of identification of psychiatric comorbidity and continuity by healthcare professionals (HCPs), difficulty in assessing the patients' decision-making capacity, evasion of responsibility between sectors, stigma towards the patient group and diagnostic overshadowing are commonly reported obstacles. At the system-level, fragmentation of the healthcare system, lack of systematic coordination between the sectors, limited access to psychiatric expertise and limited time and resources in the oncological clinic are prominent barriers. The existing studies investigating barriers are predominantly from the US or other English-speaking countries (Bentson et al., 2023; Glasdam et al., 2023; Leahy et al., 2021). Yet, a recent anthropological study from Denmark confirms that the above-mentioned barriers also exist in countries with universal healthcare systems where citizens are assured access to healthcare regardless of their social or financial background (Bruun et al., 2024; Bruun et al.). Despite the urgent need for enhancing the care for this patient group, to our knowledge only one model aiming to improve cancer care has been published, namely the BRIDGE model from the US (Irwin et al., 2019). This model includes proactive identification of psychiatric comorbidity, person-centered care by a psychiatrist, a case manager, and enhanced collaboration between psychiatry and oncology. The model was feasible in a US healthcare setting and has been shown to decrease disruptions in cancer care and reduce psychiatric illness severity and anxiety levels in a randomized controlled trial (Irwin et al., 2023). Yet, evidence-based and sustainable models for integrating psychiatry and cancer care in a European context, with more universal healthcare systems, are missing.

Thus, the aim of this study was to develop a patient-centered, interdisciplinary, cross-sectorial, collaborative care model for patients with cancer and pre-existing SMD: The CASEMED supportive cancer care model.

2. Methods

2.1. Design

This intervention development study holds a complex intervention research approach as outlined in the framework developed by the UK Medical Research Council (Skivington et al., 2021). This approach was applied to facilitate sustainable adoption and implementation in a 'real-world' setting (O'Cathain et al., 2019). A co-production participatory approach was applied, focusing on development, adaption, and rapid cycles of evaluation and refinements based on a continuous exchange of insights between the research group and stakeholders (Sandbæk et al., 2022; Hawkins et al., 2017). The study was reported following the Consolidated Criteria for Reporting Qualitative research (COREQ) checklist for qualitative research (Tong et al., 2007), the GUIDED checklist for intervention development (Duncan et al., 2020) and the TIDieR checklist for intervention reporting (Hoffmann et al., 2014). Stakeholders, including Health Care Professionals (HCP), patients and patient representatives were continuously involved in the development of the CAncer and pre-existing SEvere MEntal Disorders (CASEMED) supportive cancer care model, although not involved in the initial design of the study. The grade of involvement and reflection upon this is described in Appendix 2 using the GPIPP2 short form (Staniszewska et al., 2017).

2.2. Setting

Danish health care is based on free and equal access to medical services, which is funded by tax revenues. Furthermore, all Danish citizens are entitled to compensation for loss of income due to unemployment, disability, or illness (The Danish welfare state). There are implemented national cancer pathways for Non-specific Symptoms and Signs of Cancer to ensure standardised and early diagnosis of patients suspected to have cancer. The NSSC-CPPs thereby facilitate early and fast diagnosis, reducing waiting time and ultimately improving prognosis (Jensen et al., 2014). The oncological treatment is centered at the larger hospitals and the majority of the treatment is outpatient treatment (www.sst.dk/da/Fagperson/Sygdomme-lidelser-og-behandling/Kraeftsygdom/Pakkeforloeb-for-kraeft). The treatment of psychiatric diseases is primarily a public task and is managed by the regional authorities. Patients with SMD are treated in hospital settings (in- and outpatient clinics) while milder mental disorders are treated by general practitioners (GPs), private psychiatrists or psychologists (Mors et al., 2011). General practitioners anchor the psychiatric treatment of more than 90% of patients, and they serve as gatekeepers to the healthcare system (Jensen et al., 2014). Hence, the choice between referral to hospital-based mental health care or private psychiatrists is based on the severity and the complexity of the mental disorder. Psychiatric hospital departments work in close collaboration with general practice, community nurses and social services (https://www.rm.dk/om-os/English-Deutsch/english/health/psychiatry/Visited date).

2.3. Data collection and participants

The data collection was structured in three phases (Fig. 1). Insights from each phase were incorporated to facilitate refinements in the next phase. These iterative processes of continuous exchange between practice and research allowed for continuous evaluation and adjustments of the model by the multi-disciplinary research group.

Data were collected from March 2022 to April 2023, involving relevant patients, patient representatives (e.g., patient associations and caregivers), nurses and doctors. The patients participating in Phase III were patients with head and neck, breast or lung cancer and pre-existing SMD. The included ICD-10 codes are presented in appendix 3, and a detailed overview of the 162 participants included in the three phases can be seen in Table 1. All interviews were made by the first author.

2.4. Phase I: barrier analysis

As a basis of this study, the research group conducted a systematic literature review and two anthropological studies (Bentson et al., 2023; Bruun et al., 2024; Bruun et al.). These studies explored barriers and facilitators to optimal cancer care for patients with cancer and pre-existing SMD, focusing on patient, provider, and system levels. In Phase I, the research team analysed these studies to merge identified barriers with suggested intervention components at the three levels. The results were discussed with 102 HCPs and patient representatives through eight group and six individual informal interviews, allowing the participants to comment on ideas for intervention components, or suggest new ones (Table 1). Participants were recruited from hospital departments where the prototype would be tested and their cooperating departments. This included three psychiatric and two oncology departments, a palliative care unit, and related general practices and municipalities. The analyses allowed new barriers and intervention components to emerge and facilitated a prioritization of the existing barriers and intervention components. The informal interviews focused on prominent, clinically relevant barriers and components that could be integrated into the clinical setting. The intervention components were continuously refined by the research team using a rapid cycle approach (Johnson et al., 2015), leading to the development of the first prototype of the model.

2.5. Phase II: stakeholder workshops

During Phase II, four workshops were held with 34 participants, including nurses, physicians, a psychiatrist, general practitioners (GPs),

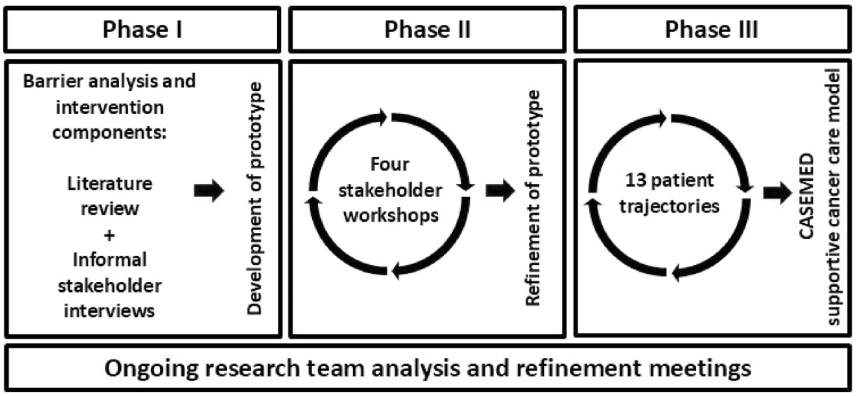

Fig. 1. Development phases of the CASEMED supportive cancer care model.

Table 1
Involved participants in the development phases.

Phase	Data type	Participants					
		Department of oncology	Department of psychiatry	General practice	Other healthcare professionals	Patients and patient representatives	Total number of participants
I	Informal interviews	24 physicians from two outpatient clinics 27 nurses from two outpatient clinics	35 physicians from three departments	Two general practitioners	10 health and social care professionals from the Specialised Palliative Care Unit One psychologist from the Department of Oncology One Advance Practice Nurse from the municipality One social nurse from a University Hospital	One representative from a cancer care organisation	102
II	Workshop I	Four oncologists (O1-4)	Three psychiatrists (Ps1-3) One research assistant (OH1)	Two general practitioners (GP1-2)			10
	Workshop II	Four nurses (N1-4)	One nurse (N5)		One psychologist from the Department of Oncology (OHCP2) One social nurse from Aarhus University Hospital (N6)	Two representatives from a cancer care organisation (PR1-2)	9
	Workshop III					Eight patient representatives from a national psychiatric care organisation (PR3-10)	8
	Workshop IV					Six patient representatives from a national psychiatric care organisation (PR10-16)	6
III	Pilot	Two oncologists O5-6 Two nurses N7-8	One psychiatrist Ps1	Three general practitioners GP3-5		Thirteen patients with cancer and pre-existing SMD (P1-13) and the relatives to six of them (PR17-22)	27

*P= Patients, PR = Patient representatives, N=Nurses, GP=General practitioners, Ps = Psychiatrists, O = Oncologists, OHCP = Other healthcare professionals, n = Numbers.

and patient representatives (Table 1). The HCPs were recruited via the research group's network and a broad invitation to doctors and nurses in the psychiatric and oncology departments at the participating hospital. Patient representatives were sourced from two national non-profit psychiatric patient organizations and one cancer organization to ensure diverse perspectives, knowledge, and expertise. This phase aimed to refine the prototype developed in Phase I using a co-production process and make it ready for pilot test. In the workshops, the participants provided feedback on the prototype, and were engaged in developing new intervention components, prioritizing existing ones, and identifying key uncertainties about the implementation of the components. The workshops were video-recorded and lasted between 37 min and 2 h (in average 78 min). A trained anthropologist took observation notes and the data were analysed to identify significant themes relevant to the refinement of the prototype, including successful patient trajectories, important psychosocial aspects to discuss with patients, and potential collaboration models between sectors. The analysis aimed to make the model flexible and easy to implement in clinical settings, using a rapid cycle approach (Johnson et al., 2015). The research group discussed drafts of the prototype based on workshop results, resolving dilemmas and reaching consensus on the refined version.

2.6. Phase III: pilot test

In Phase III, the refined prototype was tested among 13 patients from two outpatient clinics at a Danish University Hospital. The project participants were identified systematically using electronic patient records and were all newly referred patients with head and neck, breast, or lung cancer and a known pre-existing SMD (Table 1). Pre-existing SMD was defined as having a SMD diagnosis registered in a Danish hospital record within the last 10 years. All eligible patients were registered ensuring that all relevant patients were identified, thus reducing the risk of selection bias.

The first five patients tested only part of the model, while the next eight tested the full prototype. To understand the feasibility and acceptability of the prototype, feedback was collected from patients, their relatives, and HCPs. Patients provided their perspectives through focused observations and informal interviews during and after testing the prototype. HCPs were interviewed with focus on the prototype's sustainability, meaningfulness, and clinical relevance. The data were analysed to identify key uncertainties and impact of the intervention components. The findings were discussed within the research group, leading to refinements and the final version of the prototype.

2.7. Ethical considerations

The study complied with the Declaration of Helsinki, which outlines general ethical principles for good medical research practice (World Medical Association, 2013). All participants received written and oral information about the study and gave verbal and written consent to participate. They were informed that participation was voluntary and that they could withdraw from the study at any time. According to the Danish National Committee on Health Research Ethics, this study could not be considered for approval as it did not include human biological material (act number 1-16-02-249-22) (Danish National Center for Ethics, 2024).

Data storage and access complied with the General Data Protection Regulation (GDPR) of the European Union (The European Parliament and the Council of the European Union, 2016). The data are stored at The Central Region of Denmark act number 1-10-72-1-22.

