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# Inclusion in the cancer patient pathway among cancer patients with and without pre-existing mental or substance use disorders: a nationwide register-based study

Ina H. Heiberg[1,2*], Lise Balteskard[1,3], Bjarne K. Jacobsen[1,4], Jørgen G. Bramness[5,6], Ragnar Nesvåg[7], Kjell Magne Tveit[8] and Anne Høye[2,5]

## Abstract

**Background** Cancer patients with a pre-existing mental disorder or substance use disorder (SUD) have a poorer prognosis compared to other cancer patients, with suboptimal routes to diagnosis and treatment as possible contributing factors. Shorter intervals from suspicion of cancer to start of cancer treatment have been observed following the implementation of Cancer Patient Pathways (CPP) in the Nordic countries, which may have led to a better prognosis. We aimed to investigate whether incident cancer patients with and without pre-existing mental disorder or SUD were equally likely to be included in a CPP. We also investigated the associations between pre-existing mental disorder or SUD and low primary care utilization, and cancers diagnosed post-emergency or close to death in non-CPP enrolees.

**Methods** This population-based registry study included incident cancer patients aged 21–79 between 2015 and 2018 ($n = 65{,}328$). Information on pre-existing mental disorders or SUD was gathered from national registries of primary and specialised health care, prescriptions, and disability diagnosis. Propensity score analyses using inverse probability weighting along with the McNemar test were performed to evaluate the risk of non-inclusion in any CPP for all cancers combined, lifestyle-related cancers combined, and the most common cancers individually.

**Results** Cancer patients with pre-existing mental disorder or SUD had an 8% (RR = 1.08; 95% Confidence Interval (CI) 1.03–1.13) higher risk of non-enrolment in a CPP. Patients with prior hospitalisation for mental disorder or SUD, and patients with pre-existing psychosis or depression were at particular risk of non-inclusion in a CPP compared to controls, especially for cancers that often present with symptoms late in the course of the disease, such as lung cancer. In line with this, patients with pre-existing mental disorder or SUD who were not referred to a CPP faced a 34% (RR = 1.34; 95% CI 1.18–1.53%) increased risk of unrecognised cancer close to death.

**Conclusions** Cancer patients with pre-existing mental disorder or SUD have an increased risk of non-inclusion in a CPP. If not included in a CPP, they have an increased risk of having unrecognised cancer close to death. By addressing

*Correspondence:
Ina H. Heiberg
ina.heidi.heiberg@helse-nord.no

Full list of author information is available at the end of the article

barriers to CPP-inclusion, and enhancing the quality of diagnostic and treatment services, healthcare systems could achieve better cancer outcomes for vulnerable patient groups.

**Keywords** Early detection of cancer, Neoplasms, Mental disorders, Psychosis, Substance use disorder, Depression, Anxiety disorder, Norway, Cancer patient pathways

## Background

Individuals with pre-existing mental disorders and/or substance use disorders (SUD) experience worse outcomes following a cancer diagnosis compared to patients without these conditions [1, 2]. Moreover, the burden of cancer-related life years lost is increasing among this population [3]. The provision of highly specialised cancer care services may not be adequately tailored to address the unique challenges associated with multimorbidity [4]. Research indicates that individuals with mental disorder or SUD exhibit suboptimal healthcare utilization across various aspects of cancer care, including reduced participation in screening programs, lower likelihood of receiving treatments such as chemotherapy, radiotherapy, stage-specific interventions, invasive procedures, and palliative care [5–14]. While the impact of suboptimal diagnostic processes in this patient group on overall outcomes has been proposed, it remains an understudied area [15]. Prior studies have identified higher risks of prolonged diagnostic intervals [16], delayed [7] or missed cancer diagnoses [17, 18] and increased likelihood of cancer diagnosis subsequent to unrelated emergency admissions [18] among patients with mental disorder or SUD. Additionally, some studies have reported that cancer patients with comorbid mental disorder experience more advanced cancer stages at the time of diagnosis [6, 7, 10, 19], although findings have not been consistent across all studies [2]. A delayed diagnosis of cancer has been linked to poorer survival for breast, colorectal, head and neck, testicular cancer, and melanoma [20–22]. Similarly, emergency presentations have been linked to reduced survival rates for cancers such as colon, stomach, lung, liver, pancreatic, and ovarian cancer [23, 24]. Moreover, prolonged intervals between cancer diagnosis and treatment are associated with disease progression to advanced stages [25], and reduced survival [26, 27]. A recent meta-analysis indicated that even a four-week delay in initiating cancer treatment was associated with increased all-cause mortality in seven common cancer types; breast, colon, rectal, lung, cervical, bladder, and head and neck cancers [27]. Notably, the same analysis revealed that even a two-week delay in cancer surgery was associated with increased risk of death among breast cancer patients. These findings emphasize the importance of minimizing the time from initial presentation to the start of treatment, as it has the potential to enhance patient outcomes in terms of improved quality of life and improved survival.

Since 2000, many countries have implemented fast-track programs aimed at reducing system-related delay in the time from cancer suspicion to diagnosis and treatment initiation. Denmark, for instance, implemented standardised Cancer Patient Pathways (CPP) in 2008, with the goal of improving prognosis and quality of life for cancer patients. Similar CPPs were subsequently implemented in Norway in 2015. The Norwegian CPPs aim to minimize non-medically justified delays in cancer investigations, enhance continuity of care, and increase transparency and patient satisfaction. To achieve this, specific criteria for urgent referrals and recommended timelines for initiating investigations, clinical decisions, and treatment have been established for over 25 cancer types. Additionally, dedicated pathway coordinators have been appointed to ensure continuity throughout the diagnostic and treatment processes. These mechanisms collectively contribute to earlier cancer detection and quicker initiation of treatment, which can significantly improve patient outcomes and survival rates. Following the implementation of CPPs in Scandinavia, various studies have reported a decrease in the interval from the onset of cancer suspicion to the point of diagnosis [28] as well as from referral to diagnosis [28–33]. Some studies also reported a decrease in the time from referral to treatment [30, 34, 35], although other studies found no significant change [29]. While some studies noted less advanced disease at diagnosis [30, 31], not all studies reported the same findings [36].

The improvement in time to diagnosis and treatment may, however, have benefited only cancer patients who were referred to a CPP. A Danish study found that patients not referred to a CPP experienced longer diagnostic intervals compared to CPP-referred patients and compared to the same patient group in the period before CPP implementation [28]. Similar observations were made in British studies, indicating that only 40% of all cancer patients seem to have benefited from fast-track systems such as CPP or the two-week wait referral system [37, 38]. The Danish study's authors discuss possible reasons for this discrepancy, including the likelihood that the fast-track system primarily benefits patients whose initial disease symptoms involve significant cardinal signs of cancer.

Ensuring equal access to healthcare services is a priority in countries with publicly funded healthcare and was a crucial driver behind the introduction of the Norwegian CPPs. Nonetheless, research has demonstrated

that factors such as low income, living alone, female sex (in the case of lung and rectal cancer), high or low age at diagnosis, somatic multimorbidity, and metastatic disease are associated with an increased likelihood of not being included in a fast-track program [39–42]. To date, not much is known concerning how the implementation of fast-track programs like CPP may have affected cancer patients with pre-existing mental disorder or SUD, who traditionally experience poorer cancer outcomes. Pre-existing mental disorders or SUD may reduce a patient's likelihood of seeking health care and, consequently, their inclusion in CPPs. This can occur through several interconnected intrapersonal or interpersonal social processes, such as self-stigma or anticipated stigma from health care workers [43]. Having a serious mental disorder or long-term SUD will, for many, also be associated with acute health challenges continuously arising and being prioritised over other symptoms. Such acute conditions will likely also affect the sensitivity to other, more diffuse symptoms. Furthermore, mental disorders and SUD may impair patients' ability to navigate the healthcare system, adhere to appointments, or communicate effectively with healthcare providers. The timely follow-ups, coordination and patient engagement required in the context of CPPs may be particularly challenging for these patients. Additionally, patients with mental disorders or SUDs frequently have other comorbidities and complex healthcare needs that complicate routine cancer diagnosis and treatment. Healthcare providers may also misattribute physical symptoms to pre-existing mental health conditions rather than potential malignancies, leading to delays or missed opportunities for CPP referral. Low health literacy, socioeconomic challenges, social isolation, and implicit biases among healthcare professionals may also influence referral patterns and treatment decisions. A Danish study published in 2022 found that cancer patients with pre-existing mental disorder or SUD had an 8% lower probability of being diagnosed through a CPP, with particularly high risks of non-inclusion observed in patients with schizophrenia or organic mental disorder [18]. Lack of inclusion was most pronounced for cancer types with non-specific symptoms, such as colon, pancreatic, liver, and lung cancers [18]. Another 2022 study from the UK revealed that colon cancer patients with cardinal symptoms of cancer and concurrent mental disorder or SUD had 28% lower odds of receiving a fast-track specialist referral, higher risks of emergency presentation, and increased likelihood of prognostically consequential delays in cancer treatment [16]. Mental disorders and SUD are distinct, but often overlapping conditions, with many shared and some unique risk factors that may affect inclusion in CPPs. Mental disorders often involve cognitive or emotional challenges, such as anxiety or depression, which can delay timely healthcare engagement, and influence effective communication of symptoms and adherence to appointments. Conversely, SUDs are more closely associated with socioeconomic instability, homelessness, and stigmatisation, which exacerbate access barriers and delay cancer care. Social support deficits and chaotic lifestyles, particularly prevalent in severe mental disorders and SUD, hinder consistent engagement with structured healthcare pathways. Healthcare provider biases may further reduce referrals, with patients perceived as less capable of adhering to complex treatment plans. Cancer symptoms may also be misattributed to pre-existing conditions, delaying diagnosis. Cancer symptom presentation may also vary between these groups. In patients with mental disorders, cancer symptoms like fatigue may be misattributed to pre-existing conditions, such as depression, delaying cancer diagnosis and CPP inclusion. For individuals with SUD, the chronic effects of substance use, such as liver damage or infections, can mimic or obscure cancer symptoms, complicating timely and accurate diagnoses. Hence, further research is needed to examine whether health reforms like the CPP effectively target the health care needs for patients with pre-existing mental disorder or SUD. Also, there is a need for further investigations into the diagnostic trajectory for suspected cancer among individuals with mental disorder or SUD.

