



Charlesworth, Laura ORCID logoORCID: <https://orcid.org/0000-0003-3584-2729>, Fegan, Colette and Ashmore, Russell (2023) How does severe mental illness impact on cancer outcomes in individuals with severe mental illness and cancer? A scoping review of the literature. *Journal of Medical Imaging and Radiation Sciences*, 54 (2). S104-S114.

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Review Article

How does severe mental illness impact on cancer outcomes in individuals with severe mental illness and cancer? A scoping review of the literature

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*College of Health, Wellbeing and Life Sciences, Sheffield Hallam University, Sheffield, England***ABSTRACT**

Introduction: Individuals living with severe mental illness (SMI) have a reduced life expectancy of approximately 15–20 years compared to the general population^{1,2}. Individuals with SMI and comorbid cancer have increased cancer related mortality rates compared to the non SMI population. This scoping review examines the current evidence in relation to the impact on cancer outcomes where individuals have a pre-existing SMI.

Methods: Scopus, PsychINFO, PubMed, PsycArticles and the Cochrane Library were searched for peer reviewed research articles, published in English language between 2001 and 2021. Initial title and abstract screening, followed by full text screening sourced articles reporting on the impact of SMI and cancer on: stage at diagnosis, survival, treatment access or quality of life. Articles were quality appraised, and data were extracted and summarised.

Results: The search yielded 1226 articles, 27 met the inclusion criteria. The search yielded no articles that met the inclusion criteria that were from the perspective of the service user or that were focused on the impact of SMI and cancer quality of life. Three themes were developed following analysis: Cancer related mortality, stage at diagnosis, and access to stage appropriate treatment.

Discussion: The collective study of populations with comorbid SMI and cancer is complex and challenging without a large-scale cohort study. The studies yielded through this scoping review were heterogeneous and often study multiple diagnoses of SMI and cancer. Collectively these indicate that cancer related mortality is increased in the population of individuals with pre-existing SMI and the SMI pop-

ulation are more likely to have an increased likelihood of metastatic disease at diagnosis and less likely to receive stage appropriate treatment.

Conclusions: Individuals with pre-existing SMI and cancer have increased cancer specific mortality. Comorbid SMI and cancer is complex, and individuals with SMI and cancer are less likely to receive optimal treatments, experience increased interruptions and delays to treatment.

RÉSUMÉ

Introduction: Les personnes atteintes de maladie mentale grave (MMG) ont une espérance de vie réduite d'environ 15 à 20 ans par rapport à la population générale [1,2]. Les personnes atteintes d'une maladie mentale grave et d'un cancer comorbide présentent des taux de mortalité liés au cancer plus élevés que ceux de la population non atteinte d'une maladie mentale grave. Cette revue de cadrage examine les preuves actuelles concernant l'incidence sur les résultats du cancer lorsque les personnes ont une MMG préexistante.

Méthodologie: Des recherches ont été menées dans Scopus, PsychINFO, PubMed, PsycArticles et la Cochrane Library pour trouver des articles de recherche évalués par des pairs, publiés en anglais entre 2001 et 2021. Un premier tri des titres, suivi d'un tri des résumés et du texte intégral a permis de trouver des articles traitant de l'incidence de la MMG et du cancer sur le stade du diagnostic, la survie, l'accès au traitement ou la qualité de vie. Les articles ont fait l'objet d'une évaluation de la qualité, et les données ont été extraites et résumées.

Funding: No funding was received to undertake this scoping review. The PhD is part funded by the lead author and part funded by her employer. All authors have contributed to the drafting of this review.

Competing interests: There are no conflicts or competing interests to disclose.

Ethical approval: Ethical approval was not sought for the scoping review. The full PhD study has University and Health Research Authority ethical approval (IRAS 268528). There are no conflicts of interest to disclose.

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Résultats: La recherche a généré 1226 articles, dont 27 répondaient aux critères d'inclusion. La recherche n'a révélé aucun article répondant aux critères d'inclusion et présentant le point de vue de l'utilisateur de services ou portant sur l'incidence de la MMG et la qualité de vie liée au cancer. Trois thèmes ont été développés à la suite de l'analyse : La mortalité liée au cancer, le stade du diagnostic et l'accès à un traitement adapté au stade.