3. Results

Throughout the development phases the prototype was refined into a final model. The intervention components are described in detail in Table 2. In the following sections, we will present the development process by reporting the findings from phases I-III.

3.1. Phase I: development of the prototype

In this phase, we identified various barriers to optimal cancer care at the patient, provider, and system levels, along with suggestions for new intervention components (see Table 3). Patient-level barriers were seen as issues that could be addressed by providers or the healthcare system, as all stakeholders agreed that the system ought to be able to adjust to the patients' needs. Stakeholders emphasized the importance of creating a model which was not time-consuming for clinics to avoid wasting resources. The interviews supported the literature findings and helped prioritize them. The most important and implementable barriers and suggested intervention components identified in the barrier analysis are presented below.

3.1.1. Patient level: identification of psychiatric comorbidity and a person-centered approach

The stakeholders confirmed that unstable psychiatric and physical symptoms, poor self-care, and low treatment adherence were major barriers to optimal cancer care for patients with pre-existing SMD. They also highlighted the lack of identification of psychiatric comorbidity as a key issue. While most HCPs agreed on the importance of identifying psychiatric comorbidity, some worried it might stigmatize patients further. However, patient representatives emphasized that patients expect their HCPs to be aware of their psychiatric comorbidity, and not addressing these would increase stigma. The barrier analysis revealed that the most important and implementable solutions to overcome these barriers included a patient-centered approach and systematically identifying psychiatric comorbidity and symptoms through questionnaires early in the cancer treatment process in order to stabilise somatic and psychiatric symptoms.

3.1.2. Provider level: engagement of caregivers, pro-activity and a systematic approach

Corresponding to the existing literature, both clinical oncologists and psychiatrists found it challenging to assess the patients' decision-making capacity, especially when patients lacked significant caregivers. As a consequence, some HCPs feared causing more harm than good, as cancer treatments can have serious side effects if not managed promptly. Therefore, identifying and involving potential caregivers (like family members, colleagues, neighbours, or friends) and HCPs from other areas (such as GPs, psychiatric or home care nurses) at the first visit was considered essential. Stakeholders also noted a lack of understanding about the needs of these patients. They felt efforts were being made, but practices varied between clinicians with no systematic approach. This inconsistency could lead to unequal access to healthcare for patients

Table 2
The intervention components in the CASEMED supportive cancer care model

Intervention component	Description of the intervention component
Identification of psychiatric comorbidity	Systematic electronic identification of patients with pre-existing SMD* recorded in the hospital journal within the last 10 years, and highlighting the psychiatric comorbidity at the first visit at the Department of Oncology.
Patient-centered approach	Questionnaires to screen for psychiatric symptoms (SCL-92) and health-related quality of life (EORTC PAL-15) distributed to the patient at the first encounter at the Department of Oncology together with screening for alcohol or drug abuse, preferred communication form and three open-ended patient-centered questions.
Engagement of significant caregivers	The oncologist investigates the patient's private and professional network at the first visit.
Enhanced collaboration between sectors	An online opMDT* conference between the oncologist from the patients' initial consult, the patient's general practitioner and a psychiatrist, discussing the patients' resources, medication, housing conditions, nutrition, possible substance abuse, need for follow up and the need for referral to the psychiatric ward.
Education of the oncological HCPs	An online document available for the HCPs*, concerning supportive offers for patients with SMD together with an educational programme with visit from a patient with SMD.
Continuity among HCPs	Prioritising continuity among HCPs by highlighting the name og the HCP in the secretary notes and the electronic booking system.

*SMD: Severe mental disorders, opMDT: Onco-psychiatric multidisciplinary team conference, HCP: Healthcare professionals.

Tabel 3
Barriers for optimal cancer care for patients with pre-existing SMD and corresponding intervention components.

Level	Barriers	Possible intervention components			Final intervention components
		Phase I	Phase II	Phase III	
Patient level	Lack of systematic identification	Identification of psychiatric comorbidity	Addressing psychiatric comorbidity Electronic screening for SMD in the journal		**Identification of psychiatric comorbidity** Electronic screening for SMD in the journal Addressing psychiatric comorbidity at the first visit
	Unstable psychiatric symptoms (Bentson et al., 2023; Leahy et al., 2021)	Initial screening of symptoms	Screening of psychiatric symptoms and quality of life though SCL-92* and EORTC-PAL-15* questionnaires		**Patient-centered approach** Through SCL 92 and EORTC QLQ-C15-PAL questionnaires
	Social isolation (Glasdam et al., 2023) Difficulties comprehending information about diagnosis and treatment plan. (Bentson et al., 2023; Glasdam et al., 2023) Lack of social or economic resources Struggle with information about diagnosis and treatment plan (Bentson et al., 2023) Neglect of self-care needs (Bentson et al., 2023; Leahy et al., 2021)	Identification and engaging private and professional caregivers	Individual treatment plans instead of a fixed intervention		**Engagement of significant caregivers** Identification and engaging of private and professional caregivers **Patient-centered approach** Individual treatment plans instead of a fixed intervention
	Mistrust towards the health care system and HCPs Lack of consent to carry out cancer treatment and rejection of supportive initiatives form the HCP (Bentson et al., 2023; Glasdam et al., 2023) Difficulties in noticing physical abnormalities and communicating symptoms (Bentson et al., 2023) Lack of compliances and treatment adherence [15–17)	Continuity among HCPs	Enhanced notifications in the booking system and prioritising of the group		**Continuity among HCPs** Through notifications in the booking system and prioritising of the group
	Abuse of alcohol or drugs (Bentson et al., 2023; Glasdam et al., 2023; Leahy et al., 2021)		Screening for alcohol or drug abuse		**Patient-centered approach** Screening for alcohol or drug abuse
	Lack of use of electronic solutions to get in touch with the patient		Screening for preferred communication form up front		**Patient-centered approach** Screen for preferred communication form up front
Provider level	Limited resources and time to communicate with patients and coordinate with their primary psychiatric care services for cancer professionals (Bentson et al., 2023; Leahy et al., 2021) Fear of doing more harm than good Confusion in who is responsible for the different parts of the treatment between health care sector (Bentson et al., 2023) Difficulties determining whether cancer or psychiatric illness should be prioritised (Bentson et al., 2023; Glasdam et al., 2023)	Enhancing collaboration through opMDT	opMDT visitation checklist	A list of fixed subject to GPs as preparation for opMDT Correspondence letter afterwards to the GPs*	**Enhanced collaboration between sectors** Through opMDTs, checklists and a correspondence letter afterwards to the GPs.
	Lack of assessing a patient's decision-making capacity (Bentson et al., 2023; Glasdam et al., 2023) Stigma towards patients with psychiatric diseases (Bentson et al., 2023; Leahy et al., 2021) Providers feeling ill-equipped to deal with mental health needs (Bentson et al., 2023; Glasdam et al., 2023; Leahy et al., 2021) Diagnostic overshadowing (Bentson et al., 2023; Leahy et al., 2021)	Education of HCPs opMDT Continuity among HCPs	Leaning event with patients with severe mental disorders		**Education of the oncological HCPs** Through learning event with patients with severe mental disorders and development of electronic guidelines **Continuity among HCPs**
System level	Fragmentation of cancer and mental health care and lack of coordination between sectors (Bentson et al., 2023; Leahy et al., 2021) Prioritising patients with pre-existing SMD Lack of knowledges of interactions between psychopharmaca and cancer treatment (Bentson et al., 2023) Limited access or long waiting list to psychiatry (Bentson et al., 2023)	Enhancing collaboration through a opMDT		opMDT every week with the possibility of a repeated opMDT Prolonged noticed of opMDT to GPs and psychiatrist	**Enhancing collaboration between sectors** Through opMDTs every week to prolong noticed to collaborators and with the possibility of a repeated opMDT
	Lack of continuity among HCPs	Enhancing continuity among HCPs			**Continuity among HCPs**

HPC: Healthcare professionals, opMDT: Onco-psychiatric multidisciplinary team conferences, GP: General practitioners, SCL92: Symptom Checklist 92, EORTC-PAL-15: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core-15 Palliative.

with pre-existing SMD. Stakeholders shared past experiences of such inequalities, including delays in identifying challenges for patients getting cancer treatment, which could have been improved with proactive support. The stakeholders also observed that the lack of supportive elements often led to many unscheduled contacts to the oncology department, and patients either dropping out of treatment or never initiating it. Thus, a more systematic and proactive approach are needed. This includes identifying and engaging caregivers and HCPs from other sectors, and training oncology HCPs in communication and supporting patients with SMD, to improve cancer care.

3.1.3. System level: continuity and collaboration

Both physicians and nurses found that the health care system favoured standardised trajectories and did not offer many possibilities to adjust care trajectories to each patient's needs and resources. Combined with limited time in clinical everyday life, this lack of flexibility made it complicated for the HCPs to adjust the treatment plans for patients with pre-existing SMD. It was easier to assess the patient's needs when the same HCPs were in charge during the cancer treatment, and continuity was therefore considered an important intervention component. Another dominant theme raised by the stakeholders was the fragmentation of the healthcare system hampering the HCPs' coordination of care and sharing valuable information about the patient with other departments or sectors. Therefore, an online onco-psychiatric multidisciplinary team conference (opMDT) between general practice, psychiatry, oncology and other relevant specialities was developed with input from the stakeholders. An MDT is a well-known form of collaboration between different multidisciplinary sectors at the hospital, why this collaboration form was preferable to ensure easy implementation.

3.1.4. The prototype after phase I

From Phase I, a prototype of the CASEMED supportive cancer care model was developed. The prototype entailed the following components: initial screening for psychiatric comorbidity and symptoms, identification and engagement of significant caregivers and HCPs in other healthcare sectors, enhanced continuity and education of HCPs and enhanced collaboration between healthcare sectors through an opMDT.

3.2. Phase II: refinement of the prototype

3.2.1. Overall assessment of the prototype from phase I

In the workshops, the HCPs found that the prototype was manageable in the daily workflow and all intervention components were considered recognisable and meaningful to the clinicians. The patient representatives especially favoured the person-centered approach where HCPs could tailor the care plan, and the enhanced collaboration within and across sectors beneficial for the cancer care. Therefore, in this phase, no additional intervention components were added, and none were rejected. Rather, refinements were made for several intervention components (Table 3). The most important refinements are presented below.

3.2.2. A person-centered approach

In order to enhance the person-centered approach, the stakeholders found it important to stabilise psychiatric and somatic symptoms at the beginning of the cancer treatment. Some HCPs, however, worried about the load on the patients when filling out the questionnaires. Therefore, the number of questionnaires was minimized, focusing on making a broad description of their possible psychiatric and physical symptoms (symptom checklist 92, SCL-92 (Olsen et al., 2004)) and assessing their health-related quality of life (European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core-15 Palliative (EORTCQLQ-C15-PAL) (Groenvold et al., 2006)), all validated in Danish. Additionally, in order to enhance the patient-centered approach, three questions about what could help the patients through the treatment, whom to contact if they didn't show up at their appointments at the hospital and what they considered would be the biggest challenges for them during treatment were added (Appendix 4).