## Methods

### Aims and design

The aim of the study was to examine whether patients with incident cancer with and without pre-existing mental disorder or SUD had equal chances of being included in a Norwegian CPP. This was investigated by carrying out a population-based nationwide study using comprehensive, high-quality individual level data prospectively recorded in Norwegian national health registries. Another objective of this study was to explore whether non-inclusion in CPPs was associated with low general practitioner (GP) attendance, cancer diagnosis following an emergency presentation to hospital, and unrecognised cancer close to death. These factors are plausible explanations for non-inclusion in a CPP inclusion among individuals with a history of mental disorders or SUD. Previous research has shown that people with mental disorders or SUD are at higher risk for emergency cancer presentations [16, 18, 44] and undiagnosed cancer prior to death [17, 45]. Furthermore, emergency presentation is often linked to limited GP contact before a cancer diagnosis [44]. Understanding these potential barriers to CPP inclusion can provide insights into how tailored interventions might better address the needs of these vulnerable patient groups, ultimately improving access to timely and structured cancer care pathways.

The study adhered to the Declaration of Helsinki and followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [46].

### Setting

The study used national registry data from Norway, where the 5.4 million residents have low (maximum of 280 $ per year) out-of-pocket costs for primary healthcare and outpatient specialised healthcare, and free, tax-financed access to in-hospital care. Four regional health authorities are responsible for providing specialised healthcare services in their respective regions. Currently, 96% of the population has a regular GP, who acts as a gatekeeper to specialised healthcare, except in emergency situations. GPs and hospital doctors can refer patients to a CPP when there is a reasonable suspicion of cancer. The Norwegian CPPs describe detailed, cancer-type-specific criteria for urgent referral and suggest cancer-specific recommended deadlines for the initiation of investigations, clinical decisions, and treatment. Cancer pathway coordinators have been assigned the task of managing referrals, scheduling appointments, and ensuring continuity throughout the investigation and treatment process. At the time of the study period (2015–2018), there were 25 organ-specific CPPs for adult patients, as well as one for metastatic cancer of unknown origin and one for non-specific symptoms that may indicate cancer.

At the time of CPP implementation, the stated objective was for 70% of individuals referred with suspected cancer to be included in a CPP, and for 70% of confirmed cancer cases to receive treatment within the recommended time limits. Norway also has national screening programs for cervical cancer and breast cancer.

### Data sources

We obtained information on incident cancer cases, including the type, date and stage of diagnosis from the Norwegian Cancer Registry, which holds data on all cancer cases in Norway since 1951. Details about CPP inclusion, CPP type, dates, clinical decisions, and emergency presentations were acquired from the Norwegian Patient Registry, which contains information on all ICD-10-diagnoses and procedures in specialist healthcare services in Norway, including publicly funded services operated by private providers. Data on pre-existing mental disorder or SUD were collected from the following national registers: (i) the Norwegian Patient Registry; (ii) the Norwegian Directorate of Health's system for control and payment of health reimbursements in primary care, which contains information on all GP and out-of-hours primary care contacts, including ICPC-2-diagnoses; (iii) the Norwegian Labour and Welfare Administration's Database of disability pensions, which contain information on ICD-10-diagnoses in cases of disability; and (iv) the Norwegian Prescription Database, which contain information (ICD-10-codes, registry-specific reimbursement codes, and ATC-codes) on prescription drugs in Norway, except drugs supplied to hospitals and nursing homes. Information regarding demographic factors, such as year and month of birth, sex, marital status, parents' and own education, place of residence (rural, urban, or unknown), date of immigration or emigration, and month and year of death, was obtained from the Norwegian Population Registry and the National Education Database, Statistics Norway. Causes of death, and cancer cases identified solely through death certificates or incidental findings at autopsy were obtained from the Cause of Death Registry. The registries were linked using an encrypted serial number derived from the compulsory 11-digit personal identifier.

### Study population

The study population included incident cancer patients aged 21–79 years at the time of their first cancer diagnosis, not including prior non-melanoma skin cancer (ICD-10 code C44), registered in the Norwegian Cancer Registry between February 1, 2015, and December 31, 2018. We considered all cancers with a dedicated CPP, except colorectal cancer in patients aged 39 years or younger (as specified in the guideline for the specific CPP) and neuroendocrine cancer, which could not be identified within our dataset (definitions provided in supplementary table S1). Additionally, we defined a subgroup of lifestyle-related cancers (i.e., head and neck, oesophagus, stomach, colon, rectum, primary liver, bile duct, pancreas, lung, malignant melanoma, breast, female genitalia, kidney, and bladder [47–49]), where individuals with mental disorder or SUD may be at particular risk due to higher prevalence of smoking, obesity and physical inactivity. ICD-10-codes for the most common cancers (i.e., cancers of the digestive organ, lungs, female breast, female genital organs, and prostate) are provided in supplementary table S1. To account for possible start-up problems regarding the CPP implementation, we included only cancer cases occurring at least one month after the implementation of the specific CPP. Patients with a pre-existing diagnosis of dementia or organic mental disorder were excluded, as were immigrants with less than three years of residence in Norway prior to the cancer diagnosis.

### Definition of exposure groups

Exposure groups were defined based on patients' diagnoses of psychosis (e.g., schizophrenia spectrum disorder, bipolar disorder, or severe depression with psychotic symptoms), depression, anxiety disorder, or SUD, recorded between 91 days and five years prior to the cancer diagnosis as identified in the national health registries

**Table 1** Patient characteristics before propensity score weighting

| Variables, % (*n*) | Mental disorder/SUD[a] | | Psychosis | | Depression | | Anxiety disorder | | Substance use disorder | | Controls[b] | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *Patients* | | (14,106) | | (1,951) | | (10,177) | | (6,984) | | (2,372) | | (51,222) |
| Men | 43.7 | (6,163) | 45.3 | (884) | 41.1 | (4,178) | 39.2 | (2,741) | 65.0 | (1,541) | 59.0 | (30,210) |
| *Age group* | | | | | | | | | | | | |
| Age 21–49 | 15.5 | (2,189) | 15.0 | (293) | 15.5 | (1,574) | 18.9 | (1,317) | 12.3 | (291) | 12.0 | (6,127) |
| Age 50–59 | 22.0 | (3,102) | 24.3 | (475) | 22.1 | (2,247) | 23.2 | (1,618) | 25.2 | (597) | 17.1 | (8,767) |
| Age 60–69 | 36.7 | (5,179) | 37.5 | (732) | 36.3 | (3,698) | 35.6 | (2,487) | 40.6 | (962) | 33.9 | (17,355) |
| Age 70–79 | 25.8 | (3,636) | 23.1 | (451) | 26.1 | (2,658) | 22.4 | (1,562) | 22.0 | (522) | 37.0 | (18,973) |
| *Married* | 45.2 | (6,380) | 35.2 | (686) | 45.9 | (4,673) | 44.4 | (3,101) | 31.7 | (752) | 64.4 | (32,996) |
| *Urban residence* | 80.8 | (11,396) | 83.3 | (1,626) | 81.0 | (8,244) | 80.6 | (5,632) | 81.3 | (1,929) | 77.4 | (39,660) |
| *Immigrant* | 14.2 | (2,007) | 13.0 | (254) | 14.7 | (1,501) | 14.2 | (991) | 12.5 | (296) | 12.6 | (6,431) |
| *Education level* | | | | | | | | | | | | |
| None or unknown | 1.3 | (184) | 2.2 | (42) | 1.3 | (130) | 1.2 | (82) | 1.2 | (29) | 0.8 | (427) |
| Primary level | 31.7 | (4,468) | 34.0 | (663) | 31.2 | (3,177) | 33.5 | (2,343) | 39.0 | (924) | 21.2 | (10,852) |
| Intermediate level | 43.6 | (6,151) | 42.9 | (837) | 43.8 | (4,460) | 42.2 | (2,949) | 43.8 | (1,040) | 48.8 | (25,004) |
| University level | 23.4 | (3,303) | 21.0 | (409) | 23.7 | (2,410) | 23.1 | (1,610) | 16.0 | (379) | 29.2 | (14,939) |
| *Income level after tax* | | | | | | | | | | | | |
| < 25 percentile | 35.3 | (4,976) | 46.4 | (906) | 34.5 | (3,509) | 37.9 | (2,647) | 43.2 | (1,025) | 21.0 | (10,752) |
| 25–75 percentile | 50.1 | (7,062) | 44.5 | (869) | 51.4 | (5,235) | 48.6 | (3,392) | 45.3 | (1,074) | 49.7 | (25,453) |
| > 75 percentile | 14.7 | (2,068) | 9.0 | (176) | 14.1 | (1,433) | 13.5 | (945) | 11.5 | (273) | 29.3 | (15,017) |
| *Elixhauser comorbidities* | | | | | | | | | | | | |
| Cardiovascular | 25.2 | (3,554) | 23.3 | (455) | 25.0 | (2,544) | 24.4 | (1,701) | 29.9 | (710) | 22.5 | (11,531) |
| Pulmonary | 12.4 | (1,745) | 13.4 | (261) | 12.2 | (1,245) | 12.5 | (873) | 17.7 | (420) | 6.5 | (3,345) |
| Neurological | 5.2 | (739) | 7.7 | (151) | 5.2 | (527) | 4.4 | (304) | 9.7 | (230) | 1.7 | (853) |
| Weight loss, electrolyte disturbances or anemia | 7.9 | (1,118) | 10.4 | (202) | 7.6 | (772) | 7.5 | (527) | 17.5 | (414) | 2.8 | (1,448) |
| *No. of Elixhauser comorbidites* | | | | | | | | | | | | |
| None | 54.5 | (7,688) | 52.5 | (1,024) | 54.7 | (5,563) | 55.8 | (3,898) | 40.6 | (964) | 65.1 | (33,355) |
| One or two | 32.9 | (4,639) | 35.2 | (687) | 32.6 | (3,320) | 32.6 | (2,275) | 40.2 | (953) | 27.1 | (13,900) |
| Three or more | 12.6 | (1,779) | 12.3 | (240) | 12.7 | (1,294) | 11.6 | (811) | 19.2 | (455) | 7.7 | (3,967) |
| *Cancer type* | | | | | | | | | | | | |
| Digestive [c] | 19.3 | (2,727) | 19.9 | (388) | 18.8 | (1,917) | 18.4 | (1,285) | 22.5 | (533) | 19.5 | (9,981) |
| Lungs | 14.0 | (1,975) | 16.1 | (314) | 13.7 | (1,394) | 13.6 | (950) | 19.9 | (471) | 9.1 | (4,669) |
| Female breast | 18.0 | (2,545) | 17.0 | (332) | 18.9 | (1,926) | 19.7 | (1,377) | 10.3 | (245) | 13.8 | (7,069) |
| Female genital [d] | 6.5 | (913) | 7.4 | (144) | 6.6 | (668) | 7.3 | (507) | 3.1 | (74) | 5.0 | (2,569) |
| Prostate | 13.3 | (1,873) | 12.3 | (240) | 13.1 | (1,335) | 11.6 | (811) | 14.3 | (339) | 23.0 | (11,792) |
| Other | 28.9 | (4,073) | 27.3 | (533) | 28.9 | (2,937) | 29.4 | (2,054) | 29.9 | (710) | 29.6 | (15,142) |
| *Cancer stadium* | | | | | | | | | | | | |
| Localised | 39.7 | (5,601) | 35.9 | (701) | 40.4 | (4,108) | 40.7 | (2,840) | 34.0 | (807) | 40.0 | (20,483) |
| Regional | 25.2 | (3,556) | 24.9 | (486) | 24.9 | (2,537) | 25.1 | (1,753) | 27.5 | (653) | 25.8 | (13,191) |