Discussion: L'étude collective des populations souffrant de comorbidité de la maladie mentale grave et du cancer est complexe et difficile sans une étude de cohorte à grande échelle. Les études obtenues dans le cadre de cette revue de la littérature étaient hétérogènes et étudiaient souvent des diagnostics multiples de maladie mentale grave et de can-

cer. Collectivement, elles indiquent que la mortalité liée au cancer est plus élevée dans la population des personnes souffrant d'une MMG préexistante et que la population atteinte de MMG est plus susceptible d'avoir une probabilité accrue de maladie métastatique au moment du diagnostic et moins susceptible de recevoir un traitement adapté au stade.

Conclusions: Les personnes souffrant d'une MMG préexistante et d'un cancer présentent une mortalité accrue liée au cancer. La comorbidité MMG et cancer est complexe, et les personnes souffrant de PMI et de cancer sont moins susceptibles de recevoir des traitements optimaux, de subir des interruptions et des retards accrus dans le traitement.

Keywords: Cancer; Comorbidity; Mental health; Mortality; Oncology; Severe mental illness; Stage at diagnosis; Long Term Conditions

Introduction

Individuals with SMI, such as schizophrenia or bipolar disorder are reported to die prematurely when compared to the general population [1,2], with the life expectancy of individuals living with SMI being 15-20 years less compared to individuals living without SMI [3]. It is estimated that approximately 38% of individuals with SMI also experience a comorbid physical illness [4], such as cancer. There were 17 million new cases of cancer diagnosed worldwide in 2018 [5], with a greater number of individuals living with and beyond cancer with the effects of the disease and treatment.

Prior to a diagnosis of cancer, the uptake of cancer screening has been shown to be reduced in the SMI population [6]. Non-attendance at screening reduces the potential for early detection and in several cancer histological types, can decrease overall survival rates [7]. Many individuals with a diagnosis of SMI have experienced reduced acceptance of physical health complaints by their primary care clinician and decreased access to diagnostic tests and treatment [8]. Following a cancer diagnosis, individuals with SMI are reported to experience reduced quality of life and reduced ability to manage physical side effects, compared to those without SMI [9-11].

Although the overall mortality gap for individuals with SMI is well documented, the impact on outcomes specific to comorbid cancer and SMI is not fully understood or explained. To date, a scoping review has not been undertaken to understand the impact of comorbid SMI and cancer on cancer outcomes. This review aimed to identify and synthesise the research undertaken to demonstrate the impact on outcomes when an individual experiences comorbid SMI alongside a cancer diagnosis.

Methods

A scoping review provides preliminary assessment of the available research literature, and it can be utilised to answer a broad research question [12,13]. This scoping review was conducted using the methodological framework proposed by Ar-

sky and O'Malley [13]. The PRISMA-ScR [14] checklist was used to ensure transparency, rigour and a systematic approach to the review. CASP checklists were completed to appraise articles [15].

Identifying the research question

The review aimed to address the following research question: how does severe mental illness impact on cancer outcomes? All cancer and SMI diagnoses were included as defined by authors in the studies retrieved, with the exclusion of dementia. Outcomes were defined using search terms outlined in Table 1.

Identifying relevant studies

The review was conducted using a systematic search of the literature for the period 2001 – 2021 and written in English. The following information databases were searched; Scopus, PsychINFO, PubMed, PsycArticles and the Cochrane Library. Grey literature was not sought, however reference lists of included studies were searched for additional relevant literature.

Study selection

Identified articles were imported into Refworks. Initial title and abstract screening occurred followed by full text screening conducted by a single author.

Charting the data

In line with Arsky and O'Malley's framework [13], key items were charted from the research data. Where available, the following categories were documented; Author, year of publication, study location, intervention type, and comparator, period of follow up and control group, study populations, cancer histology, SMI diagnoses, how SMI diagnoses determined, aims of the study, methodology, outcome measures and significant findings.

Table 1
Search terms.