3.2.3. Enhancing continuity among HCPs

All participants agreed that continuity was a key component to achieving a beneficial treatment alliance. Some expressed a need for a "case manager", described as a HCP who was specially assigned to guide and support the patient all the way through the system. Several concerns emerged during the discussions about adding a case manager to the model. A major concern against implementation was the financial resources to cover the salary. Therefore, a case manager was not included in the final model. Instead, continuity should be prioritised in daily clinical practice. However, some HCPs experienced that continuity was desirable but sometimes difficult to organise. A HCP explained:

> *"Continuity is something that we all want, but my experience tells me that it is something that can be difficult to fulfil, even though it is actually in everyone's interest and everyone wants it"* Physician at the department of oncology (O3)

To accommodate these barriers for achieving continuity, we added enhanced notifications in the booking system to make it clear which HCP were responsible for the individual patient.

3.2.4. Education of HCPs

Some oncology HCPs expressed a lack of knowledge about how to enhance care for and communication with patients with SMD. At the same time, they articulated frustration with the inconsistencies in the care and support offered to patients with SMD, as the different offers often were locally anchored in the municipalities and were distributed geographically unequally. The HCPs worried that an even greater information load concerning the care and support offers would be added to the clinic. Therefore, an easily accessible online document was developed containing information about local care initiatives, including contact information. Further, the oncology clinics were offered a visit by a patient with a psychiatric diagnosis for the HCPs to hear a personal experience. The purpose was to enhance the dialogue and reduce stigma, as these were the most prominent themes raised by the participants at the workshops.

3.2.5. Enhancing the collaboration between sectors

In Phase I, the need for an enhanced collaboration between sectors were highlighted and the HCPs in the workshops all agreed that it was crucial that the collaboration approach was easily acceptable and where it was possible to bring all the stakeholders together in the same session to ensure quick and informed decisions between the sectors. The stakeholders found the opMDTs valuable and only a few technical adjustments were suggested during the workshops.

> *"I think that it (the opMDT) will facilitate our work, by getting a good start and making it more appropriate from the start. Patients are so different, so it is important to get all the way around"* Nurse from the radiotherapy department (N4)

Therefore, an opMDT checklist was developed in collaboration with the participants to cover all important topics, including questions about substance abuse and preferred communication methods. During workshops, it was thoroughly discussed whether it was beneficial and meaningful to have the patients participate in the opMDT or not. While including patients would enhance a person-centered approach, it would also increase their workload and lengthen the opMDT. The GPs felt this would make it harder for all HCPs to participate. Patient representatives agreed, preferring full sector representation due to past disagreements over responsibilities. Ultimately, it was decided not to include patients, which also had the benefit that it made the conference an open space for HCPs to discuss different treatment solutions. GPs were invited to the online conference via a correspondence letter, with instructions to communicate relevant attention points about the patient or trajectory if

they were unable to attend. At this point stakeholders identified two key uncertainties: first, whether the patients would have the necessary resources to participate in the model, second, if the HCPs would be able to prioritize the opMDT in the daily clinic. Therefore, it was decided that the opMDT ought to be held in the afternoon when both hospital doctors and GPs were less likely to have appointments.

3.2.6. The prototype after phase II

The refinements in the end of Phase II included; electronic screening for psychiatric comorbidity and addressing the comorbidity at the first visit, screening for physical symptoms and quality of life through two questionnaires and three additional questions. As to that, electronic guidelines and learning events were developed to enhance the education for the oncology HCPs. To ensure continuity, enhanced notifications in the electronic booking system were also added.

3.3. Phase III: the final CASEMED model

3.3.1. Overall assessment

In general, the HCPs found the prototype from Phase II beneficial for the patients. It was easy to implement, and the continuity was preferable for both the patients and the HCPs. All the HCPs found that the interdisciplinary discussions in the opMDT enhanced the cancer care. The GPs especially valued the greater insight into the oncological treatment gathered from the opMDT, helping them understand what their patients were going through and in what way they could support them. The oncologist and psychiatrist found the discussions particularly beneficial when the GPs attended as they added valuable information about the patients. The patients also expressed that they felt safe when their case was discussed both by multiple HCPs but also by their GP, who often knew them well.

3.3.2. Participation

The electronic system detected 21 patients electable for participation during the time of the pilot test. Thirteen patients agreed to participate in the project, whereas four patients declined and another four did not get the offer due to logistics. A patient elaborated on why he did not want to participate:

> *"I don't feel mentally ill. I had a major depression eight years ago, but right now I am fine"* Patient at the department of oncology (P1)

Another patient did not experience a need for a more targeted intervention and said:

> "*I already have a nice team of doctors, psychologists and nurses around me. I don't need further support*" Patient at the department of oncology (P4)

Thus, non-participation was related to patients not perceiving the need for additional care. Consequently, it was not the most physical or mentally ill patients who declined participation, quite the contrary. All but one patient succeeded in filling in the questionnaires. The patient who did not answer the questionnaires but participated in the intervention was an elderly woman with disseminated mammary cancer, brain metastasis and paranoid schizophrenia. She was living in a nursing home and described as having performance status 3 (WHO-performance scale). In all, the participants found the prototype acceptable, thus no adjustments were added to this part.

3.3.3. The opMDT

The GPs participated online in three cases and in another four cases by correspondence letter. Generally, the GPs were positive towards the prototype of the model and the topics discussed at the opMDT. They found it meaningful to participate but struggled with the short notice. To accommodate this, the prototype was changed to ensure the GPs minimum of one week's notice and the opMDT were made weekly. It was also decided that if a treatment didn't go as planned it would be possible to arrange a new opMDT to coordinate the further treatment plan. A GP expressed that he was unsure about what information the department of oncology wanted, as he wished to be as prepared as possible. Therefore, a list of relevant fixed topics to discuss at the conferences was also attached to the initial correspondence letter to the GP, to make the preparation as precise as possible. Several GPs expressed that they wanted to participate but were unable to attend due to logistics. To ensure that they still got the relevant information, a correspondence letter with a copy of the conclusion of the opMDT stated in the patient's hospital file was sent to the GPs after the opMDT, whether the GP participated in the opMDT or not, to enhance the collaboration and communication between the sectors.

3.3.4. The final model

Results from all three phases were combined to create the final model, called the CASEMED supportive cancer care model (Fig. 2).

Fig. 2 illustrates how the model is expected to work and under which conditions. It represents the connection between the planned activities (intervention components), intended results (output and outcome), and the context in which the model is delivered.

As presented in Fig. 2, we expect this model to improve cancer care for patients with pre-existing SMD. Ideally, each patient experiences a cancer trajectory where their personal preferences are taken into account and where they are met by a high grade of continuity and collaboration across sectors. Identifying SMD aims to normalize it as a comorbidity, similar to other physical comorbidities, reducing stigma and increasing focus on this group in both the short and long term. The opMDT, collaboration with general practitioners, and continuity among staff will improve collaboration between patients and HCPs, as well as among HCP themselves, in the short term. In the long term, this improved collaboration could reduce the fragmentation of the healthcare system. Ultimately, the model aims to support the delivery of cancer care and, over time, improve survival rates among people with cancer and pre-existing SMD.

4. Discussion

4.1. Main findings

In this study, we developed the CASEMED supportive cancer care model, a patient-centered, cross-sectorial, interdisciplinary, and collaborative care model between general practice, the department of psychiatry and the department of oncology to enhance cancer care for patients with pre-existing SMD. The final model included early identification of psychiatric comorbidity, screening of symptoms, engagement of significant caregivers, continuity among HCPs, education of the oncology HCPs and finally enhanced collaboration between sectors through the opMDT. The study indicated that the model fitted well with the existing workflow at the local oncology department, using known communication and collaboration strategies (correspondence letters, MDTs, telephone consultations etc.). The intervention components were perceived as meaningful for both doctors, nurses, patients, and their relatives.

4.2. Strengths and limitations

The main strengths of this study lie in its comprehensive approach, applying various data sources like barrier analysis, interviews, group discussions, and workshops with patients, patient representatives, and HCPs. The involvement across health care sectors and of both patients and professionals offered valuable insights into different perspectives and clarified existing procedures and capabilities across all levels. The iterative method enabled the research team to tackle and adjust implementation issues during the design phase to overcome common clinic barriers.

Limitations include a small pilot sample size, diverse patient

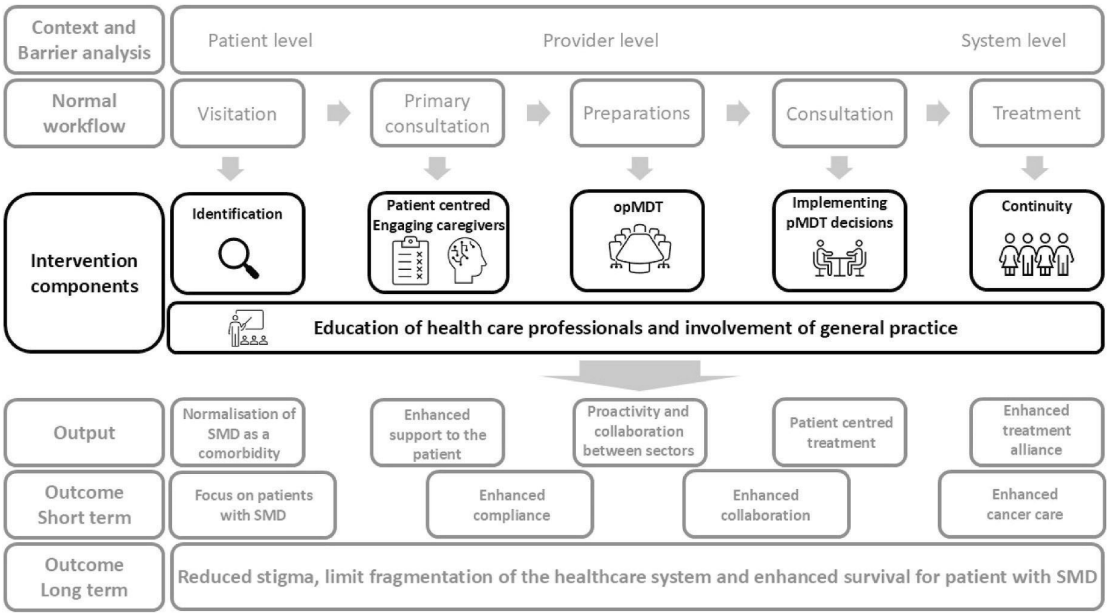

Fig. 2. The CASEMED supportive cancer care model.

populations, and lack of a full-scale feasibility study. Also, professional participants were more dominantly involved in the early phases compared to patients. The model was tested in only two oncology clinics, missing broader insights. Understanding key uncertainties about engaging primary care, prioritising patients, and ensuring continuity among HCPs require a full-scale feasibility study.

4.3. Discussion of results

Despite increasing international recognition that psychosocial care is essential for quality cancer care (Jacobsen and Wagner, 2012; Pirl et al., 2014), and growing awareness that patients with pre-existing SMD experience inequities in cancer treatment, research on potential solutions remains limited. Oncology teams have little guidance and limited resources regarding how to effectively integrate psychosocial care into the clinic. To our knowledge, we have conducted the first systematically developed model targeting patients with cancer and pre-existing SMD in Europe integrating both knowledge from research and co-production with stakeholders.