**Table 1** (continued)

| Variables, % (*n*) | Mental disorder/SUD[a] | | Psychosis | | Depression | | Anxiety disorder | | Substance use disorder | | Controls[b] | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Metastatic | 14.3 | (2,018) | 17.0 | (332) | 13.9 | (1,418) | 14.1 | (982) | 16.9 | (402) | 13.0 | (6,677) |
| Unknown | 20.8 | (2,931) | 22.1 | (432) | 20.8 | (2,114) | 20.2 | (1,409) | 21.5 | (510) | 21.2 | (10,871) |

[a] Abbreviations: SUD = substance use disorder

[b] Incident cancer patients with no pre-existing mental disorder or SUD

[c] ICD-10-codes C15-C16, C18-C22, C24-C25

[d] ICD-10-codes C53-C56

(definitions provided in supplementary table S2). A five-year time limit was set to enhance the likelihood that the diagnosis of mental disorder or SUD remained relevant and necessitated ongoing or recent treatment. Individuals who met multiple criteria were eligible for inclusion in multiple groups. The comparison group consisted of cancer patients without any pre-existing diagnosis of mental disorder or SUD during the last five years before the cancer diagnosis, indicated by the absence of recorded F-diagnoses in the ICD-10 coding system, and also the absence of ICPC-2-codes or ATC-codes indicative of psychosis, depression, anxiety disorder, or SUD (see table S2 for a full list of relevant diagnostic and ATC-codes).

### Definition of outcomes

The main outcome measure was non-inclusion in a CPP. For certain cancers (female genital cancer, prostate cancer, lymphoma, thyroid cancer, and head and neck cancer), the majority of patients enrolled in a CPP fulfilled the inclusion criteria by having a confirmed cancer diagnosis prior to embarking on the CPP. However, their inclusion was vital to expedite investigations and the commencement of treatment procedures. Consequently, those who were not included in any CPP during the 90 days before or after the cancer diagnosis were considered as not included in any CPP. Inclusion in the same organ-specific CPP as the final diagnosis was not required, as approximately 5% of patients followed a CPP different from the final cancer diagnosis.

Secondary outcomes included low frequency of GP encounters prior to the cancer diagnosis, cancer diagnosis after emergency presentation in specialised health care, and cancer diagnosed close to death, and were investigated in the subset of patients who were not included in any CPP. Low frequency of GP attendance prior to the cancer diagnosis was defined as fewer than three GP encounters during the last two years before the cancer diagnosis, corresponding to the lowest decile in the data set. Cancer emergency presentations were defined as cases in which the first cancer diagnosis registered in the Cancer Registry coincided with an emergency admission or an emergency outpatient consultation in specialised health care. Cancers diagnosed close to death refer to cases where patients died within 60 days of their first cancer diagnosis, including cases reported to the Cancer Registry solely by death certificate and cancer cases incidentally discovered during autopsies. The 60-day time frame is approximate (+/- 15 days), as we only had information on the month and year of death.

### Statistical methods

We initially present the demographic, socioeconomic, and clinical characteristics of the sample according to their exposure status (Table 1). To ensure balance in

baseline characteristics, we employed propensity score analyses with inverse probability weighting (IPW) to create exposure and control groups. First, we estimated the propensity score of patients having a pre-existing mental disorder or SUD diagnosis using gradient boosting models with autotuning, as implemented in the gradboost procedure [50] in SAS Vyia. Based on prior research, we included sex, age at diagnosis, education levels of both the patient and their parents, income, gross assets, marital status, place of residence, and immigrant status as potential confounders [39, 40, 42]. In line with recommendations [51] we also included covariates deemed likely to predict outcome [39–42], including cancer type, stadium, and Elixhauser comorbidity groups (types and number). Time-dependent covariates were measured in the year preceding the cancer diagnosis. Data on cancer stage was missing for 21.1% of cases, while less than 1% of cases lacked information on education level, place of residence, or marital status. The machine learning algorithm used for propensity score estimation inherently handled missing data without relying on imputation or parametric assumptions. Separate models were built for mental disorder or SUD collectively, and for psychosis, depression, anxiety disorder, and SUD individually.

Next, we generated output data sets with balanced distributions of covariates between the exposed and unexposed groups. This was achieved by utilizing the estimated propensity scores as weights and applying inverse probability weighting through the psmatch procedure in SAS [52]. The weight was set to one for those with a pre-existing mental disorder or SUD diagnosis and to (propensity score/(1-propensity score)) for those without a pre-existing mental disorder or SUD diagnosis, corresponding to the average treatment effect on the treated (ATT). The balance and common support between the exposure and control groups were assessed for each covariate in the different subsets. Successful balancing was indicated by standardised mean differences (SMD) < 0.10 and variance ratios within the interval of 0.5-2.0. After IPW, the SMDs for all covariates, except one in the SUD-specific analysis, fell below the recommended threshold of 0.10 (see supplementary table S3). Additionally, all of the variance ratios were within the acceptable range of 0.5-2.0, further indicating appropriate balance in the comparison groups (see supplementary table S4).

Finally, we employed McNemar test, as implemented in the clinstat SAS macro [53], to estimate the risk ratios (RRs) with 95% confidence intervals (CI) in the weighted datasets. Statistical tests were two-sided, with a significance level of 0.05. The analyses were conducted for mental disorder (i.e., psychosis, depression, or anxiety disorder) or SUD combined, and separately for psychosis, depression, anxiety disorder, and SUD. We present sex-specific results for all included cancers combined and lifestyle-related cancers combined, as well as analyses for some of the most frequent types of cancer including both sexes (if relevant).

To ensure the robustness of our findings, we performed several sensitivity analyses where we varied the definitions or inclusion criteria. These included: (i) using a hierarchical ordering of diagnoses (psychosis > depression > anxiety disorder > SUD), (ii) including only mental disorders or SUD cases diagnosed in specialised health care, (iii) including only inpatients with mental disorders or SUD, (iv) excluding cases with multiple exposures, (v) excluding cancers with screening programs, (vi) excluding cases diagnosed with cancer before the start of a CPP, and (vii) excluding patients in CPPs that may have been unrelated to the specific cancer under investigation. Additionally, considering that aggressive disease at the time of cancer diagnosis could impact the likelihood of inclusion in a CPP, we conducted sensitivity analyses by excluding those who died within 60 days (+/- 15 days) of their first cancer diagnosis. We also included sensitivity analyses where the significance level was set to 0.01.

## Results

### Descriptive data

The study included a total of 65,328 incident cancer cases, which accounted for approximately two thirds of all cancer cases in the relevant age group in Norway during the study period (2015–2018) (as cancer cases without a dedicated CPP or with a previous cancer diagnosis were not included in the analytical population).

Among the included cases, 14,106 (21.6%) had a pre-existing diagnosis of mental disorder or SUD (i.e., psychosis, depression, anxiety disorder, or SUD). A total of 1,951 (3.0%) had a pre-existing diagnosis of psychosis; 10,177 (15.6%) had a pre-existing diagnosis of depression; 6,984 (10.7%) had a pre-existing diagnosis of anxiety disorder; 2,372 (3.6%) had a pre-existing diagnosis of SUD, whereas 51,222 (78.4%) had no pre-existing mental disorder or SUD diagnosis (see Table 1). Of the patients with psychosis, depression, anxiety disorder, or SUD, respectively 85%, 54%, 67% and 58% had at least one of the other included mental disorders or SUD diagnoses. The distribution is shown in the Venn diagram [54] in Fig. 1 below.

Table 1 and supplementary tables S3 and S4 demonstrate considerable baseline differences in the included covariates between the exposed and unexposed groups before employing IPW. However, a satisfactory balancing of the included covariates was demonstrated when applying IPW, as described in the methods section.