	Concept 1: Severe Mental Illness	Concept 2: Cancer	Concept 3: Outcomes
Synonyms/ Alternatives	Psychiatric Schizophren* Psychosis Bipolar Manic Depress* Serious mental illness Psychotic	Oncology Neoplasm Malignancy Tumo* Carcinoma	Treatment QOL Quality of life Survival Stage Stage at diagnosis Mortality Prevention Incidence

Collating, summarising and reporting the results

Data were extracted using NVivo 12 software [16], identifying codes relevant to outcomes: all-cause mortality, cancer related mortality, access to treatment, treatment compliance, stage at diagnosis, metastatic disease at diagnosis and health-care utilisation.

Results

The search yielded 1226 articles. Articles over 20 years old were removed, alongside biochemical articles and duplicates resulting in 411 articles remaining Fig. 1. Following title and abstract screening, 108 articles remained for full text screening and 27 articles met inclusion criteria (Appendix 1). The search yielded no articles meeting the inclusion criteria that were from the perspective of the service user or that were focused on the impact of SMI and cancer quality of life Fig. 1.

Study design and characteristics

All 27 studies were variations of cohort studies, consisting mostly of retrospective cohort studies. Studies were conducted across several countries, with the highest single country contribution from the United States of America (n=10). Data from studies were extracted by outcome: all-cause mortality, cancer related mortality, access to treatment, treatment compliance, stage at diagnosis, metastatic disease at diagnosis and healthcare utilisation. Several studies reported on more than one outcome with most studies focused on mortality rates. Results were categorised into three themes: cancer specific mortality, stage at diagnosis and, access to stage appropriate treatment.

Discussion

Theme 1 - cancer specific mortality

Studies reported mortality rates in cohorts with SMI and cancer. With the exception of one study, all studies assessing mortality rates in the cancer and SMI population demonstrated higher mortality compared to non-SMI populations. Findings in this section are reported by cancer histological type. Some results in this section are presented as hazard ratios. This is a common method used to compare probability of events across two

cohorts, in this case cancer only or cancer and SMI. A hazard ratio of 1 indicates equal events, those above 1 indicate greater probability and those less than 1 indicate reduced probability.

Collective cancer histological types

Several studies reported cancer histological types collectively, demonstrating increased cancer mortality risk in individuals with SMI and cancer compared to those with cancer only.

In one article, cancer specific mortality rates in psychiatric patients were compared to the general population of Western Australia [17]. Findings indicated higher mortality in both males and females with cancer and psychiatric illness compared to those with cancer only. A further study [18] provides similar findings, in which cancer mortality was 72% higher in males and 59% higher in females in contact with mental health services. Chang et al [19] reported similar findings in which individuals with SMI had significantly poorer survival. The hazard ratio was reported as 1.74; statistically significant for schizophrenia (1.90) and schizoaffective disorder (2.33). Hemmington [20] et al reported mortality in the 12 months from cancer decision to treat. In the SMI group this was reported as 32.4% compared to 18.3% in the population without SMI.

Batty et al [21] compared survival times from first cancer diagnosis to cancer death in men with and without a psychiatric hospital admission. Men with psychiatric illness had increased risk of death at 2, 5 and 10 years following cancer registration and were more than twice as likely to die from their cancer. Crump et al [22] presented similar findings specific to bipolar disorder, in which a hazard ratio of 1.30 for females and 1.09 for males was reported.

Breast cancer

A Finnish nationwide population study [23] reported increased breast cancer mortality in populations with non-affective psychosis, mood disorder and substance use disorder, with hazard ratios of 1.51, 1.16 and 1.34. These findings are supported by Cunningham et al [24], in this study individuals with schizophrenia, schizoaffective disorder, bipolar affective disorder or other nonorganic psychosis were more likely to die from their breast cancer than females without a history of mental illness. A further Danish population-based cohort study also reported the increase in breast cancer mortality in cases of comorbid SMI observed by other studies [25]. The increased