4.3.1. A systematic approach to patient-centeredness

The model promotes a systematic focus on psychosocial topics and patient preferences, aiming to save time in clinics. Many HCPs expressed a need for more time to create effective, sustainable treatment plans and coordinate care for patients with pre-existing SMD, as noted in previous studies (D'Alton et al., 2021). Involving patients with SMD in research and identifying psychiatric comorbidities can reduce mental illness stigma (Thornicroft et al., 2022; Amanda Maranzan, 2016). Even though lack of education was a frequent topic among the HCPs, another way to address patients with complex medical and social challenges could have been though contextualising care (Weiner and Schwartz, 2015) Addressing patients with complex challenges through contextualized care, brings care beyond standard guidelines and checklists.

4.3.2. Enhancing cancer care through collaboration and continuity

Our study supports the BRIDGE model's emphasis on interdisciplinary collaboration to improve cancer care for patients (Irwin et al., 2019). The CASEMED model fosters interdisciplinary engagement and may mitigate social inequality in cancer care. Involving psychiatric expertise early in cancer diagnosis can reduce care disruptions and improve patient outcomes. The study also emphasises the importance of continuity among HCPs to enhance cancer care, as literature shows it enhances safety and reduces mortality (Pereira Gray et al., 2018). Applying such continuity in oncology clinics could yield similar benefits.

4.3.3. Dissemination of the model in a wider context

Although the intervention components have been developed in collaboration with patients with head and neck, breast and lung cancer and pre-existing SMD, it can be argued that this model is not exclusive to supporting this group of patients. The model is not specific to cancer diagnoses or cancer treatment types nor does the different psychiatric disorders have any impact on the different components of the intervention. The model has a patient-centered approach with a focus on collaboration, interdisciplinarity and continuity why this model might also be suitable for other vulnerable patients irrespective of their cancer or psychiatric disorders. The components of the model could be transferred to other specialities at the hospital, with consideration for adaptation when moving the model to another context (Moore et al., 2021).

4.4. Implications and further studies

Overall, the key uncertainties raised by the stakeholders before Phase III seemed to be proven wrong, but to strengthen the reliability of these findings, a feasibility study is currently being conducted at the participating hospital. Here, all consecutively referred patients with head and neck, breast and lung cancer and pre-existing SMD are invited to participate in the CASEMED supportive cancer care model. This study will use a mixed methods approach to ensure a thoroughly evaluation of the feasibility of the model.

5. Conclusion

We partnered with patients, caregivers, GPs, psychiatrists, oncologists, nurses and patient representatives to develop the CASEMED supportive cancer care model. The model included a patient-centered, cross-sectorial, interdisciplinary approach to ensure optimal cancer care for patients with pre-existing SMD. Intervention components consisted of early identification of psychiatric comorbidity, screening of symptoms,

engagement of significant caregivers, continuity among HCPs, education of the oncology HCPs, and finally, enhanced collaboration between sectors through the opMDT. The model holds potential to enhance the cancer care for patients with cancer and pre-existing SMD.

CRediT authorship contribution statement

Louise Elkjær Fløe: Writing – review & editing, Writing – original draft, Visualization, Validation, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Josefine Maria Bruun:** Writing – review & editing, Resources, Data curation. **Jesper Grau Eriksen:** Writing – review & editing, Supervision, Methodology, Formal analysis, Conceptualization. **Poul Videbech:** Writing – review & editing, Supervision, Formal analysis, Conceptualization. **Mette Asbjørn Neergaard:** Writing – review & editing, Supervision, Methodology, Funding acquisition, Conceptualization. **Anna Mygind:** Writing – original draft, Supervision, Methodology, Formal analysis, Data curation, Conceptualization.

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Declaration of competing interest

The authors declare that there is no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejon.2024.102748.

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11.4 Paper IV

Feasibility of a supportive cancer care intervention for patients with pre-existing severe mental disorders – The CASEMED Model

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Abstract

Background

Patients with pre-existing severe mental disorders (SMD) face barriers to optimal cancer treatment. Structured interventions may improve care, but knowledge about their feasibility in daily clinical practice is needed.

Aim

To assess the feasibility of the CASEMED Model.

Methods

This mixed-methods feasibility study was conducted at Aarhus University Hospital and included patients with pre-existing SMD and breast, lung, or head and neck cancer. The intervention components included early detection of psychiatric comorbidity, screening for physical and psychiatric symptoms, involvement of caregivers, continuity, education, and enhanced cross-sector collaboration through an onco-psychiatric multidisciplinary team conference (opMDT). Data were collected from patient records and interviews focusing on intervention delivery, acceptability, burden, unintended consequences, and mechanisms of change.

Results

Of 27 eligible patients, 23 (85%) participated. Patients had breast (48%), lung (26%), or head and neck cancer (26%) and were diagnosed with moderate to severe depression (65%), bipolar affective disorders (26%), or schizophrenia and other psychotic disorders (9%). Overall, the intervention was feasible and well-accepted, with minimal burden reported. It facilitated a multidisciplinary approach, patient-centered care and cross-sector collaboration. The main implementation barriers included difficulties identifying the appropriate target population, lengthy questionnaires, lack of continuity among oncological professionals, and low general practitioner participation in opMDTs.

Conclusion

This feasibility study demonstrates that the CASEMED Model is acceptable and feasible, with a low level of burden and few implementation barriers. The intervention facilitated a multidisciplinary approach with potential to enhance cancer care. Further research is needed to confirm its effectiveness and generalizability in other healthcare settings.

Background

Patients with severe mental disorders (SMD), defined in this study according to the World Health Organization as moderate to severe depression, bipolar affective disorder, schizophrenia, and other psychotic disorders, constitute a particularly vulnerable population with a two- to threefold higher mortality risk compared with the general population [1]. Approximately 6.6% of the Danish adult population lives with SMD, corresponding to roughly 3,200 newly diagnosed cancer patients with pre-existing SMD each year, and the incidence is rising [2,3].

Barriers to optimal cancer treatment for patients with pre-existing SMD are identified at multiple levels [4]. At the patient level, unstable psychiatric symptoms, cognitive deficits, suboptimal self-care, and challenges with consent and adherence to treatment are prominent barriers [4-9]. At the provider level, lack of identification of psychiatric comorbidity, lack of continuity of healthcare professionals (HCPs), difficulties in assessing patients' decision-making capacity, stigma towards the patient group, and diagnostic overshadowing are frequently reported obstacles [4-8]. At the system level, fragmentation of healthcare systems and lack of systematic coordination between mental health and oncology services also remain significant barriers to optimal cancer care [4-6].

Despite the high mortality rate and multiple barriers to optimal cancer treatment, knowledge concerning healthcare utilization and supportive initiatives in this population remains limited [10,11]. Previous studies have suggested a need for systematic and patient-centered support across care pathways. Only two interventions have been described in the literature: the American Bridge intervention [12] and the Danish CASEMED Model [13]. These interventions were developed in different healthcare systems but share a patient-centered, cross-sector, multidisciplinary approach that integrates psychiatry into oncology clinics to facilitate optimal cancer care for patients with pre-existing SMD.
To assess the viability of the CASEMED Model before committing substantial resources to its implementation, this feasibility study was conducted.

Methods

Study Design

This mixed-methods feasibility study was guided by the United Kingdom Medical Research Council's framework for developing and evaluating complex interventions [14]. The study was reported in accordance with the COnsolidated criteria for REporting Qualitative research (COREQ) checklist for qualitative data [15], the Good Reporting of a Mixed Methods Study (GRAMMS) guideline [16], and the Template for Intervention Description and Replication (TIDieR) checklist for intervention reporting [17].

Setting

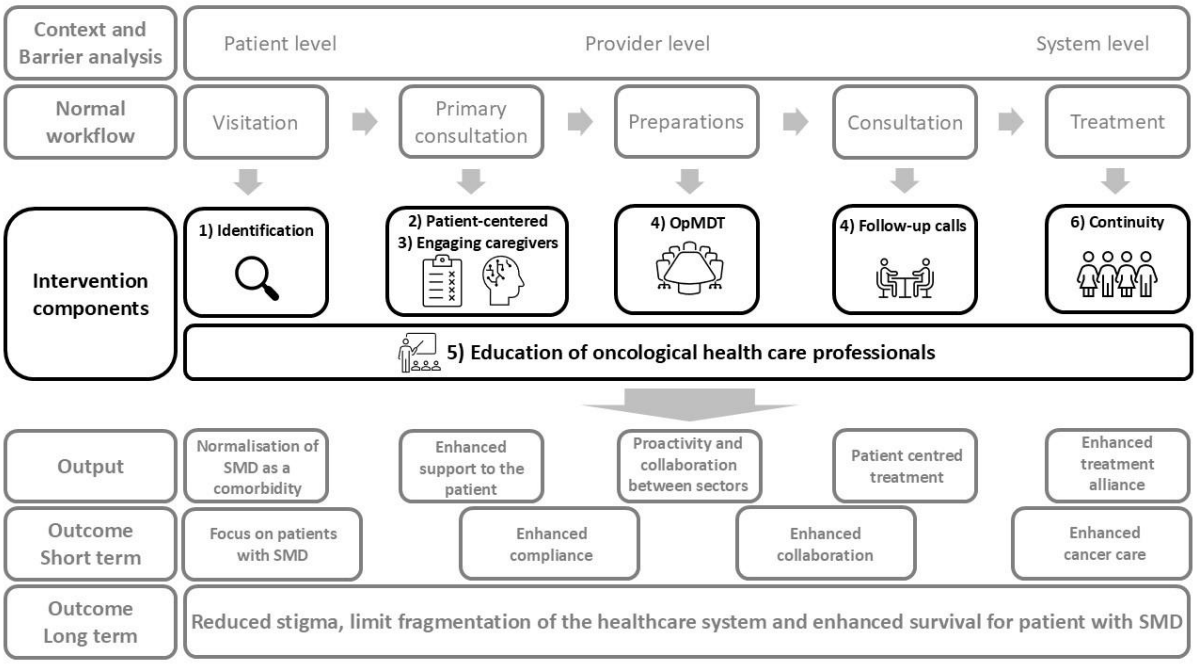
The Danish healthcare system is tax-funded and provides free-of-charge access to somatic and mental healthcare. Medical oncology and radiotherapy are centralized at large hospitals and are primarily delivered in an outpatient setting [18]. Patients with SMD are treated in hospital-based psychiatric services, whereas milder conditions are typically managed by general practitioners (GPs), psychiatrists in private practice, or psychologists [19]. GPs, psychiatrists and psychologists work together in close collaboration with community nurses and social services. GPs in this study received remuneration for their participation, although such compensation is not standard in Denmark.

The CASEMED Model

The CASEMED Model includes: (1) early identification of psychiatric comorbidity, (2) patient-centered approach e.g. through screening for physical and psychiatric symptoms, (3) engagement of significant caregivers, (4) enhanced cross-sector collaboration through the onco-psychiatric multidisciplinary team conference (opMDT), (5) education of oncology HCPs, and (6) continuity among HCPs (Figure 1).The intervention aims to improve cancer care for patients with pre-existing SMD through multidisciplinary collaboration, cross-sector communication, and a patient-centered approach. It emphasizes the importance of respecting patient preferences and addressing SMD like any other comorbidity in order to reduce stigma.

The intervention aims to enhance cancer care quality, reduce system fragmentation, and ultimately improve clinical outcomes and survival. The CASEMED Model was developed and pilot-tested at Aarhus University Hospital in Denmark. Detailed descriptions of the intervention are provided elsewhere [13].