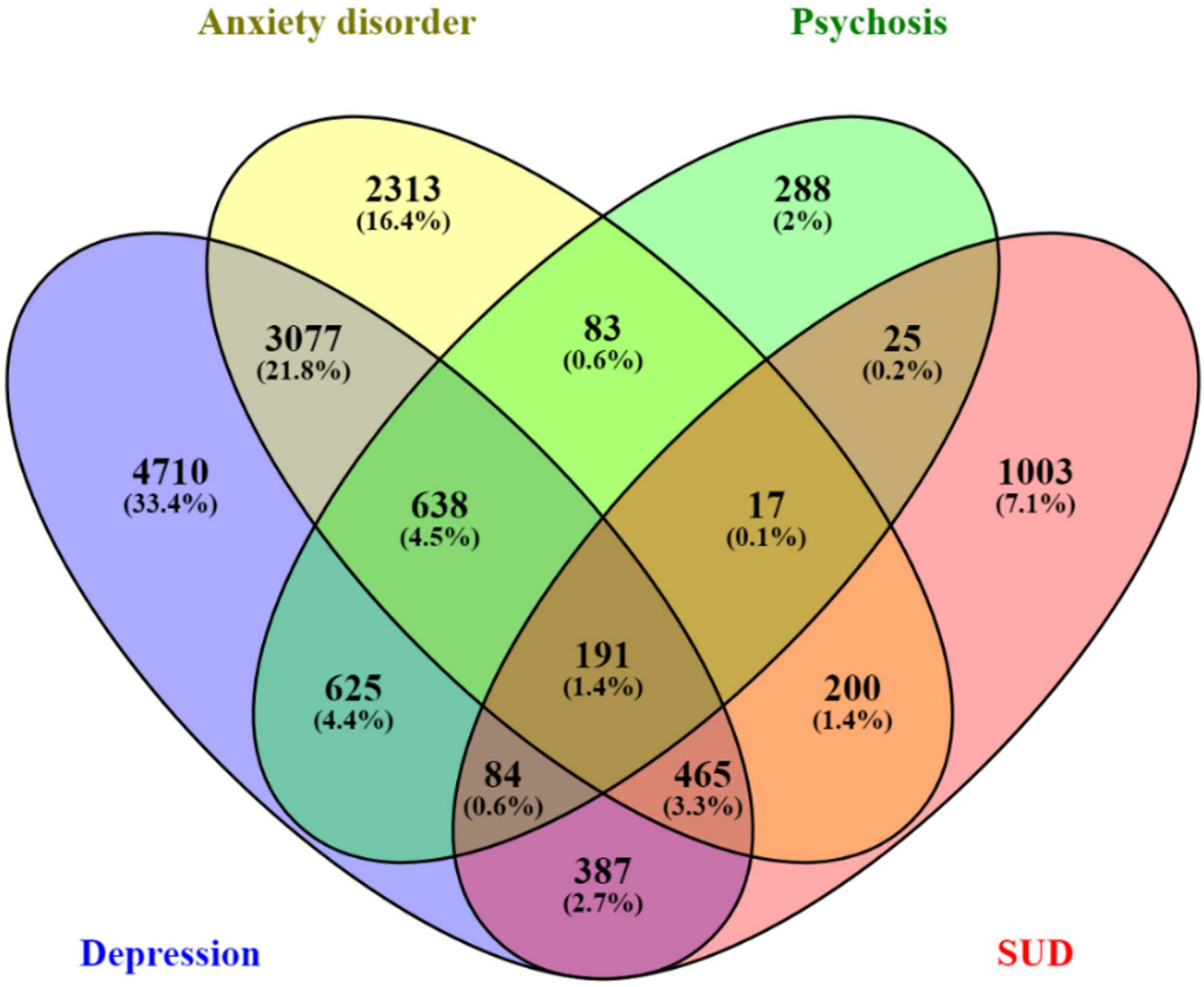


**Fig. 1** Venn diagram showing the extent of overlap between individual mental disorder and substance use disorder (SUD). Number of subjects with the different combinations of mental disorders and SUD

#### Risk of non-inclusion in a CPP

When considering all included cancers combined, we found an 8% increased risk of non-inclusion in a CPP for cancer patients with pre-existing mental disorder or SUD in comparison to controls (RR = 1.08; 95% CI 1.03–1.13) (Table 2), corresponding to 233 (95% CI 99–360) fewer included patients than expected. Subgroup analyses indicated an accentuated tendency in individuals with pre-existing psychosis (RR = 1.15; 95% CI 1.02–1.29), and an increased risk was also observed for patients with pre-existing depression (RR = 1.07; 95% CI 1.02–1.13). However, no significant differences were noted regarding non-inclusion in a CPP between cancer patients with and without pre-existing anxiety disorder or SUD when considering all cancers collectively.

In the examination of combined lifestyle-related cancers, we identified a parallel 8% increased risk of non-inclusion among cancer patients with pre-existing mental disorder or SUD (RR=1.08; 95% CI 1.02–1.14). Notably, individuals with pre-existing psychosis exhibited a 20% higher risk of non-inclusion in a CPP (RR=95% CI 1.04–1.39) compared to cancer patients without pre-existing mental disorder or SUD in the subset of lifestyle-related cancers. No significant differences were observed for non-inclusion in a CPP among patients with lifestyle-related cancers with pre-existing depression, anxiety disorder, or SUD.

Regarding the most common cancer types, the analyses show that lung cancer patients with pre-existing mental disorder or SUD had a 21% (RR = 1.21; 95% CI 1.04–1.40%) higher risk of non-inclusion in any CPP, compared to controls (Fig. 2). Moreover, patients with pre-existing mental disorder or SUD, and patients with pre-existing depression individually, also had an increased risk of non-inclusion in a CPP for cancers categorized as "other cancers" (see Fig. 2). The "other cancer"

**Table 2** Risk ratios (RR) for non-inclusion in a CPP for all cancers combined and lifestyle-related cancers combined, according to prior mental disorder or SUD exposure and sex

| | Any cancer [a] | Lifestyle related cancer [b] |
|---|---|---|
| | Adjusted RR (95% CI) | Adjusted RR (95% CI) |
| **Prior mental disorder/SUD** | | |
| Both genders | 1.08 (1.03–1.13) * | 1.08 (1.02–1.14) * |
| Men | 1.08 (1.01–1.15) * | 1.08 (0.99–1.19) |
| Women | 1.08 (1.01–1.15) * | 1.07 (0.99–1.15) |
| **Prior psychosis** | | |
| Both genders | 1.15 (1.02–1.29) * | 1.20 (1.04–1.39) * |
| Men | 1.17 (1.00-1.38) | 1.20 (0.96–1.51) |
| Women | 1.12 (0.94–1.33) | 1.20 (0.99–1.45) |
| **Prior depression** | | |
| Both genders | 1.07 (1.02–1.13) * | 1.06 (0.99–1.13) |
| Men | 1.07 (0.99–1.16) | 1.04 (0.93–1.16) |
| Women | 1.07 (1.00-1.16) | 1.06 (0.97–1.16) |
| **Prior anxiety disorder** | | |
| Both genders | 1.05 (0.99–1.12) | 1.04 (0.95–1.13) |
| Men | 1.06 (0.96–1.16) | 1.06 (0.92–1.22) |
| Women | 1.04 (0.96–1.14) | 1.02 (0.91–1.13) |
| **Prior SUD** | | |
| Both genders | 1.06 (0.96–1.19) | 1.12 (0.98–1.28) |
| Men | 1.06 (0.93–1.21) | 1.15 (0.97–1.36) |
| Women | 1.06 (0.87–1.29) | 1.06 (0.85–1.33) |

Abbreviations: RR = risk ratio; CPP = cancer patient pathway; CI = confidence interval; SUD = substance use disorder

[a] All cancer types with dedicated CPPs, excluding neuroendocrine cancer

[b] Cancer of the breast, colon, rectum, head & neck, bladder, kidney, female genitalia, lung, oesophagus, stomach, bile duct, and primary liver cancer

* Significant result at p-level 0.05

group encompasses kidney cancer, where a more than 30% increased risk was observed for mental disorder or SUD combined, and depression individually (results not shown in tables or figures). No significant differences were observed between exposure groups for non-inclusion in any CPP for digestive, female breast, female genital, and prostate cancer types.

### Sensitivity analyses

A series of sensitivity analyses of all cancers combined demonstrated the robustness of the results, as variations in definitions and inclusion criteria did not substantially alter the findings. The statistically significant results for cancer patients with pre-existing mental disorder or SUD remained consistent across all sensitivity analyses (see Fig. 3).

The statistically significant results for cancer patients with pre-existing psychosis or depression also remained consistent across all sensitivity analyses, except for the analyses that excluded individuals who died shortly after the cancer diagnosis, the sensitivity analyses where the significance level was set to 0.01, and the sensitivity analysis that only included cases diagnosed in specialised health care (depression only). The outcomes for the remaining exposed groups were generally consistent across various sensitivity analyses, with a significant deviation observed in analyses that exclusively included cases with prior hospitalisations for mental disorder or SUD. In the sensitivity analyses including only exposed inpatients and controls, an elevated risk of non-inclusion in a CPP was identified for all subgroups of mental disorder or SUD, ranging from 26% (RR = 1.26; 95% CI 1.08–1.46) among patients with pre-existing SUD to 76% among patients with pre-existing psychosis (RR = 1.76; 95% CI 1.41–2.20) (see Fig. 3).

### Risk of low GP attendance, emergency diagnosis or unrecognised cancer shortly before death

In the subgroup of patients not enrolled in any CPP, cancer patients with pre-existing mental disorders or SUD had a 47% lower risk of low GP attendance compared to controls (RR = 0.53; 95% CI 0.46–0.61) (see Table 3). The propensity for low GP attendance varied across exposure groups. While cancer patients with pre-existing psychosis or SUD demonstrated a comparable likelihood of low GP attendance in the two years leading up to their initial cancer diagnosis as controls did, those with pre-existing depression or anxiety disorder exhibited an almost 60% reduced risk of low GP attendance compared to controls (see Table 3).

Regarding the risk of cancer diagnosis after emergency contacts with specialised care, we found a 10% elevated risk of emergency presentation among patients with pre-existing mental disorder or SUD who were not included in any CPP (RR = 1.10; 95% CI 1.00–1.21). In subgroup analyses across distinct exposure groups, we observed a 28% higher risk of emergency presentation among patients with pre-existing SUD not included in any CPP (RR = 1.28; 95% CI 1.05–1.56). No significant differences were identified between cancer patients with or without pre-existing psychosis, depression, or anxiety disorder in terms of emergency presentation risk.