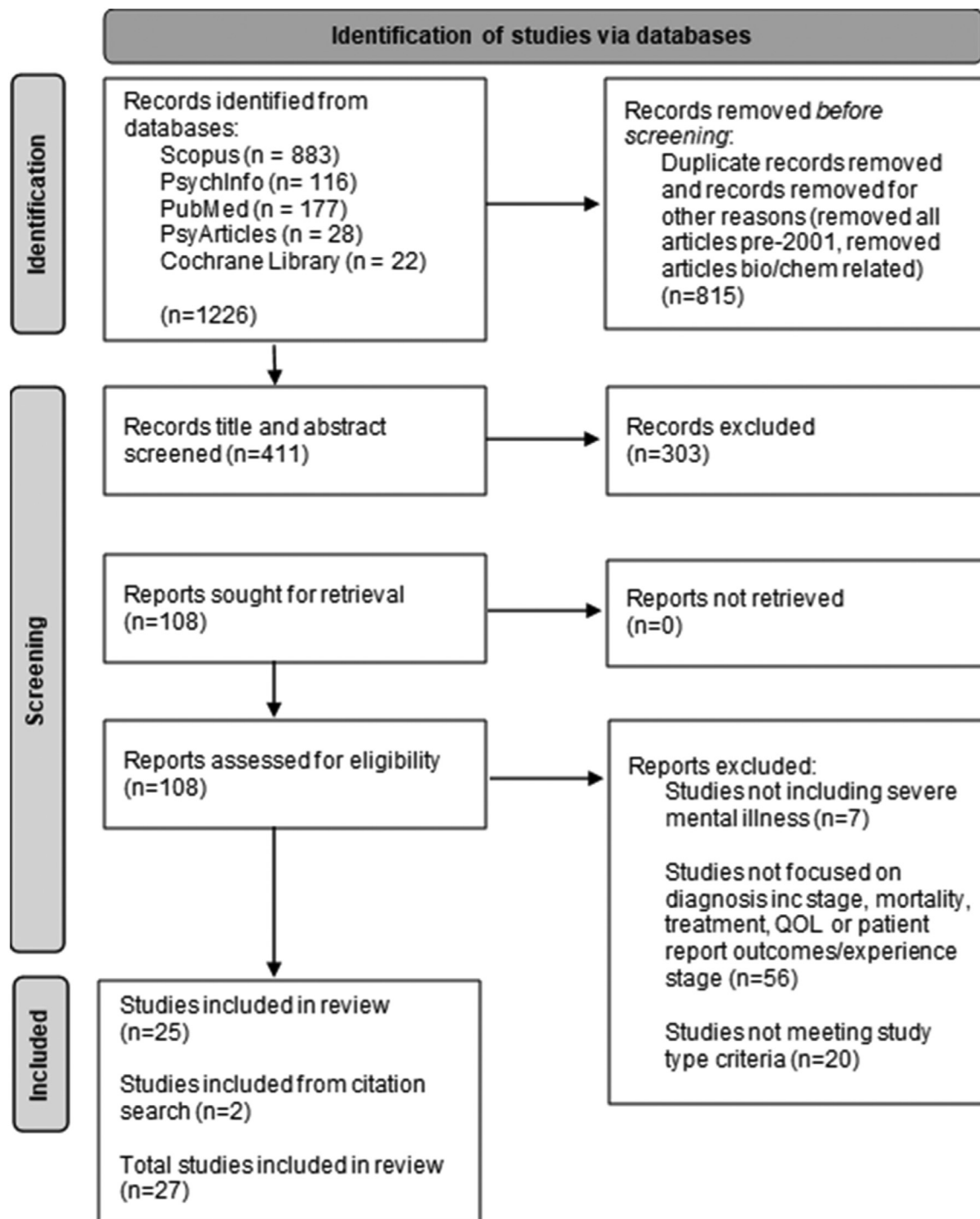


Fig. 1. PRISMA flowchart.

mortality risk in breast cancer and SMI populations is further supported by a study by Iglay et al [26] in which the mortality in individuals over the age of 68 years with breast cancer and bipolar disorder, schizophrenia or other psychotic disorders was reported as 1.20. It should be considered that this study has a 5 year follow up only and reports on the over 68-year population only.

Colorectal cancer

Manderbacka et al stratified the effect of SMI on mortality rates in colorectal cancer [27]. After controls, this was reported as 1.72 for men and 1.37 for women with psychosis and colorectal cancer. This increase in mortality is supported by Cunningham et al [24] who reported a nationwide study of adults aged 18-64 years with colorectal cancer and SMI, in which indi-

viduals with schizophrenia, schizoaffective disorder, bipolar affective disorder or other nonorganic psychosis were three times more likely to die from their cancer. Furthermore, a retrospective cohort study [28] reported on the survival of older adults with colon cancer. The study population included individuals over the age of 67 years between 1993 and 2005 with hazard ratios of; 1.04 for mood disorder, 1.16 for psychotic disorder and 1.12 for substance use disorders.