Figure 1: The CASEMED Model



Intervention component	Description of the intervention component
1) Identification of psychiatric comorbidity	Systematic electronic identification of patients with pre-existing SMD recorded in the hospital journal within the last 10 years, and enunciation the psychiatric comorbidity at the first visit at the Department of Oncology.
2) Patient-centered approach	Questionnaires to screen for psychiatric symptoms and health-related quality of life distributed to the patient at the first encounter at the Department of Oncology together with screening for alcohol or drug abuse, preferred communication form and three open-ended patient-centered questions, about barriers and facilitators for optimal cancer care.
3) Engagement of significant caregivers	The oncologist investigates the patient's private and professional network at the first visit.
4) Enhanced collaboration between sectors	An online opMDT conference between the oncologist from the patients' initial consult, the patient's general practitioner and a psychiatrist, discussing the patients' resources, medication, housing conditions, nutrition, possible substance abuse, need for follow up and the need for referral to the psychiatric ward.
5) Education of the oncological HCPs	An online document available for the HCPs, concerning supportive offers for patients with SMD together with an educational programme with visit from a patient with SMD focusing on lived experiences and communication.
6) Continuity among HCPs	Prioritising continuity among HCPs by highlighting the name og the HCP in the secretary notes and the electronic booking system.

*SMD: Severe mental disorders, opMDT: onco-psychiatric multidisciplinary team conference, HCP: Health care professional.

At their first visit to the Department of Oncology, patients were identified through an electronic record system. To screen for physical and psychiatric symptoms, they completed a validated quality-of-life questionnaire (European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core-15 Palliative [EORTC-QLQ-C15-PAL]) [20] and a validated psychiatric questionnaire (Symptom Checklist-92 [SCL-92]) [21]. The oncologist also evaluated the patient's private caregivers (relatives or friends) and professional support network. An online opMDT meeting involving the patient's GP, oncologist, and psychiatrist (either the patient's own or a project-appointed) was held. A palliative care specialist was additionally invited if a single-item EORTC QLQ-C15-PAL score exceeded three, indication a significant burden in need of being addressed by a clinician. An opMDT checklist

ensured that all key areas were addressed, and meeting schedules were provided in advance to the oncologist, palliative care specialist, and project-appointed psychiatrist to optimize participation. After the opMDT, a follow-up call to the patient was made to communicate recommended clinical actions. Examples of such actions included additional consultations, psychiatric referrals, medication adjustments, or assignment of a navigator (a public support person). The patient decided which recommendations to pursue. Continuity of care was reinforced through enhanced notes in the booking system, and once during the project period, oncology HCPs attended a one-hour educational session focused on providing care and communication for patients with SMD (Figure 1).
The research project leader (LEF) coordinated patient inclusion, distributed questionnaires, arranged opMDT meetings, and conducted follow-up calls.

Participants
Patients were identified via the hospital's electronic system, which screened new referrals for lung, breast, or head and neck cancer and a prior hospital contact for SMD within the past ten years. The research project leader thereafter notified the oncologists in person about the patient. In this study, SMDs were defined as moderate to severe depression (ICD-10: F32.1–9, F33.1–9), bipolar affective disorder (ICD-10: F30–31), or schizophrenia and other psychoses (ICD-10: F20–25, F28–29) [22]. The validity of these diagnoses in the electronic system is generally high [23], but they were further validated with patients and by a psychiatrist via record review. Recruitment occurred at the first oncology visit (April 1, 2023 - June 1, 2024). Exclusion criteria were absence or less than five days of oncological treatment. If patients were not currently under psychiatric care, they were assigned to one of two hospital-based project psychiatrists for the opMDT.

Outcomes
Inspired by the implementation outcomes suggested by Proctor et al. [24], the quantitative and qualitative outcomes investigating feasibility included intervention delivery, acceptability, burden, other negative consequences, and mechanisms of change (Table 1).

Table 1 Operationalization of outcomes

Central concept	Operationalization	Quantitative measures	Qualitative measures
Delivery+	Reach (Reaching the target group).	Percentages of recruited patients out of the eligible group. Patient characteristics.	Which experience did the HCPs have regarding the recruited patients and the patients' reasons for nonparticipation?
	Fidelity (Did we deliver the intervention as intended).	HCP participation in opMDT Number of the patients who filled out the questionnaires.	
Acceptability*	Was the intervention acceptable for the patient to participate in, for the HCP to use, and in what way?		How did the HCPs perceive the overall intervention as well as each of the key components? Which reflections did the patients have about participation?
Burden*	Did the HCPs or the patients find the intervention burdensome?	Average time for the opMDT and the follow-up calls to the patients informing them of clinical actions.	Did the HCPs find participation in the intervention burdensome and how long time did they use on preparation for the opMDT?
Negative consequences#			Did the HCPs or patients experience any negative consequences of the intervention and in what way?
Mechanisms of change+	1) Identification of psychiatric comorbidity.	Number of patients where the psychiatric diagnosis was mentioned in the journal after the opMDT.	How did the patients experience the focus on their psychiatric disease?
	2) Patient-centered approach.	Percentage of patients receiving the planned oncological treatment.	Which experiences did the HCPs have regarding any changes in patient relationship? In what way did the patients experience the HCPs' approach to them, their psychiatric disease and their living situation? Are there any supportive initiatives for the HCPs that the patients missed during their treatment?
	3) Engagement of significant caregivers.		In what way were the private and professional caregivers engaged and what thoughts did the patients have about support from them?
	4) Enhanced collaboration between sectors.	Number and kind of supportive clinical actions suggested at the opMDT. Number and kind of clinical actions accepted by the patients. Number and kind of clinical actions declined by the patients.	Which experiences did the HCPs have regarding any changes in collaboration between sectors due to the opMDT? What did the patients think about the collaboration between sectors?
	5) Education of the oncological HCPs.	Number of education sessions.	Which reflections did the oncological HCPs have about the education?
	6) Continuity among HCPs.	How many doctors and nurses did the patient engage with during their treatment? Where they seen by a senior consultant by the first visit?	Which reflections did the HCPs and patients have regarding continuity? Did the patients experience continuity and why?

HCP: Healthcare professionals, opMDT: onco-psychiatric multidisciplinary team conference.

+ Inspired by Moores et al [25]

* Inspired by TFA framework [26]

Inspired by Bonell [27]

Data collection

Quantitative data were obtained from patient questionnaires and patient records. At baseline, patients completed questionnaires covering demographics and patient-centered concerns related to cancer treatment together with validated scales assessing health-related quality of life (EORTC-QLQ-C15-PAL) and psychiatric symptom burden (SCL-92), in all totalling 110 items [13]. Questionnaires served both as part of the intervention and as quantitative outcomes. Three months after treatment initiation, patient records were reviewed for patient characteristics, scheduled consultations, hospital admissions, and continuity among oncological HCPs (Table 2). Performance status (PS), reflecting patients' daily functional level, was assessed by the oncologist at the first visit.

Qualitative data were collected through semi-structured interviews with 10 patients and 18 HCPs, including five oncologists, four oncology nurses, two project psychiatrists, one palliative care specialist, three GPs who had participated in opMDTs and three who had not (Appendix S1). Recruitment aimed to capture diverse perspectives on the intervention, its context, and cross-sector collaboration. Interview guides, developed by the multidisciplinary research team, explored acceptability, operational feasibility, and negative consequences (Appendix S2). Field notes during recruitment, opMDTs, and follow-up calls and interviews were conducted by LEF, a female MD with oncology registrar experience and training in qualitative methods, who had no prior relationship with patients or GPs but was college to the oncologist, project psychiatrist and nurses. Interviews were conducted in person or by phone and recorded and transcribed verbatim. Duration ranged from 6 to 50 minutes (median 17 minutes). No interviews were repeated or returned for validation. Hospital HCPs were interviewed near study end, while GPs and patients were interviewed approximately three months post-inclusion.

Data analysis and statistics

Quantitative outcomes were analysed using descriptive statistics in Stata version 18.0. Interviews and field notes were analysed deductively, categorizing data according to intervention delivery, acceptability, burden, other negative consequences, and mechanisms of change, the last reflecting the six CASEMED Model components. LEF performed initial coding, which was quality-checked by MAN. After separate analyses, quantitative and qualitative findings were integrated using a triangulation protocol [28].

Ethics

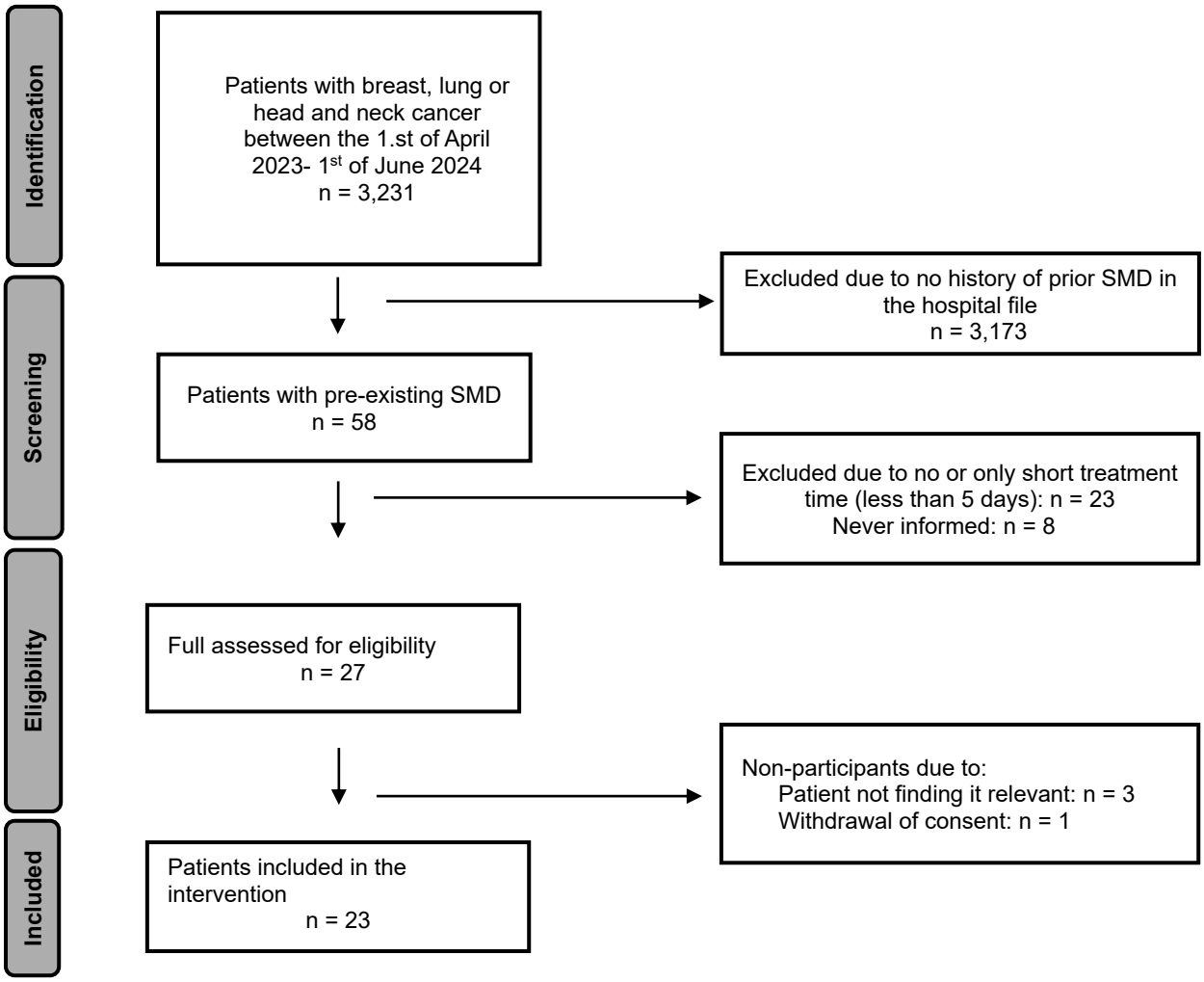
The study adhered to the Declaration of Helsinki [29] and the EU General Data Protection Regulation (GDPR). Data storage was approved by the Central Denmark Region (act no. 1-10-72-1-22). Ethical approval was not required under Danish law (act no. 1-16-02-249-22). Participants received written and oral information, were assured anonymity, voluntariness, and the right to withdraw at any time. All provided written informed consent.