Notably, unrecognised cancer close to death among those not referred to any CPP was significantly more likely among those with pre-existing mental disorder or SUD (RR = 1.34; 95% CI 1.18–1.53). Subgroup analyses revealed a consistent pattern, with the same trend observed among cancer patients with pre-existing psychosis, depression, or SUD. The risk was 59% higher among those with pre-existing psychosis (RR=1.59; 95% CI 1.17–2.17), 26% higher among those with pre-existing depression (RR = 1.26: 95% CI 1.08–1.48), and 84% higher among those with pre-existing SUD (RR = 1.84; 95% CI 1.44–2.35) (see Table 3). Among those not referred to any

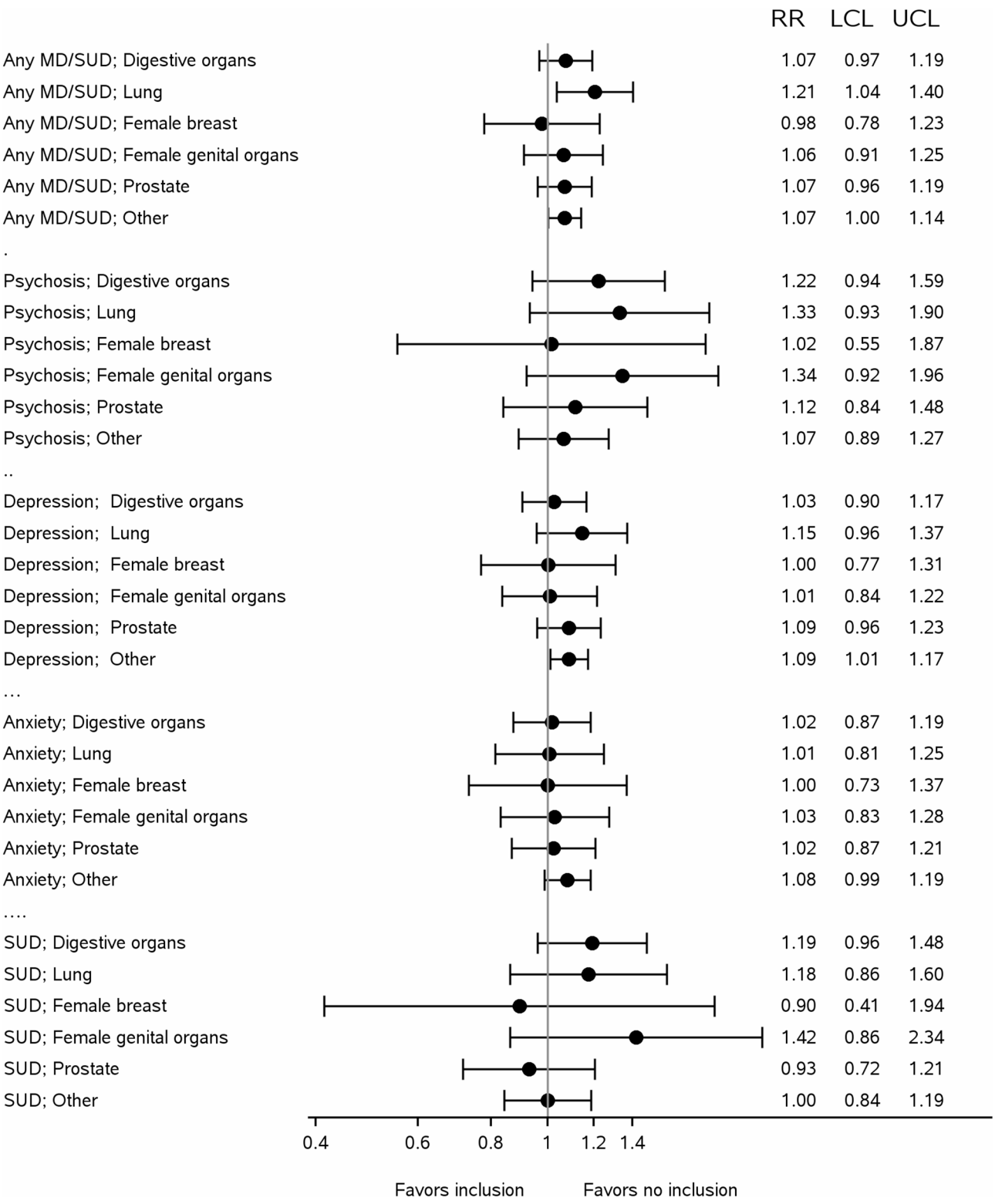


**Fig. 2** Risk ratios (RR) with lower (LCL) and upper (UCL) 95% confidence limits for non-inclusion in a Cancer Patient Pathway, according to type of mental disorder/SUD and cancer type. Abbreviations: MD = mental disorder (psychosis, depression, or anxiety disorder); SUD = substance use disorder

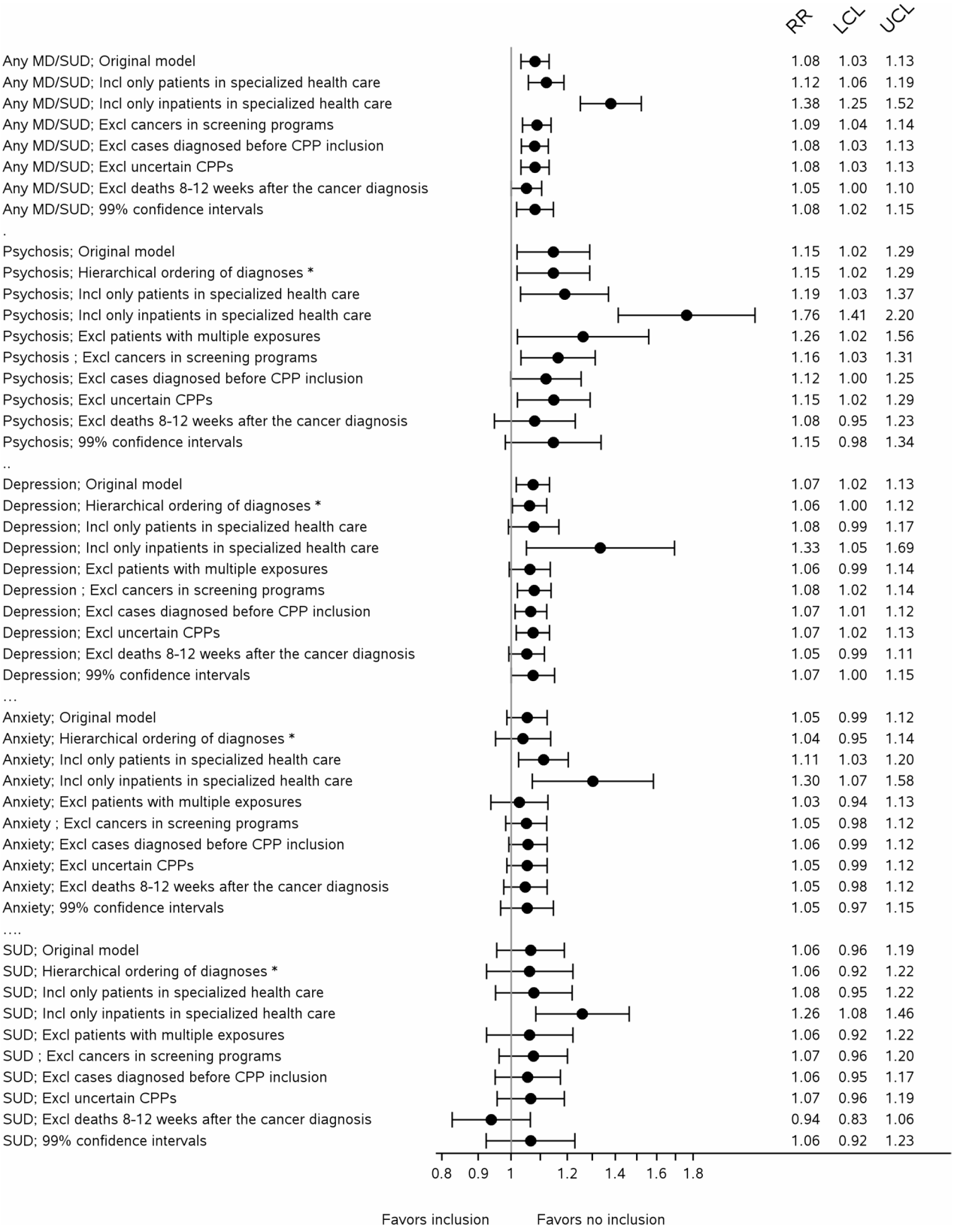


**Fig. 3** Sensitivity analyses. Risk ratios with 95% Confidence Intervals for non-inclusion in a Cancer Patient Pathway, according to differing inclusion criteria and type of mental disorder/SUD. * Hierarchical ordering: Psychosis > Depression > Anxiety disorder > Substance use disorder (SUD). Abbreviations: MD = mental disorder (psychosis, depression, or anxiety disorder); SUD = substance use disorder; RR = risk ratio; LCL = lower confidence limit; UCL = upper confidence limit

**Table 3** Adjusted risk ratios (RR) for low GP attendance prior to cancer diagnosis, cancer diagnosis after emergency presentation, or cancer diagnosis at time of death among cancer patients not included in any CPP, according to pre-existing mental disorder/sud exposure and sex

| | Low GP attendance prior to cancer diagnosis | Cancer diagnosis after emergency presentation | Cancer diagnosis unrecognized close to death |
|---|---|---|---|
| **Prior mental disorder/SUD** | | | |
| Both genders | 0.53 (0.46–0.61)* | 1.10 (1.00-1.21)* | 1.34 (1.18–1.53)* |
| Men | 0.59 (0.49–0.72)* | 1.14 (0.99–1.31) | 1.38 (1.15–1.66)* |
| Women | 0.46 (0.37–0.57)* | 1.07 (0.94–1.21) | 1.30 (1.07–1.57)* |
| **Prior psychosis** | | | |
| Both genders | 0.83 (0.61–1.13) | 1.11 (0.88–1.40) | 1.59 (1.17–2.17)* |
| Men | 0.85 (0.55–1.31) | 1.15 (0.81–1.63) | 1.52 (1.01–2.29)* |
| Women | 0.81 (0.52–1.26) | 1.09 (0.80–1.47) | 1.68 (1.05–2.68)* |
| **Prior depression** | | | |
| Both genders | 0.43 (0.36–0.51)* | 1.08 (0.96–1.21) | 1.26 (1.08–1.48)* |
| Men | 0.47 (0.36–0.60)* | 1.03 (0.86–1.23) | 1.10 (0.87–1.39) |
| Women | 0.39 (0.30–0.51)* | 1.12 (0.96–1.29) | 1.42 (1.14–1.76)* |
| **Prior anxiety disorder** | | | |
| Both genders | 0.41 (0.33–0.51)* | 1.03 (0.90–1.18) | 1.09 (0.90–1.33) |
| Men | 0.45 (0.33–0.62)* | 1.14 (0.92–1.40) | 1.17 (0.88–1.55) |
| Women | 0.37 (0.27–0.51)* | 0.97 (0.81–1.15) | 1.02 (0.77–1.36) |
| **Prior SUD** | | | |
| Both genders | 0.84 (0.62–1.13) | 1.28 (1.05–1.56)* | 1.84 (1.44–2.35)* |
| Men | 0.96 (0.67–1.35) | 1.41 (1.10–1.81)* | 1.83 (1.38–2.44)* |
| Women | 0.54 (0.28–1.03) | 1.08 (0.78–1.49) | 1.84 (1.14–2.96)* |

Abbreviations: GP = general practitioner; SUD = substance use disorder

* Significant result at p-level 0.05

CPP, patients with pre-existing anxiety disorder had similar likelihood as controls for unrecognised cancer close to death.