Lung cancer

Arffman et al [29] extracted data for individuals with lung cancer and SMI. Increased cancer mortality risk was observed for women with psychosis and small cell lung cancer (SCLC) or squamous cell carcinoma (SCC). Hazard ratios were reported as 1.76 (SCLC) and 1.67 (SCC). Males with psychosis and SCC had a hazard ratio of 1.24. A further study [30] focused on lung cancer and SMI but specifically in the over 66 years population, in which a small increase in cancer mortality in the schizophrenia population was observed. Although not statistically significant, it should be noted that this sample was limited to individuals aged 66 years and over.

Prostate cancer

In a study of SMI and locoregional high grade, non-metastatic prostate cancer in individuals aged 67 years and over, individuals with prostate cancer and SMI had an increased risk of cancer mortality at 5 years and a hazard ratio in this cohort of 1.41 [31].

Gastrointestinal cancer

Premature mortality in individuals with SMI and gastrointestinal cancer is reported by John et al [2], with a cancer specific mortality ratio of 1.5. In all studies reported in this section, increased mortality was associated with comorbid SMI. The magnitude of increased mortality is varied across the evidence base with a small number of studies reporting minimal increase in mortality risk and others indicating gross inequalities in mortality between the cancer only and the cancer in SMI populations.

Theme 2 - stage at diagnosis

A total of thirteen studies reported stage at diagnosis variations between the cancer only and the cancer and SMI populations. Several studies also noted an absence of data to enable reporting of stage at diagnosis. Findings in this section are reported by cancer histological type.

Collective cancer histological types

Kisely et al [17] compared all-cause mortality rates in psychiatric patients compared to the non-SMI population. Mortality rates in both males and females were increased and the proportion of cancers that were diagnosed with metastatic disease at presentation was significantly higher. Individuals with breast and lung cancer had the greatest increase in metastatic disease at presentation, however in some cancer types such as

prostate cancer, no increase in metastatic disease at presentation was observed. Manderbacka et al [32] presented findings from a nationwide study of individuals with all cancer types and substance misuse, psychosis and mood disorder. In all SMI diagnoses, an increase in metastatic disease was observed when compared to those without SMI. This was most significant in individuals with substance misuse or psychosis. Toender et al [33] presented similar findings.

Breast cancer

Ribe et al [25] explained that females with SMI were less likely to present with localised disease, however following adjustment for tumour stage, this did not significantly impact on mortality rates. The findings of Ribe et al [25] are supported by Iglay et al [26] who identified that individuals with SMI were more likely to have disease at advanced stage, an increase in mortality was also observed. Interestingly, individuals with SMI were also reported to be more likely to be smokers. It should be noted that the increased use of tobacco observed in this study in the SMI population could also be a contributing factor to mortality. Ahlgren [23] reported that individuals with breast cancer and non-affective psychotic disorder were diagnosed with metastatic disease at presentation more often when compared to individuals without SMI. Dalton et al [34] did not report stage at diagnosis but observed that females with breast cancer and schizophrenia were reported to have larger tumours compared to females without SMI.

Colorectal cancer

Manderbacka [27] demonstrated an increased likelihood of unknown stage at diagnosis in individuals with colorectal cancer who also had substance use disorder or psychosis. Females with psychosis had the greatest increase in metastatic disease at presentation. Although stage at diagnosis was accounted for, this did not explain the mortality rates observed in this population. It should be noted that only individuals who were hospitalised for SMI were included within this study and therefore the overall number of individuals with SMI is likely to be under reported. Baillargeon [28] also reported on individuals with colorectal cancer and SMI, focused specifically on older adults greater than 67 years. This study identified marginal decreases in individuals diagnosed with stage 1 cancer in the SMI population but no increase in stage 4 disease for those with SMI and colorectal cancer. The study also acknowledged the significant proportion of individuals with SMI who had unknown stage at diagnosis. Similar findings were observed in a study conducted by Cunningham [24]. When compared to those without SMI, a reduced proportion of individuals with colorectal cancer and schizophrenia or bipolar disorder were diagnosed with localised cancer at presentation. The SMI population also experienced a greater proportion of distant metastatic disease at presentation when compared to individuals without SMI.