Results

Inclusion of patients

Among 58 patients with pre-existing SMD referred during the study period, 23 were excluded due to no or only short palliative treatment, and eight were never informed, mainly due to vacation by the research project leader (Figure 2). In total, 23 of 27 eligible patients (85%) participated. Three non-participants cited minor or asymptomatic SMD as their reason, and one patient withdrew consent due to fear of stigma from the municipality.

Figure 2: Inclusion process in the feasibility study of the CASEMED Model



Patient characteristics

Among the 23 included patients, 74% were female. The distribution of SMD diagnoses was as follows: fifteen had moderate to severe depression, six had bipolar disorder, and two had schizophrenia or other psychoses (Table 2). Breast cancer was the most common diagnosis (48%), while lung and head and neck cancers each accounted for 26%. Patients ranged in age

from 37 to 80 years, with a median age of 58 years (interquartile range (IQR) 50-66 years). Most patients were in good PS, with 87% scoring between 0 and 1.

Sixty-five percent of patients received social benefits, 43% lived alone, and 30% had current alcohol or drug abuse. A majority (78%) used digital healthcare applications effectively (e.g. applications to book blood samples or keep track of hospital appointments), and 9% were under current hospital-based outpatient psychiatric care. Not surprisingly the patients reported a relatively hight psychiatric symptom burden (Global Severity Index) and low health-related-quality of life both overall, but also when looking into the functional and the emotional scales.

During the three-month observation period from treatment initiation, patients attended a median of one unscheduled in-person oncology consultation (IQR 0-1.5) and one unscheduled telephone consultation (IQR 0-3) at the Department of Oncology. Half of the patients experienced at least one acute hospital admission at the Department of Oncology, with an average duration of 3.8 days. Notably, a small subset of patients accounted for most unscheduled visits and admissions, for example, just three patients accounted for 79 out of 88 total admission days.

Table 2. Patient characteristics

Female gender, n (%)	**17** (74)
Age, median (IQR)	**58** (50-66)
WHO performance scale (PS), n (%)	
PS 0	**11** (48)
PS 1	**9** (39)
PS 2	**3** (13)
Cancer type, n (%)	
Breast	**11** (48)
Head and neck	**6** (26)
Lung	**6** (26)
Severe mental disorder, n (%)	
Moderate to severe depression	**15** (65)
Affective bipolar disorder	**6** (26)
Schizophrenia and other psychosis	**2** (9)
Currently treated at the Department of Psychiatry n (%)	**2** (9)
Lives alone, n (%)	**10** (43)
On public support, n (%)	**15** (65)
Uses online health applications (yes), n (%)	**18** (78)
Abuse of alcohol or drugs	
Current abuse	**7** (30)
Former abuse	**4** (17)
No current or former abuse	**12** (52)
SCL-92 Global Severity Index*, median (IQR)	**0.72** (0.58-1.08)
EORTC health-related-QOL measure*, mean (IQR)	**59.3** (50.0-83.3)
Physical functioning, mean (IQR)	**67.4** (46.7-93.3)
Emotional functioning, mean (IQR)	**68.14** (41.7-91.7)
Unscheduled consultations+, n, median (IQR)	
With oncological physician	**19**, 1 (0-1.5)
Unscheduled telephone consultations +, n, median (IQR)	**60**, 1 (0-3)
Hospital admissions+, n, median (IQR)	**13**, 0 (0-5)
Hospital admission in days+, n, median (IQR)	**88**, 0 (0-39)

*Five missing data because of the lack of completed questionnaires

+During the first three months of treatment

Intervention delivery

All 23 patients' treatments were discussed at the opMDT as planned, with no technical issues reported. Project psychiatrist attendance was consistent at 100%, whereas GP attendance was low (17%), despite 61% having intended to participate. The GPs did not have the opMDT in their schedule beforehand but were only noticed 7-14 days ahead. In general, they reported that their attendance was limited by structural barriers as vacations and the need to attend acute patients in the clinic. A follow-up meeting 2-4 weeks after the first opMDT was suggested to overcome this barrier. Clinicians also highlighted the need to refine patient selection, noting that individuals with complex psychiatric or social needs benefited most, while those with remitted moderate depression and no active psychiatric symptoms appeared to gain less benefit from the intervention.

Acceptability, burden and other negative consequences

Overall, nurses, oncologists, and psychiatrists experienced that the intervention was acceptable and easily integrated into daily hospital workflows (See Table 3). Patient participation was high (85%), and 78% completed the questionnaires, although some found them lengthy. Patients generally experienced the intervention as minimally burdensome and well-integrated into their existing treatment pathways. The time spent on the opMDT (median 12 minutes), and the follow up calls to patients (median 11 minutes) informing them of recommended clinical actions was presumed meaningful by the participants. The patients reported that the systematic yet patient-centered format, including options for additional consultations and continuity in oncology care, was reassuring.

Mechanisms of change

Identification of psychiatric comorbidity

Following the opMDT, psychiatric comorbidity was documented in 70% of the following records, indicating an awareness of the comorbidity. Patients reported feeling comfortable discussing psychiatric concerns and valued supportive responses. While HCPs initially feared increasing stigma, they observed positive patient reactions when psychiatric comorbidity was addressed. Both groups valued the opportunity to openly address psychiatric issues, and the intervention legitimized the conversations, revealing previously unmet needs. HCPs also reported increased confidence in managing complex psychiatric needs and emphasized the importance of early planning to prevent treatment disruptions. An oncologist elaborated how using the intervention facilitated a timely effort:

"*It (using the intervention) also means that we start off better, both we, and I think the patient too, because it opens up the conversation, and we set things up early. (…) Because otherwise, they aren't always so receptive to our good ideas. I mean, when things have gone sideways*" (O1).

Patient-centered approach

All patients initially received guideline-based treatment plans, and 19 completed the planned oncological treatment, indicating that treatment decisions were generally feasible and well-supported. Some patients found the psychiatric questionnaires lengthy, and the psychiatrist found that the questionnaire responses had limited value. Instead, the psychiatrist preferred information based on past psychiatric electronic patient records. In contrast, quality-of-life questionnaires were actively used in the opMDT by oncologists and palliative care specialists. Patients felt acknowledged and supported, especially when individual accommodations such as solo hospital transport or preferred treatment times were arranged.

Engagement of significant caregivers

The involvement of private caregivers was often described as decisive in patients' ability to cope with cancer treatment, especially emotionally. The opMDT was perceived as effective in identifying professional support options, such as professional caregivers, and supportive initiatives, including meal services and domestic help. This ensured optimal support for the patient throughout their cancer treatment, as perceived by a patient:

"We have also reached out for free prepared meals, because those are things my husband takes care of more than usual, and it's tough for him, so it's a great support" (P8).

In that way, the opMDT was assessed as important in supporting private caregivers, who often assumed new roles during treatment, underscoring the need for systems that recognize and support this engagement. By identifying private caregivers at the start of treatment and discussing professional support options during the opMDT, the intervention helped integrate these caregivers more systematically into the care process.

Collaboration between sectors

The opMDT was the cornerstone in collaboration between sectors and was proven feasible and well-received by patients and HCPs across sectors. Of the 23 patients, 20 received at least one clinical action facilitated by the opMDT, most commonly additional appointments (n =14) or medication adjustments (n = 8). Four patients (two partially, two fully) declined clinical actions, primarily referrals to psychiatric services or involvement of a support person, citing a preference for independent management. Despite this, most patients felt reassured by the interdisciplinary discussion, even when few or no clinical actions were initiated.
All HCPs found the opMDTs beneficial, particularly when the GP participated, as this enhanced decision-making, patient safety, and collaboration. One oncologist reported increased confidence in prescribing prednisolone after psychiatric input, which helped assess the risk of psychosis as a potential adverse effect. Psychiatrists also highlighted improved patient safety through medication reviews and early risk identification. GPs noted that, although collaboration with the Department of Oncology had previously been positive,

the opMDT further reduced communication barriers and provided reassurance, as it enabled GPs to voice their concerns about patient challenges. A GP explained how the intervention enhanced the collaboration between sectors:

"I have had the opportunity to further communicate things we have been able to align on, and the general exchange of what we can expect from each other, that is what it (the opMDT) is good for (…) That thing about having had contact with the specialists who are there, right? That means a lot (..). I just think that the personal contact one has had, then I kind of know that we'll probably make things work (…). I think I have used less energy on the patient course, I have become more reassured because I know that you also pay special attention to the patient." (GP1).

Even though not all patients were in contact with their GP during treatment, those who had, described them as informed and engaged.

Education of the oncological HCPs

The education sessions were feasible and generally well-received, and oncologists and nurses experienced that it facilitated a more inclusive perspective on people with SMD, fostering confidence and reducing stigma around psychiatric comorbidity. An oncologist elaborated how the sessions enhanced the relation to the patients:

"As soon as you think that we are the same kind, you are in a better position to build a relationship with a patient. And that puts you in a better position to treat them properly" (O3).

The nurses described the education as a foundation for ongoing team dialogue and felt inspired by new tools, such as distraction techniques and environmental adjustments, to better support patients with complex needs.

Continuity among the oncological HCPs

Despite the intervention initiatives, the relational continuity of care remained limited. Forty-five percent of patients saw the same physician for at least half of their scheduled consultations, while 50% experienced similar continuity with a nurse. Generally, patients found HCPs kind and attentive but emphasized that relational continuity fostered trust and emotional safety and enabled deeper, more meaningful conversations. HCPs observed that continuity build trust and supported treatment adherence. Barriers towards enhancing continuity included variable clinic working hours and shift rotations. Patients initially seen by a specialist oncology physician had notably better continuity, hence 80% saw the same specialist in at least half of their scheduled consultations.