## Discussion

### Main findings

When analysing all cancers with dedicated CPPs combined in this nationwide study of more than 65,000 incident cancer patients, we found that a pre-existing diagnosis of mental disorder or SUD was associated with a slightly increased risk of non-inclusion in any CPP compared to controls. The risk was particularly elevated among patients with a history of hospitalisation due to mental disorder or SUD, among patients with pre-existing psychosis, and for cancers that can be difficult to diagnose at an early stage (i.e., lung cancer). Additionally, in the subgroup of patients not included in any CPP, patients with pre-existing psychosis, depression or SUD faced a higher risk of unrecognised cancer shortly before the time of death compared to controls, which was not explained by more advanced stage at diagnosis.

### Comparison with related studies

There are only a few prior studies that have examined inclusion in fast-track cancer programs for people with pre-existing mental disorder or SUD. These studies are not directly comparable to our study, as the exposure groups, age groups, cancer groups and definitions of inclusion in a fast-track program differ. In a Danish study, Virgilsen et al. categorised individuals as part of any CPP if they were diagnosed with cancer subsequent to their inclusion in a CPP [18]. In contrast, our study encompassed instances of cancer identified through screening, and cancer cases where adherence to Norwegian guidelines necessitates a confirmed cancer diagnosis prior to inclusion in a CPP for further diagnostic work-up. Consequently, a higher proportion of new cancer cases were counted as included in our study; 79% compared to 63% in the Danish study. However, both studies found that persons with pre-existing mental disorder or SUD had an 8% increased risk of non-inclusion in any CPP, where patients with pre-existing psychotic disorders were at particular risk. The Danish study found that the risk of non-inclusion was most prominent for cancer types that can be difficult to diagnose at an early stage, such as lung cancer or cancers in the digestive organs. Majano et al. also reported that colon cancer patients with concurrent mental disorder or SUD and cardinal symptoms of cancer had lower odds of a fast-track specialist referral [16]. In concordance with the Danish study, we found that lung cancer patients with a history of mental disorder or SUD were at particular risk of non-inclusion in a CPP, but found no differences between patients with cancer in the digestive organs with and without pre-existing mental disorder or SUD. Differences in definitions, including the exclusion of patients with dementia/organic mental disorder, and patients over 79 years of age in our study may have contributed to this difference in results. We found no differences between male and female cancer patients with pre-existing mental disorder or SUD regarding non-inclusion in a CPP. We are not aware of previous gender-specific studies of inclusion in CPP for cancer patients

with pre-existing mental disorder or SUD, but the finding may be in variance with a Norwegian study that found lower odds of inclusion for female lung and rectum cancer patients compared to males in the general cancer population [40].

To our knowledge, there are no existing studies that have specifically examined the relationship between non-inclusion in any CPP and low GP attendance, cancer emergency presentations, or unrecognised cancer close to time of death among cancer patients with and without pre-existing mental disorder or SUD. However, prior studies have reported a higher risk of a cancer diagnosis after emergency presentation among patients with existing mental disorder or SUD [16, 18, 44]. Additionally, these studies have highlighted that non-attendance in primary care is common among patients who receive a cancer diagnosis following an unplanned contact with the specialist health service [44]. In our study, we found that the in the subgroup of cancer patients who were not included in any CPP, risk of emergency presentations was higher among patients with pre-existing SUD, but similar between patients with and without psychosis, depression, or anxiety disorder. Therefore, this factor did not explain the observed differences in non-inclusion between cancer patients with and without pre-existing psychosis, anxiety disorder or depression in our study. Furthermore, it is worth noting that patients with pre-existing mental disorder or SUD had a higher frequency of GP attendance prior to the cancer diagnosis, which also does not contribute to explaining the observed differences. We have previously reported higher primary care utilization but lower use of somatic specialist health services in patients with pre-existing psychosis who died of cardiovascular disease [55].

The finding of a higher risk of unrecognised cancer close to death among patients with pre-existing psychosis is in accordance with a prior study reporting an increased risk of cancer diagnosis less than 30 days before death among patients with schizophrenia [17]. The Danish study referred to previously [18] found an increased risk of cancer first recognised on the death certificate among patients with pre-existing mental disorder or SUD. We found, however, that the risk of a first cancer diagnosis close to the time of death for patients varied with gender and the type of mental disorder or SUD, where men and women with pre-existing psychosis or SUD had an increased risk compared to other cancer patients, as did women, but not men, with pre-existing depression or anxiety disorder. Although the outcome measures are not the same in these studies, our findings contribute to nuance the picture of the importance of gender and type of mental disorder or SUD in relation to unrecognised cancer close to death.

### Possible mechanisms

Various factors related to the disease, patient, provider, and healthcare system levels could contribute to the observed findings. Prior research has shown that factors such as low income, living alone, female sex (in the case of lung and rectum cancer), high or low age at diagnosis, somatic multimorbidity, and metastatic disease are associated with an increased likelihood of non-inclusion in a fast-track program [39–42]. While these factors were accounted for in the analysis, residual confounding cannot be ruled out.

Our findings revealed that among cancer patients who were not included in any CPP, those with pre-existing psychosis or SUD had a marked increased risk of unrecognised cancer close to death compared to controls, as did women with pre-existing depression or anxiety disorder. These findings indicate that persons with these disorders may be less likely to fully utilize the specialised somatic healthcare resources available to them compared to individuals without these conditions [55]. The mechanisms behind this probably vary with the type of mental disorder or SUD. For the most severely ill, factors such as neglect or reduced awareness of symptoms, reduced capacity, cognitive deficits, lack of ability to consent, and behavioural aspects, likely contribute to the observed results [56]. These factors can affect interpretation and dissemination of new or changed symptoms, patient-provider communication, and healthcare-seeking behaviour, including reduced uptake of screening services [57].

A decreased sensitivity to pain in patients with psychosis has been hypothesised in some studies [58], but the findings may be explained by negative symptoms or a reduced ability to express pain [59]. Stigma associated with mental disorder or SUD may further discourage individuals from seeking healthcare [60]. Lack of consent may also contribute, as Norwegian legislation allows treatment of somatic illness without consent only in cases of acute or imminent danger of serious illness or death. An additional concern arises from the fact that many individuals with severe mental disorders receive follow-up care from health professionals lacking sufficient expertise in somatic issues. Consequently, crucial risk factors or identified somatic illnesses may not receive the necessary attention.

The phenomenon of "negative pragmatism" also likely contributes to the reported findings, wherein practitioners may downplay the significance of somatic follow-up due to the patients' pre-existing acute challenges [61]. Moreover, the presence of multimorbidity as such can significantly affect doctors' diagnostic reasoning and examinations, both due to competing priorities, as alternative explanations for symptoms, and in the assessments of what is feasible actions [62]. This impact may be particularly noteworthy for women with pre-existing

depression or anxiety disorder who were not included in any CPP, who, despite higher GP attendance, faced an elevated risk of a delayed cancer diagnosis. This heightened risk may be associated with the phenomenon known as diagnostic overshadowing [63], where early indications of cancer may be mistakenly interpreted as manifestations of psychiatric symptoms, leading to delays in the recognition and diagnosis of the underlying malignancy. On a systemic level, the challenges are compounded by fragmented care and a lack of coordination within the healthcare system, which poses particular challenges for patients with severe mental disorder or SUD [64, 65].

#### Generalizability

Many European countries have nationwide, tax-funded healthcare systems that promote standardization across regions. National cancer registries are common, supporting systematic monitoring and evaluation of CPPs. However, CPP implementation varies across Europe. England have cancer patient pathways resembling the structured Nordic CPPs, while Germany, France, Spain, the Netherlands, and Italy have systems designed to ensure structured diagnostic and treatment processes, albeit with differing levels of specificity and national coverage [66, 67]. Our findings are most applicable to countries with health care systems similar to those in Northern Europe. Nevertheless, the global healthcare community shares the goal of reducing system-related delays in cancer care, emphasizing efficient diagnostics and treatment, interdisciplinary collaboration, and patient involvement to improve satisfaction and outcomes. Consequently, these insights hold relevance for diverse healthcare models worldwide.

#### Implications

A close cooperation between specialist psychiatric and somatic health care is crucial to identify patients at risk and address the complex needs of patients with severe mental disorder or SUD. This includes structural measures to allow sufficient time for comprehensive assessments, effective communication during healthcare attendance at all levels, and possibly enrolment in assertive community treatment programs. Specialists in psychiatry and drug/addiction medicine may also find themselves compelled to assume broader responsibilities for their most critically ill patients, akin to the multifaceted role undertaken by GPs.

GPs play an important role in both identification and follow-up of cancer, particularly highlighted in the context of patients with severe mental disorder or SUD. This role may include yearly somatic screening of patients with severe mental disorder or SUD, as well as active outreach to vulnerable patients. Emphasizing preventive, evidence-based measures to reduce cancer risk factors such as smoking, low levels of physical activity and unhealthy diets, is also of crucial importance.

Developing and implementing more accurate risk assessment instruments can also play a significant role in identifying patients at higher risk of emergency presentation or non-inclusion in a CPP. These instruments should consider both medical factors and social determinants of health to provide a comprehensive evaluation of individual patient needs. The presence of shared risk factors for non-inclusion and emergency presentation suggests that certain sociodemographic and clinical characteristics, such as low income, living alone, high or low age at diagnosis, somatic comorbidity, and non-attendance in primary care, should serve as warning signals for healthcare personnel. By recognising these risk factors, healthcare providers can effectively target high-risk individuals for proactive intervention and support.

Addressing the disparities in non-inclusion and emergency presentations should not be limited to improving access to fast-track systems. Equally important is the provision of high-quality diagnostic and treatment services once cancer is recognised. This includes ensuring timely referrals, appropriate treatment planning and multidisciplinary care coordination, in order to reduce the observed lack of equity for these patients.