Lung cancer

Studies by Bergamo [30] and Arffman [29] reported on individuals with lung cancer and SMI. Bergamo [30] studied indi-

viduals aged 66 years and over with lung cancer and schizophrenia. The study observed a greater likelihood of receiving a diagnosis of early-stage lung cancer compared to the general population. Although an increase in localised cancer was observed, individuals with schizophrenia and lung cancer experienced poorer outcomes. In contrast, Arffman [29] observed a reduction in localised disease at presentation in males and females with non-affective psychotic disorder, and marginal differences in localised and metastatic disease at presentation in individuals with substance use disorder and mood disorder. A key finding from this study was that 25% of individuals with non-affective psychotic disorder had unknown stage at diagnosis.

Several studies indicate a greater risk of metastatic disease at presentation in the SMI and cancer population. The increase in unknown stage at diagnosis in the SMI population makes true comparisons challenging. Where later stage at diagnosis is observed and accounted for, this does not fully account for the increase in mortality observed in the SMI population.

Theme 3 - access to stage appropriate treatment

A total of thirteen studies reported on access to stage appropriate treatment, which included treatment compliance or treatment delays. Nine of the thirteen studies report specifically on schizophrenia, with a further four studies reporting on mental illness diagnoses collectively, findings in this section are reported to reflect this.

Schizophrenia

Dalton et al [34] reported that the likelihood of individuals with breast cancer and schizophrenia or related disorders, not being allocated to guideline treatment, was increased when compared to those without schizophrenia. Individuals with schizophrenia were more likely to have received non-breast conserving surgery and more likely to have received a mastectomy compared to individuals without. This population were also more likely to receive hormone therapy but less likely to have received chemotherapy alone or chemotherapy combined with hormone therapy when compared to individuals without schizophrenia. Irwin et al [35] reported a small (n=95) single centre study of predictors of disruptions in breast cancer care for individuals with schizophrenia. In this population, 50% of individuals with schizophrenia experienced at least one disruption in their care for breast cancer and 20% did not receive stage appropriate treatment. Individuals with schizophrenia and early-stage breast cancer were twice as likely to receive a mastectomy when compared to individuals without. The population of individuals with schizophrenia were also less likely to receive adjuvant chemotherapy or radiation therapy. In contrast, Sharma [36] reported that schizophrenia does not adversely affect the treatment of women with breast cancer in a small, single centre study of 37 individuals.

In another study [37], individuals with breast cancer and schizophrenia experienced a delay in diagnosis, with several individuals not receiving the surgery indicated. A total of 7 individuals delayed or refused surgery and 4 individuals delayed or

refused indicated chemotherapy treatment. In a further study, Hwang et al [38] aimed to quantify the clinical course of individuals with breast cancer and schizophrenia that were eligible for adjuvant chemotherapy. Data were available for 46 individuals, of these 39 were offered chemotherapy with 12 individuals refusing or uncompliant, although no explanation was provided to expand on how compliance was defined or supported in this population. Of 38 individuals with adequate data that should have been offered post operative endocrine therapy, 25 individuals were offered treatment and 8 refused or were non-compliant.

Fond et al [39] reported on end-of-life care in individuals with schizophrenia and cancer. The study compared access to palliative care and high intensity end of life care between those with and without schizophrenia. Patients with schizophrenia were less likely than the control group to receive high intensity end of life care, including chemotherapy, surgery, endoscopy, imaging or blood transfusions and were more likely to receive palliative care. A further study [40] focused on palliative and high intensity end of life care in patients with schizophrenia and lung cancer in comparison to a control group without SMI. Individuals with schizophrenia were more likely to be admitted to palliative care units in the last 31 days life and were less likely to receive chemotherapy, surgery, artificial nutrition, and imaging compared to those without.

Mateen et al [41] reported on individuals with pre-existing schizophrenia or schizoaffective disorder and lung cancer diagnosis, comparing disparity between individuals who received less aggressive “state of the art” treatment for curable lung cancer relative to cancer stage. Within this small cohort, 5 of 17 patients experienced disparity in their cancer care. A further study [30] focused on lung cancer in elderly individuals with schizophrenia and identified that this population were less likely to receive stage appropriate treatment for non-small cell lung cancer.