Table3. Combined analysis of the CASEMED Model feasibility study

Quantitative analysis	Integrated analysis	Qualitative analysis
	Delivery	
Participation in intervention of eligible patients asked: **23/27** (85%) Number of opMDTs: **23/23** (100%) <u>Participation in opMDT:</u> Known oncologist present: **12/23** (52%) GP present: **4/23** (17) % GP intended to participate: **14/23** (61%) Psychiatrist present: **23/23** (100%) Palliative specialist present when requested up on: **7/11** (64%) Completed questionnaires: **18/23** (78%)	The main parts of the intervention were delivered as intended. The participation percentage were high and non-participation were mainly due to patients not feeling the need for extra support. Thus, the participation of GPs at the opMDT were lower than expected. The GPs expressed that they wanted to participate and found it relevant, but were a times unable to attend due to vacations, conferences and acute patients in the clinic. The GPs furthermore elaborated that they didn't find that changing the setting of the opMDT would change that.	• Patients were easily enrolled. • Non-participation was primarily due to "no need" by patients or oncologists. • Absences due to leave and conferences further reduced oncologists' involvement in opMDTs. • GP participation was hindered by understaffing, acute care duties, and leave. • Some HCPS where in doubt if the inclusion criteria accurately captured the intended target population.
	Acceptability	
	Overall, the intervention was perceived acceptable for both patients and HCPs. The different intervention components fitted well into the daily clinic.	• The patients found the intervention acceptable and meaningful. • The HCPs found that the intervention components fitted well into the clinical workflow at the hospital.
	Burden	
Time spent on each opMDT in minutes: Median (IQR): **12** (8;15) Time spent on each follow-up call after opMDT in minutes: Median (IQR): **11** (8;14)	The form of the opMDT were acceptable and feasible, and the burden for the HCPs to participate in the intervention were minimal. The time spend on coordination at the opMDT were found valuable and cost effective by all HCPs. Thus, a few GPs found it hard to find time to participate and the lack of future remuneration were a barrier for implementation. From the patient perspective the questionnaires were too long.	• All HCPs found the timing and format of the opMDT appropriate. • No HCPs reported difficulties preparing for the opMDT. • Some GPs reported difficulty integrating the opMDT into their clinical schedule. • Some patients found the questionnaires long. • GPs noted a lack of future remuneration under current Danish welfare agreements. • Technical aspects functioned well.
	Negative consequences	
	Only minor negative unintended consequences were detected.	• Oncology nurses felt excluded from opMDTs but found documentation (notes and checklists) useful.
	Mechanisms of change	
The psychiatric diagnosis was mentioned in the electronic journal after the opMDT: **16/23** (70%)	**1) Identification of psychiatric comorbidity** The identification of psychiatric comorbidity and enunciation of it, were possible and found meaningful for both patients and HCPs as it helped to reduce stigma towards patients with pre-existing SMD.	• Patients found it meaningful when HCPs acknowledged their psychiatric comorbidity. • Patients felt positively received when they raised the comorbidity themselves. • HCPs felt the intervention legitimized discussing psychiatric comorbidity. • HCPs observed that patients responded well to these discussions. • One oncologist noted that HCPs were sometimes surprised by the burden of pre-existing SMD, which was not initially apparent.
Percentage of the patients receiving the planned oncological treatment: **19/23** (82%) Patients treated after guidelines**: 23/23** (100%)	**2) Patient-centered approach** In general, the patients received the planned treatment and found that their need and personal preferences were taken into account during their cancer treatment.	• Patients felt that HCPs generally considered their personal preferences, e.g. time at day for treatment • Some patients still experienced the system as very rigid at times e.g. in relation to arranging blood samples.
	3) Engagement of significant caregivers	

	The opMDT helped integrate private and professional caregivers as other supportive measures well into the cancer trajectory. Professional caregiver support was preserved crucial to support private caregivers so they could focus on emotional support of the patients.	• The patients found the caregivers well integrated into the cancer treatment and the majority of patients identified private caregiver support as critical to treatment adherence especially dude to emotional support. • HCPs elaborated that opMDT initiated focus on possible professional caregivers and supportive measures. • Professional caregiver support was primarily provided by psychiatric nurses, navigators, and practical services such as meal assistance and domestic help. • The patients were grateful for the professional caregiver support, which they felt eased the work of their private caregivers.
<u>opMDT clinical actions:</u> Number of patients receiving any intervention **20/23** (87%) Adding a resource person: **3/23** (13%) Chancing in medicine: **8/23** (35%) Extra appointments: **13/23** (57%) Referred to the psychiatry: **3/23** (13%) <u>Patients declining offers from the opMDT:</u> Partly: **2/23** (9%) All: **2/23** (9%)	**4) Enhanced collaboration between sectors** The opMDT were found very useful by all HCPs especially when the GPs attended. It made the patients feel safer and it made the treatment decisions easier for the oncologists. Medical adjustments and extra appointments in the oncological clinic were the most common clinical actions. The main clinical action that patients did not accept were the offer of a navigator. The patients elaborated that they wanted to see if they could manage the treatment by themselves.	• GPs valued the collaboration and input from specialists; some noted reduced workload with maintained care quality. • Hospital HCPs found interdisciplinary input reassuring and valued GP attendance for deeper patient insight. • One oncologist reported that the opMDT improved decision-making and patient reassurance. • Most patients were unaware of collaboration due to limited GP contact; those with contact found GPs well-informed.
Numbers of clinics receiving education: **3/4** (75%)	**5) Education of the oncological HCPs** The education program was easily implemented into the clinical workflow. It lowered stigma and the nurses were inspired by new tools, such as distraction techniques and environmental adjustments.	• The education program was valued by both nurses and oncologists. • It enhanced HCPs' understanding of challenges faced by patients with pre-existing SMD. • The program contributed to reduced stigma and improved communication around psychiatric comorbidity. • In one oncological clinic nurses were inspired to implement new tools as distractions techniques and environmental adjustments to support patients with SMD in daily practice.
Seen by the same physician in minimum 50% of the scheduled consultations: **10/22**, (45%) Seen by the same physician in > 50% of the scheduled consultations**: 6/22**, (27%) Seen by the same nurse in minimum 50% of the scheduled consultations: **11/22** (50%)+ Seen by the same nurses in > 50% of the scheduled consultations: **9/22** (41%) Continuity when seen by a consultant at the first visit: Seen by the same physician in minimum 50% of the scheduled consultations: **12/15** (80%) Seen by the same physician in > 50% of the consultations: **6/15** (40%)	**6) Continuity among HCPs** The patients and the HCP found continuity crucial as it enhanced the depth of the relationship, enhanced the compliance, and made treatment decisions easier for the HCPs. Thus, the criteria for continuity were not fulfilled, the patients reflected that all the HCPs they had meet were very nice, helpful and engaging.	• Patients valued continuity, as it enhanced their sense of safety and reduced the need to repeatedly explain their situation. • Even when continuity was lacking, patients generally found new HCPs to be kind and engaging. • HCPs observed that continuity deepened the therapeutic relationship over successive encounters. • The HCPs perceived continuity to improve treatment adherence and support more informed clinical decision-making.

*Only 22 patients included as one only had one contact

+ the patients have been seen in 2-3 different clinics: ambulatory, outpatient clinic and radiotherapy.

Discussion

Main findings

This feasibility study demonstrates that a collaborative, patient-centered cancer care intervention for patients with pre-existing SMD is both acceptable and feasible in a real-world setting. The intervention was successfully integrated into routine clinical workflows, with high patient participation and imposing minimal burden on patients and HCPs. Both patients and HCPs considered the intervention meaningful and supportive of high-quality cancer care and valued the opportunity to openly address psychiatric issues. Together with the educational components, incorporating the patient perspective, the intervention appeared to reduce stigma, while the opMDT format facilitated collaboration between sectors, enhanced HCPs' decision-making and coordination of supportive measures. Nonetheless, several challenges towards fully implementation were identified. Identifying the right target population, maintaining continuity among oncological HCPs and ensuring consistent GP participation in opMDTs proved challenging, despite strong interest expressed by both groups. Despite these limitations, the intervention promoted a multidisciplinary and patient-centered approach and enhanced the HCPs' decision-making and the cancer trajectories for patients with cancer and pre-existing SMD.

Discussion of results

Comparison with prior studies

The Lancet Oncology Commission highlights an increasing imbalance in cancer care, where technological and biomedical advances have outpaced attention to the human aspects of care. While precision medicine and efficiency have progressed, fundamental elements such as compassion, dignity, and relational care are at risk of being overlooked. The Commission argues that the core crisis in cancer care lies not only in disease outcomes, but in fragmented and impersonal systems that undermine meaning, trust, and psychological safety for patients [30].

The feasibility and acceptability of the CASEMED Model for both patients and HCPs align with findings from the American BRIDGE intervention [12]. While the BRIDGE intervention uses a more fixed approach with a designated case-manager and regular patient assessments, the adaptive strategy in the CASEMED Model was perceived to be acceptable and feasible, supporting patient-centered care and contribute to the interventions' sustainability. A designated case-manager might have enhanced patient engagement but would likely reduce the possibility of direct implementation in a Danish context due to resources such as cost and time in the clinic thereby reducing the sustainability of the model. Both interventions alike underscore the importance of adapting care for patients facing social, physical, and psychiatric challenges. This aligns with the concept of cumulative complexity, which emphasizes the need for patient-centered and context-sensitive care rather than standardized approaches that may overlook the lived experiences of patients in complex life situations [31]. As complexity increases, so does the need for patient-centered

support that aligns with the patient's capacity to ensure that care remains manageable and effective [31].
Although this study was not designed to evaluate the effectiveness of the intervention, the mechanisms of the intervention were evaluated, finding that it facilitates patient-centered care and cross-sector collaboration. The interventions core components have been identified in other studies across the cancer trajectory as improving the quality of cancer care [32-34].

Barriers to implementation
The study identified four main barriers against fully implementation. Firstly, psychiatrists and oncologists questioned whether the inclusion criteria captured the intended population. At times, patients with minimal psychiatric burden were sometimes included, while socially marginalized patients with evident needs but no documented psychiatric history were excluded. While the former group often declined participation due to lack of perceived relevance, clinicians noted that the latter group might have benefited. Future studies could consider physician-initiated inclusion based on suspected but undiagnosed conditions or social vulnerability or using other definitions or screening tools for SMD e.g. the Global Assessment of Functioning (GAF) Scale [35]. Thust this would require additional education of the HCPs and time in the clinic and thereby might not be as sustainable. Secondly, some patients found the questionnaire burdensome to fill in, and the clinicians' perceived benefit of the questionnaires was limited. To ensure successful future implementation, it should be considered to only include relevant SCL-92 subscales, as the EORTC-PAL-15 questionnaires contained both key cancer symptoms and overall quality of life. Thirdly, although the CASEMD model addressed continuity in several ways, relational continuity of care remained a concern [36,37]. Given its known association with reduced mortality, continuity was preserved as particularly important for this high-risk group [38]. Despite these challenges, patients generally reported feeling heard and acknowledged by all HCPs. This may be partly explained by the strengthened informational continuity achieved through the opMDTs, where the patient's psychiatric history and insights from general practitioners were systematically integrated into cancer care. In addition, management continuity was enhanced through the opMDT by facilitating coordination and shared decision-making across sectors, thereby supporting a more coherent and aligned care trajectory [36,37]. Despite targeted efforts, relational continuity was not consistently achieved. However, assigning a specialised physician at the initial oncology visit increased continuity from 45% to 80%, highlighting a potentially effective strategy for future implementation. Finally, GP participation in the opMDTs was low (17%), largely due to structural barriers. To overcome this barrier, a follow-up meeting 2–4 weeks after the initial opMDT was proposed.