#### Strengths and limitations

The study has several strengths, including its population-based design and use of comprehensive nationwide data without selection bias. The inclusion of exposure and control groups balanced in terms of baseline characteristics minimised bias due to measured confounders. The use of a non-parametric method for estimating propensity scores that captured both main effects and interactions in included covariates provided robustness to possible model misspecification. Moreover, the outcome analyses were conducted independently of the modelling. However, limitations should be acknowledged. Propensity score methods cannot balance unmeasured confounders that are uncorrelated with the included variables in the model, which introduces the possibility of residual confounding. The diagnosis used are set by physicians or psychologists for clinical purposes, potentially making them susceptible to variations in diagnostic practices. The definition of enrolment in a CPP is not straightforward, and the inclusion of patients with a confirmed cancer diagnosis might be questioned. Excluding these patients did, however, not change results. The chosen observation period for inclusion may have also impacted the outcomes. If the time from suspicion of cancer to inclusion in a CPP is consistently longer for patients with mental disorders or SUD, compared with patients without such disorders, we may have underestimated the proportion included. Exploratory sensitivity analyses with

different definitions of mental disorder or SUD and CPP inclusion yielded similar results. We cannot rule out that some statistically significant results may have been spurious findings due to multiple testing. However, the use of complete and unselected nationwide data, along with consistent results, may allow for generalization to other countries with similar healthcare systems.

## Conclusions

Cancer patients with pre-existing mental disorder or SUD have an increased risk of non-inclusion in a CPP, with the most severely mentally ill at particular risk. Additionally, in the subgroup of patients not included in any CPP, patients with pre-existing psychosis, depression, or SUD face a higher risk of unrecognised cancer shortly before the time of death, which was not explained by more advanced cancer stage. These findings emphasize the need for an integrated and patient-centred approach to cancer care, particularly for individuals with severe mental disorders. By addressing barriers to CPP-inclusion, allowing sufficient time during healthcare attendance, improving risk assessment, and enhancing the quality of diagnostic and treatment services, healthcare systems can work towards achieving better outcomes for these vulnerable patient groups.

### Abbreviations

| | |
|---|---|
| ATT | Average Treatment Effect on the Treated |
| ATC | Anatomical Therapeutic Chemical |
| CI | Confidence Intervals |
| CPP | Cancer Patient Pathway |
| GP | General Practitioner |
| ICD-10 | International Statistical Classification of Diseases and Related Health Problems, 10th Revision |
| ICPC-2 | International Classification of Primary Care, 2nd Edition |
| IPW | Inverse Probability Weighting |
| LCL | Lower Confidence Limit |
| MD | Mental Disorder |
| NorPD | The Norwegian Prescription Registry |
| RR | Risk Ratio / Relative Risk |
| SD | Standard Deviation |
| SMD | Standardised Mean Differences |
| SUD | Substance Use Disorder |
| UCL | Upper Confidence Limit |

## Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12889-025-23180-7.

Supplementary Material 1

Supplementary Material 2

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### Author contributions

AH, LB, IHH, and BKJ conceived and designed the study. IHH managed and analysed the data and was primarily responsible for reporting and writing. IHH, AH, BKJ and LB prepared an initial draft of the manuscript. All authors contributed to manuscript revisions and reviewed and approved the final manuscript.

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### Data availability

The data that support the findings of this study are available from the Norwegian Patient Registry, the Norwegian Directorate of Health's system for control and payment of health reimbursements in primary care, the Norwegian Labour and Welfare Administration's Database of disability pensions, the Norwegian Prescription Database and Statistics Norway. Restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. According to the contract signed with the registries involved, the researchers are not allowed to forward data, or subsets of data, to other researchers, except for project members named in the Data Protection Impact Assessment. Any researcher with an approved exemption from professional secrecy requirements for the use of personal health information in research from the Regional Committee for Medical and Healthcare Research Ethics will, however, be able to create an identical data set by applying to the relevant registries.

## Declarations

### Ethics approval and consent to participate

The study protocol received approval from the Regional Committee for Medical and Health Research Ethics (REC North). Additionally, REC North granted the legal basis for utilizing personal health information in research, which includes exemptions from confidentiality requirements and the need for consent (Approval: 2019/59177/REK nord). All registry owners provided consent for the utilization of their data. Given the use of pre-existing registry data, obtaining written or verbal consent to participate was neither feasible nor required for this study.

### Consent for publication

Not applicable.

### Competing interests

The authors declare no competing interests.

### Experiments on humans or human tissue samples

Not applicable.

### Disclaimer

Data from the Norwegian Patient Registry and the Norwegian Cancer Registry have been used in this publication. The interpretation and reporting of these data are the sole responsibility of the authors, and no endorsement by the Norwegian Patient Registry or the Norwegian Cancer Registry is intended nor should be inferred.

### Author details

[1]Center for Clinical Documentation and Evaluation (SKDE), Tromsø, Norway
[2]Division of Mental Health and Substance Abuse, University Hospital of North Norway, Tromsø, Norway
[3]Department of Oncology, University Hospital of North Norway, Tromsø, Norway
[4]Department of Community Medicine, UiT The Arctic University of Norway, Tromsø, Norway
[5]Department of Clinical Medicine, UiT The Arctic University of Norway, Tromsø, Norway
[6]Section for Clinical Addiction Research (RusForsk), Division of Mental Health and Addiction, Oslo University Hospital, Oslo, Norway
[7]Division for Mental and Physical Health, the Norwegian Institute of Public Health, Oslo, Norway
[8]Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, Oslo, Norway

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**References**


1. Kisely S, Crowe E, Lawrence D. Cancer-related mortality in people with mental illness. JAMA Psychiatry. 2013;70(2):209–17.
2. Toender A, Munk-Olsen T, Vestergaard M, et al. Impact of severe mental illness on cancer stage at diagnosis and subsequent mortality: A population-based register study. Schizophr Res. 2018;201:62–9.
3. Erlangsen A, Andersen PK, Toender A, Laursen TM, Nordentoft M, Canudas-Romo V. Cause-specific life-years lost in people with mental disorders: a nationwide, register-based cohort study. Lancet Psychiatry. 2017;4(12):937–45.
4. Søgaard M, Thomsen RW, Bossen KS, Sørensen HT, Nørgaard M. The impact of comorbidity on cancer survival: a review. Clin Epidemiol. 2013;5(Suppl 1):3–29.
5. Solmi M, Firth J, Miola A, et al. Disparities in cancer screening in people with mental illness across the world versus the general population: prevalence and comparative meta-analysis including 4 717 839 people. Lancet Psychiatry. 2020;7(1):52–63.
6. Kaerlev L, Iachina M, Trosko O, Qvist N, Ljungdalh PM, Norgard BM. Colon cancer patients with a serious psychiatric disorder present with a more advanced cancer stage and receive less adjuvant chemotherapy - A nationwide Danish cohort study. BMC Cancer. 2018;18(1):1050.
7. O'Rourke RW, Diggs BS, Spight DH, et al. Psychiatric illness delays diagnosis of esophageal cancer. Dis Esophagus: Official J Int Soc Dis Esophagus. 2008;21(5):416–21.
8. Irwin KE, Henderson DC, Knight HP, Pirl WF. Cancer care for individuals with schizophrenia. Cancer. 2014;120(3):323–34.
9. Bergamo C, Sigel K, Mhango G, Kale M, Wisnivesky JP. Inequalities in lung cancer care of elderly patients with schizophrenia: an observational cohort study. Psychosom Med. 2014;76(3):215–20.
10. Ishikawa H, Yasunaga H, Matsui H, Fushimi K, Kawakami N. Differences in cancer stage, treatment and in-hospital mortality between patients with and without schizophrenia: retrospective matched-pair cohort study. Br J Psychiatry: J Mental Sci. 2016;208(3):239–44.
11. Huang HK, Wang YW, Hsieh JG, Hsieh CJ. Disparity of end-of-life care in cancer patients with and without schizophrenia: A nationwide population-based cohort study. Schizophr Res. 2018;195:434–40.
12. Lawrence D, Kisely S. Inequalities in healthcare provision for people with severe mental illness. J Psychopharmacol (Oxford England). 2010;24(4 Suppl):61–8.
13. Kisely S, Alotiby MKN, Protani MM, Soole R, Arnautovska U, Siskind D. Breast cancer treatment disparities in patients with severe mental illness: A systematic review and meta-analysis. Psycho-oncology. 2023;32(5):651–62.
14. Seppänen AV, Daniel F, Houzard S, Le Bihan C, Coldefy M, Gandré C. Breast Cancer care pathways for women with preexisting severe mental disorders: evidence of disparities in France? J Clin Med 2023; 12(2).
15. Renzi C, Kaushal A, Emery J, et al. Comorbid chronic diseases and cancer diagnosis: disease-specific effects and underlying mechanisms. Nat Rev Clin Oncol. 2019;16(12):746–61.
16. Majano SB, Lyratzopoulos G, de Wit NJ, et al. Mental health morbidities and time to Cancer diagnosis among adults with Colon Cancer in England. JAMA Netw Open. 2022;5(10):e2238569.
17. Brink M, Green A, Bojesen AB, Lamberti JS, Conwell Y, Andersen K. Excess medical comorbidity and mortality across the lifespan in schizophrenia.: A nationwide Danish register study. Schizophr Res. 2019;206:347–54.
18. Virgilsen LF, Vedsted P, Falborg AZ, Pedersen AF, Prior A, Jensen H. Routes to cancer diagnosis for patients with pre-existing psychiatric disorders: a nationwide register-based cohort study. BMC Cancer. 2022;22(1):472.
19. Wootten JC, Wiener JC, Blanchette PS, Anderson KK. Cancer incidence and stage at diagnosis among people with psychotic disorders: systematic review and meta-analysis. Cancer Epidemiol. 2022;80:102233.
20. Neal RD, Tharmanathan P, France B, et al. Is increased time to diagnosis and treatment in symptomatic cancer associated with poorer outcomes? Systematic review. Br J Cancer. 2015;112(Suppl 1):S92–107.
21. Whittaker TM, Abdelrazek MEG, Fitzpatrick AJ, et al. Delay to elective colorectal cancer surgery and implications for survival: a systematic review and meta-analysis. Colorectal Disease: Official J Association Coloproctology Great Br Irel. 2021;23(7):1699–711.
22. Johnson BA, Waddimba AC, Ogola GO, Fleshman JW Jr., Preskitt JT. A systematic review and meta-analysis of surgery delays and survival in breast, lung and colon cancers: implication for surgical triage during the COVID-19 pandemic. Am J Surg. 2021;222(2):311–8.
23. McPhail S, Swann R, Johnson SA, et al. Risk factors and prognostic implications of diagnosis of cancer within 30 days after an emergency hospital admission (emergency presentation): an international Cancer benchmarking partnership (ICBP) population-based study. Lancet Oncol. 2022;23(5):587–600.
24. Danckert B, Falborg AZ, Christensen NL, et al. Routes to diagnosis and the association with the prognosis in patients with cancer - A nationwide register-based cohort study in Denmark. Cancer Epidemiol. 2021;74:101983.
25. Jensen AR, Nellemann HM, Overgaard J. Tumor progression in waiting time for radiotherapy in head and neck cancer. Radiother Oncol. 2007;84(1):5–10.
26. Liu Y, Zhang T, Wu Q, et al. Relationship between initiation time of adjuvant chemotherapy and survival in ovarian cancer patients: a dose-response meta-analysis of cohort studies. Sci Rep. 2017;7(1):9461.
27. Hanna TP, King WD, Thibodeau S, et al. Mortality due to cancer treatment delay: systematic review and meta-analysis. BMJ. 2020;371:m4087.
28. Jensen H, Tørring ML, Olesen F, Overgaard J, Fenger-Grøn M, Vedsted P. Diagnostic intervals before and after implementation of cancer patient pathways - a GP survey and registry based comparison of three cohorts of cancer patients. BMC Cancer. 2015;15:308.
29. Nilbert M, Bläckberg M, Ceberg J, Hagberg O, Stenhoff R, Liedberg F. Diagnostic pathway efficacy for urinary tract cancer: population-based outcome of standardized evaluation for macroscopic haematuria. Scandinavian J Urol. 2018;52(4):237–43.
30. Nilssen Y, Brustugun OT, Tandberg Eriksen M, et al. Decreasing waiting time for treatment before and during implementation of cancer patient pathways in Norway. Cancer Epidemiol. 2019;61:59–69.
31. Dyrop HB, Safwat A, Vedsted P, et al. Cancer patient pathways shortens waiting times and accelerates the diagnostic process of suspected sarcoma patients in Denmark. Health Policy. 2013;113(1–2):110–7.
32. Larsen MB, Hansen RP, Hansen DG, Olesen F, Vedsted P. Secondary care intervals before and after the introduction of urgent referral guidelines for suspected cancer in Denmark: a comparative before-after study. BMC Health Serv Res. 2013;13:348.
33. Schmidt I, Thor J, Davidson T, Nilsson F, Carlsson C. The National program on standardized cancer care pathways in Sweden: observations and findings half way through. Health Policy. 2018;122(9):945–8.
34. Abuhasanein S, Jahnson S, Aljabery F, et al. Standardized care pathways for patients with suspected urinary bladder cancer: the Swedish experience. Scandinavian J Urol. 2022;56(3):227–32.
35. Lyhne NM, Christensen A, Alanin MC, et al. Waiting times for diagnosis and treatment of head and neck cancer in Denmark in 2010 compared to 1992 and 2002. Eur J cancer (Oxford England: 1990). 2013;49(7):1627–33.
36. Jensen H, Tørring ML, Fenger-Grøn M, Olesen F, Overgaard J, Vedsted P. Tumour stage and implementation of standardised cancer patient pathways: a comparative cohort study. Br J Gen Practice: J Royal Coll Gen Practitioners. 2016;66(647):e434–43.
37. Jensen H, Tørring ML, Olesen F, Overgaard J, Vedsted P. Cancer suspicion in general practice, urgent referral and time to diagnosis: a population-based GP survey and registry study. BMC Cancer. 2014;14:636.
38. Meechan D, Gildea C, Hollingworth L, Richards MA, Riley D, Rubin G. Variation in use of the 2-week referral pathway for suspected cancer: a cross-sectional analysis. Br J Gen Practice: J Royal Coll Gen Practitioners. 2012;62(602):e590–7.
39. Olsen F, Jacobsen BK, Heuch I, Tveit KM, Balteskard L. Equitable access to cancer patient pathways in Norway - a National registry-based study. BMC Health Serv Res. 2021;21(1):1272.
40. Nilssen Y, Brustugun OT, Eriksen MT, Haug ES, Naume B, Møller B. Patient and tumour characteristics associated with inclusion in Cancer patient pathways in Norway in 2015–2016. BMC Cancer. 2020;20(1):488.
41. Baun ML, Jensen H, Falborg AZ, Heje HN, Petersen LK, Vedsted P. Ovarian cancer suspicion, urgent referral and time to diagnosis in Danish general practice: a population-based study. Fam Pract. 2019;36(6):751–7.
42. Wiering B, Lyratzopoulos G, Hamilton W, Campbell J, Abel G. Concordance with urgent referral guidelines in patients presenting with any of six 'alarm' features of possible cancer: a retrospective cohort study using linked primary care records. BMJ Qual Saf. 2022;31(8):579–89.
43. Fortuna KL, DiMilia PR, Lohman MC, et al. Feasibility, acceptability, and preliminary effectiveness of a Peer-Delivered and technology supported