Other SMI diagnoses

Wiegard et al [42] reported on rectal cancer and psychiatric illness disparity in surgical management. In this population, individuals with psychiatric illness were less likely to receive sphincter sparing surgery for rectal cancer compared to those without psychiatric illness. The study also compared length of stay data and postoperative complications with no significant differences identified between cohorts. In a study focused [31] on the impact of SMI in older individuals with prostate cancer, SMI was associated with reduced likelihood of receiving surgery, or radiation therapy concurrent with hormone therapy within 12 months following cancer diagnosis. Baillargeon et al [28] also studied the impact of mental illness on cancer treatment in the older population, focused on colon cancer. Individuals with pre-existing mental illness had a greater chance of non-receipt of treatment across all categories of mental illness compared to individuals without pre existing mental illness. Another study [23] identified that individuals with breast cancer and SMI received radiation therapy treatment significantly less often than individuals without SMI.

In summary, the studies reviewed indicate reduced access to stage appropriate treatment in individuals with SMI and cancer compared to individuals without SMI.

Summary

In response to the research question; how does severe mental illness impact on cancer outcomes? The studies from this scoping review collectively demonstrate that individuals with SMI and cancer experience inequalities in cancer outcomes when compared to individuals without SMI. The findings of this review demonstrate that individuals with comorbid SMI and cancer have increased cancer related mortality, often have greater probability of metastatic disease at the time of cancer diagnosis and have reduced access to stage appropriate treatment compared to individuals without SMI.

Complexity of comorbid SMI and cancer

The collective study of populations with comorbid SMI and cancer is complex and challenging without a large-scale cohort study. The studies yielded through this scoping review are heterogenous and often study multiple diagnoses of SMI and cancer. The complexity is further expanded when considering wider potential confounding factors such as, the impact of medication, how SMI is diagnosed and reported time period prior to and post cancer diagnosis. Although some clear themes and implications can be drawn from the review of the studies within this scoping review, due to the heterogenous nature of the studies and populations, the above factors should be considered when interpreting the findings. Several studies within this review also indicate absence of data, in several cases this is absence of stage at diagnosis and comorbidity data, which also impacts on the conclusiveness and interpretation of the findings; in addition to potential underreporting of SMI within the literature.

It is acknowledged that individuals with SMI undertake increased health risk behaviours [43,44], however the impact of modifiable risk factors is not captured across many of the studies included within this review. It is known that continued smoking in individuals with cancer can increase mortality and treatment related toxicity [45,46]. Should a greater number of individuals within the SMI population continue to smoke when compared to the non SMI population, this could also increase mortality and adversely impact on treatment toxicity. Further research to include accurate smoking behaviour at diagnosis, during treatment and follow up would provide more definitive outcomes relating to the impact of smoking status on cancer related mortality and treatment toxicity and compliance in this population.

The heterogenous nature of the studies in relation to SMI diagnosis in this study provides some useful considerations for further research. The largest cohort of specific diagnosis studied focuses on schizophrenia. It is important to consider that SMI diagnoses manifest very differently depending on the specific diagnosis; this can be observed in some of the studies in-

cluded within this review in which individuals with schizophrenia, schizoaffective disorder or psychosis have less favourable outcomes when compared to other specific diagnosis.

Unexplained mortality gap

Synthesis of the studies within this review indicate that even when contributing factors such as comorbidities, stage at diagnosis and treatment are adjusted for, a mortality gap remains in cohorts with SMI and cancer when compared to the non-SMI population. Except for one study, no studies were yielded where clinician or patient decision making was explored. This could be an influencing factor associated with timely access to stage appropriate treatment and therefore be one possible explanation for the currently unexplained mortality gap. There is also a paucity of research considering treatment tolerance. The search strategy failed to yield any studies assessing quality of life from the perspective of the individual, with only one study focused on toxicity post treatment. Without evidence to consider if greater treatment related toxicity is experienced, treatment compliance cannot be fully understood and again this could therefore be an explanation for the unexplained mortality gap.