Implications
Clinical implications
Given the limited preparation time required from clinicians for participating in the opMDT and the fact that most intervention components were easily embedded within existing

clinical workflows, the findings suggest that the CASEMED Model, with minor refinements, can be implemented into routine clinical practice without the need for substantial additional resources. A prerequisite is that education, continuity, remuneration for the GPs participation and the opMDTs are prioritised, and that the intervention components carried out by the research project leader, are taken care for by other clinicians. Moreover, because the intervention components are not tailored to a specific cancer type or psychiatric diagnosis, the CASEMED model is likely transferable and adaptable to a range of other clinical settings. Patients with SMD frequently present with multiple complex chronic comorbidities, and an adaptation may extend the interventions applicability to support patients with pre-existing SMD during hospital admissions for a range of medical conditions beyond oncology. Thereby addressing the broader needs of patients with psychiatric comorbidity.

Research implications

This study supports the feasibility of integrating psychiatry into oncology care for patients with pre-existing SMD, improving detection and management of comorbidities without adding substantial burden. The structured patient-centered approach may inform future interventions for populations with complex needs. Larger, more diverse studies are needed to confirm these findings, evaluate long-term clinical and psychiatric effect, and assess cost-effectiveness.

Study limitations

Firstly, as only 23 patients were included, the representativeness of the sample for the broader population of patients with pre-existing SMD is modest; however, as this was a feasibility study, the primary aim was to evaluate intervention mechanisms rather than to draw causal conclusions about effectiveness, which should be assessed in future randomized controlled trials, or langer scale studies.. Secondly, the incidence of patients with pre-existing SMD was lower than expected (1.8% vs 6.6%) [2], presumably partly because we primarily included patients with good PS. Consequently, the intervention did not reflect the experiences of patients with SMDs who never reached oncology services or received only short-term palliative care. Notably, 40% of newly referred cancer patients with SMDs received no treatment or only short-term palliative care, likely due to more advanced disease and lower PS [39]. Thirdly, the study was conducted at a single university hospital in Denmark, which may limit generalizability as local adaptation would be needed for broader implementation. Finally, as mentioned above, some intervention components, such as opMDT scheduling and documentation, were managed by the research project leader and not evaluated in routine practice. However, as these are typically clinic responsibilities, they are assessed unlikely to hinder future implementation.

Conclusion

This feasibility study suggests that the CASEMED Model, with smaller refinements, is feasible within the daily clinical setting, without the need for substantial additional resources. Patients and HCPs found the intervention acceptable and supportive of high-quality cancer care facilitating cross-sector collaboration and a person-centered and multidisciplinary approach. Importantly, it seems that early and integrated psychiatric involvement in cancer care can enable patients with pre-existing SMD to initiate and adhere to cancer treatment. However, future studies are needed to assess whether the CASEMED Model improves cancer treatment adherence and survival to determine its effectiveness and generalizability.

Statement and declarations

Author contributions

LEF (female) collected the quantitative data and conducted the semi-structured interviews of the participants and field-notes. LEF performed the analysis, and MAN performed quality control check on the analyses. LEF drafted the manuscript. All authors engaged in designing the study, discussing the analyses and revision of the manuscript.

AI-statement

During the preparation of this manuscript the first author used “ChatGPT” in order to refine the grammar on already written sections. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

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Conflict of interest

The authors declare that there is no conflict of interest.

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12 Appendix

12.1 Appendix S1

Final search string constructed for PubMed and subsequently converted to Embase, Psycinfo, and Scopus.

Database	Date final search	Search syntax	Other criteria	References (n)
PubMed	Date 19.10.2024 Time 15.05	("neoplasms"[MeSH Terms] OR "neoplasm*"[MeSH Terms] OR "cancer"[Title/Abstract] OR "neoplasm"[Title/Abstract]) AND ("mental disorders"[MeSH Terms:noexp] OR "Depression"[MeSH Terms] OR "mental disorder"[Title/Abstract] OR "bipolar disorders"[Title/Abstract] OR "major depression"[Title/Abstract] OR "unipolar depression"[Title/Abstract] OR "schizophrenia"[Title/Abstract] OR "severe mental illness"[Title/Abstract] OR "SMI"[Title/Abstract] OR "severe mental disease"[Title/Abstract] OR "SMD"[Title/Abstract]) AND ("survival"[MeSH Terms] OR "Survival Analysis"[MeSH Terms] OR "mortality"[MeSH Terms] OR "survival"[Title/Abstract] OR "mortality"[Title/Abstract])) NOT ("meta-analysis"[Publication Type] OR "review"[Publication Type] OR "systematic review"[Publication Type])) AND 2003/01/01:2024/10/19[Date - Publication]	English language January 2003-19/10-2024	2038
EMBASE	Date 19.10.24 Time 15.47	('neoplasm'/de OR neoplasm:ab,ti) AND ('schizophrenia'/de OR 'schizophrenia spectrum disorder'/exp OR schizophrenia:ab,ti OR 'major depression'/de OR 'major depression':ab,ti OR 'bipolar disorder'/de OR 'bipolar disorder':ab,ti OR 'severe mental illness'/exp OR 'severe mental illness':ab,ti OR 'severe mental disorder'/exp OR 'severe mental disorder':ab,ti) AND ('survival'/de OR survival:ab,ti OR 'mortality'/de OR mortality:ab,ti) AND [2003-2024]/py	English language January 2003-19/10-2024 Limited to articles as publications	240
Psycinfo	Date 19.10.2024 Time 17.56	((MJMAINSUBJECT.EXACT("Neoplasms") OR ab(Neoplasm) OR ti(neoplasm))) AND ((MJMAINSUBJECT.EXACT("Mental Disorders") OR ab(Mental Disorders) OR ti(Mental Disorders)) OR (MJMAINSUBJECT.EXACT("Bipolar Disorder") OR ab(Bipolar Disorder) OR ti(Bipolar Disorder)) OR (MJMAINSUBJECT.EXACT("Schizophrenia") OR ab(Schizophrenia) OR ti(Schizophrenia)) OR (MJMAINSUBJECT.EXACT("Serious Mental Illness") OR ab(serious mental illness) OR ti(serious mental illness)) OR (MJMAINSUBJECT.EXACT("Major Depression") OR ab(major depression) OR ti(major depression)) OR (MJMAINSUBJECT.EXACT(“Serious Mental Disorder”) OR ab(serious mental disorder) OR ti(serious mental disorder))) AND ((MJMAINSUBJECT.EXACT(“Survival”) OR ab(survival) OR ti(survival) OR (MJMAINSUBJECT.EXACT(“Mortality”) OR ab(mortality) OR ti(mortality))))	English language January 2003-19/10 2024 Limited to articles as publicationtype	316
Scopus	Date 19.10.2024 Time 15.59	(TITLE-ABS-KEY (cancer OR neoplasms) AND TITLE-ABS-KEY ("mental disorders" OR "bipolar disorder" OR "major depression" OR "unipolar depression" OR "schizophrenia" OR "smi" OR "smd" OR "severe mental disorder") AND TITLE-ABS-KEY (survival OR mortality)) AND PUBYEAR > 2002 AND PUBYEAR < 2024 AND (LIMIT-TO (LANGUAGE , "English")) AND (LIMIT-TO (DOCTYPE , "ar"))	English language January 2003-19/10-2024 Limited to articles as publicationtype	2142

12.2 Appendix S2

Characteristics for interviewed participants in Study IV

Profession	**Sex**	**Age**
Patient (P1)	Female	75
Patient (P2)	Male	68
Patient (P3)	Female	43
Patient (P4)	Male	38
Patient (P5)	Male	57
Patient (P6)	Male	58
Patient (P7)	Female	59
Patient (P8)	Female	49
Patient (P9)	Female	59
Patient (P10)	Female	57
Oncology nurse (N1)	Female	60
Oncology nurse (N2)	Female	35
Oncology nurse (N3)	Female	35
Oncology nurse (N4)	Female	32
Psychiatrist (Ps1)	Male	45
Psychiatrist (Ps2)	Female	43
General Practitioner (GP1)	Male	60
General Practitioner (GP2)	Male	48
General Practitioner (GP3)	Female	54
General Practitioner (GP4)	Male	52
General Practitioner (GP5)	Male	44
Palliative Care Physician (PC1)	Female	56
Oncologist (O1)	Male	64
Oncologist (O2)	Female	55
Oncologist (O3)	Female	62
Oncologist (O4)	Female	52
Oncologist (O5)	Female	60

12.3 Appendix S3

Interview guides for semi-structured interviews

Participant	Question	Component
Patients	*"In what way did the department of oncology handle the fact that you had a psychiatric diagnosis?"*	Mechanisms of change - Identification of psychiatric comorbidity - Patient centred approach
	"What has it been like that there has been focus on your psychiatric disease?"	Mechanisms of change - Identification of psychiatric comorbidity - Patient centred approach Negative unintended consequences
	"In what way did you experience that your personal needs were met during your cancer treatment?"	Mechanisms of change - Patient centred approach
	"In what way have your private caregivers been involved in the treatment?"	Mechanisms of change - Engagement of significant caregivers
	"How do you perceive the collaboration between the department of oncology, general practice and the psychiatry?"	Mechanisms of change - Enhanced collaboration between sectors
	"Do you feel that you were often met by known HCPs, and what has that meant to you?"	Mechanisms of chance - Enhanced collaboration between sectors - Patient centred approach
	"Do you have any good advice for the cancer department regarding the treatment of future patients?"	Negative unintended consequences
	Other comments	
General Practitioner	*"Have you participated in a pMDT, and how did you experience it?"*	Acceptability
	"Does the components in the intervention make sense to you?"	Acceptability
	"What extra effort did it require from you to participate?"	Acceptability Burden
	"In your opinion has the intervention had any consequences for the patient's course of treatment?"	Acceptability
	"Has it had any impact on when or how you will contact the cancer department?"	Mechanisms of change - Enhanced collaboration between sectors
	<u>Questions to nonparticipants in opMDTs</u>	
	"What was the barrier to not participating in the opMDT?"	Acceptability Burden
	"Do you think the intervention would have had an effect on the patient's course of treatment?"	Acceptability
	"Do you think the intervention would have had an effect on the collaboration between general practice and the cancer department?"	Mechanisms of change - Enhanced collaboration between sectors
	"How many opMDT have you participated in?"	Delivery

Oncologists, nurses and psychiatrists	*"How much preparation time have you spent per patient?"*	Burden
	"What did it require from you to participate in the opMDTs?"	Burden
	"How do you feel the intervention has impacted the patient relationship?"	Mechanisms of chance - Patient centred approach
	"In what way has the CASEMED Model changed your perspective on patients with cancer and concurrent psychiatric illness?"	Acceptability Mechanisms of chance - Patient centred approach
	"How do you feel the CASEMED Model has affected the treatment of this patient group?"	Acceptability
	"In what way has the CASEMED Model influenced collaboration across sectors?"	Mechanisms of change - Enhanced collaboration between sectors
	"Which elements have you found particularly effective, and in what way?"	Acceptability
	"Which elements have you found inappropriate, and in what way?"	Negative unintended consequences
	<u>Questions only for oncologist:</u>	
	"How many CASEMED patients have you been a responsible for?"	Mechanisms of chance - Continuity among HCPs
	"In what way was it clear to you that you were responsible for the patients?"	Mechanisms of chance - Continuity among HCPs
	"In what way do you think the patient perceived you as responsible?"	Mechanisms of chance - Patient centred approach
	"In what way did the patient's psychiatric diagnosis affect the course of treatment?"	Mechanisms of chance - Patient centred approach
	"What did you learn from the education program, and did it influence your perspectives or practice in the daily clinic?"	Mechanisms of chance - Education of the oncological HCPs