Self-Management intervention for older adults with serious mental illness. Psychiatr Q. 2018;89(2):293–305.
44. Virgilsen LF, Falborg AZ, Vedsted P, Prior A, Pedersen AF, Jensen H. Unplanned cancer presentation in patients with psychiatric disorders: A nationwide register-based cohort study in Denmark. Cancer Epidemiol. 2022;81:102293.
45. Crump C, Winkleby MA, Sundquist K, Sundquist J. Comorbidities and mortality in persons with schizophrenia: a Swedish National cohort study. Am J Psychiatry. 2013;170(3):324–33.
46. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. Int J Surg (London England). 2014;12(12):1495–9.
47. Khan N, Afaq F, Mukhtar H. Lifestyle as risk factor for cancer: evidence from human studies. Cancer Lett. 2010;293(2):133–43.
48. Larsson SC, Burgess S. Appraising the causal role of smoking in multiple diseases: A systematic review and meta-analysis of Mendelian randomization studies. EBioMedicine. 2022;82:104154.
49. Masuda T, Ogawa K, Kamatani Y, Murakami Y, Kimura T, Okada Y. A Mendelian randomization study identified obesity as a causal risk factor of uterine endometrial cancer in Japanese. Cancer Sci. 2020;111(12):4646–51.
50. SAS Institute. The GRADBOOST Procedure. 2023. https://documentation.sas.com/doc/en/vdmmlcdc/8.1/casml/viyaml_gradboost_syntax01.htm (accessed August, 22th 2023).
51. Faries D, Zhang X, Kadziola Z, Siebert U, Kuehne F, Obenchain R, Haro JM. Real world health care analysis. Causal methods and implementation using SAS (R). Cary, NC, USA: SAS Institute; 2020.
52. SAS Institute. SAS/STAT® 14.2 User's Guide The PSMATCH Procedure. 2023. https://support.sas.com/documentation/onlinedoc/stat/142/psmatch.pdf (accessed August, 22th 2023).
53. Caswell J. accessed May 11th. Clinical Descriptors for Two-Way Tables with Independent Unweighted or Weighted Samples: A SAS Macro to Calculate P, OR, ARR, NNT, RR, and Their Confidence Intervals. https://www.academia.edu/37692312/Clinical_Descriptors_for_Two_Way_Tables_with_Independent_Unweighted_or_Weighted_Samples_A_SAS_Macro_to_Calculate_P_OR_ARR_NNT_RR_and_Their_Confidence_Intervals (2023).
54. Oliveros JC, Venny. An interactive tool for comparing lists with Venn's diagrams. 2007–2015. https://bioinfogp.cnb.csic.es/tools/venny/ (accessed 29th Nov 2023 2023).
55. Heiberg IH, Nesvåg R, Balteskard L, et al. Diagnostic tests and treatment procedures performed prior to cardiovascular death in individuals with severe mental illness. Acta Psychiatr Scand. 2020;141(5):439–51.
56. Fagiolini A, Goracci A. The effects of undertreated chronic medical illnesses in patients with severe mental disorders. J Clin Psychiatry. 2009;70(Suppl 3):22–9.
57. Hwong A, Wang K, Bent S, Mangurian C. Breast Cancer screening in women with schizophrenia: A systematic review and Meta-Analysis. Psychiatric Serv (Washington DC). 2020;71(3):263–8.
58. Stubbs B, Thompson T, Acaster S, Vancampfort D, Gaughran F, Correll CU. Decreased pain sensitivity among people with schizophrenia: a meta-analysis of experimental pain induction studies. Pain. 2015;156(11):2121–31.
59. Urban-Kowalczyk M, Pigońska J, Śmigielski J. Pain perception in schizophrenia: influence of neuropeptides, cognitive disorders, and negative symptoms. Neuropsychiatr Dis Treat. 2015;11:2023–31.
60. Clement S, Schauman O, Graham T, et al. What is the impact of mental health-related stigma on help-seeking? A systematic review of quantitative and qualitative studies. Psychol Med. 2015;45(1):11–27.
61. Skeie I. Health improvements needed in persons with mental disorders and substance use disorders. Tidsskrift for Den Norske Laegeforening: tidsskrift for Praktisk medicin. Ny Raekke 2024; 144(1).
62. Fleischhacker WW, Cetkovich-Bakmas M, De Hert M, et al. Comorbid somatic illnesses in patients with severe mental disorders: clinical, policy, and research challenges. J Clin Psychiatry. 2008;69(4):514–9.
63. Happell B, Ewart SB, Bocking J, Platania-Phung C, Stanton R. That red flag on your file': misinterpreting physical symptoms as mental illness. J Clin Nurs. 2016;25(19–20):2933–42.
64. Gandré C, Coldefy M. Disparities in the use of general somatic care among individuals treated for severe mental disorders and the general population in France. Int J Environ Res Public Health 2020; 17(10).
65. Brämberg EB, Torgerson J, Norman Kjellström A, Welin P, Rusner M. Access to primary and specialized somatic health care for persons with severe mental illness: a qualitative study of perceived barriers and facilitators in Swedish health care. BMC Fam Pract. 2018;19(1):12.
66. National Disease Registration Service. Cancer diagnostic pathways. 2024. https://digital.nhs.uk/ndrs/our-work/ncras-work-programme/cancer-diagnostic-pathways (accessed 13 Dec 2024).
67. The German Cancer Society. Clinical Practice Guidelines. 2024. https://www.krebsgesellschaft.de/gcs/german-cancer-society/guidelines.html (accessed Dec 16, 2024 2024).

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