Although this scoping review did not focus specifically on delayed cancer diagnosis, several studies do report on stage at diagnosis. Collectively, SMI is a factor leading to later cancer diagnosis. In several studies this has been accounted for in the cancer related mortality statistics, but it is an important factor that could have a further impact on clinician and patient decision making which is not explored by the literature. Diagnostic overshadowing can occur when professionals make assumptions about the health symptoms an individual presents with, where physical symptoms are sometimes attributed to mental ill health and not explored otherwise. Diagnostic overshadowing and reduced health seeking behaviours including reduced uptake of cancer screening programmes are some potential explanations for less favourable stage at diagnosis.

Future research to explore the impact of SMI on quality of life in individuals with cancer, from the perspective of the individual would add greater understanding to this complex issue.

Conclusion

The findings from this scoping review show that individuals with pre-existing SMI and cancer experience inequalities in cancer outcomes compared to those without. Individuals with comorbid SMI and cancer have increased cancer related mortality, are often at greater risk of metastatic cancer at diagnosis, are less likely to receive optimal treatments and experience increased interruptions and delays to treatment. Although confounding factors such as later stage or metastatic disease at diagnosis accounts for some of the inequalities observed in mortality, this is not fully explained by stage at diagnosis alone. Accurate note taking regarding decision making from the perspective of the primary care givers and individuals with SMI and cancer would add further narrative to explain this phenomenon alongside further information surrounding smoking status.

Declarations

This scoping review was completed as part of a PhD study to identify the perception of needs of individuals with severe mental illness and cancer.

Appendix 1

Summary of Evidence

Authors [Correlating Reference]	Year/location	Intervention type (follow up and control group)	Study population
Toender, Munk – Olsen, Vestergaard et al [33]	2018 Denmark	Whole Danish population between 1978-2013. Cancer incidence and mortality were compared in individuals with and without SMI.	All Cancer types SMI schizophrenia, schizoaffective disorder, bipolar affective disorder SMI
Manderbacka, Arffman, Suvisaari et al [32]	2017 Finland	Total population of Finland with a first cancer diagnosis between 1993 and 2013. 5 year cancer mortality risk Impact of SMI on mortality compared	Finnish population with first cancer diagnosis between 1993 and 2013 Lung, Breast, Colon and Rectum and Prostate cancer. Psychosis, Substance Use Disorder and Mood Disorder based on hospital admission 1 year or more before cancer diagnosis Finnish population with first cancer diagnosis between 1993 and 2013
Manderbacka, Arffman, Lumme et al [27]	2018 Finland	Whole Finnish population – individuals with colorectal cancer between 1990 and 2013 with hospital admissions associated with SMI.	Colorectal cancer SMI defined as Psychosis, Substance Use Disorder and Mood Disorder based on hospital admission 1 year or more before cancer diagnosis
Ahlgren-Rimpilainen, Arffman, Suvisaari et al [32]	2020 Finland	Mortality in women with breast cancer and SMI compared to women without a history of SMI between 1990 and 2013	Finnish population with first breast cancer diagnosis between 1993 and 2013 Breast cancer SMI defined as Psychosis, Substance Use Disorder and Mood Disorder based on hospital admission 1 year or more before cancer diagnosis
Arffman, Manderbacka, Suvisaari et al [23]	2019 Finland	Mortality in individuals with lung cancer and SMI compared to individuals without a history of SMI between 1990 and 2013	Finnish population with first lung cancer diagnosis between 1993 and 2013 Lung cancer SMI defined as Psychosis, Substance Use Disorder and Mood Disorder based on hospital admission 1 year or more before cancer diagnosis
Bergamo, Sigel, Mhango et al [30]	2014 USA	Lung cancer in elderly patients with schizophrenia compared to individuals without schizophrenia	The Surveillance, Epidemiology, and End Results (SEER) database linked to Medicare records used to identify primary non-small cell lung cancer (NSCLC) patients ≥66 years of age. Schizophrenia prior to lung cancer diagnosis identified using medicare care inpatient, physician and outpatient ICD 9 codes
Cunningham, Sarfati, Stanley et al [24]	2015 New Zealand	Breast and colorectal cancer linked to psychiatric hospitalisation records for adults. Cancer-specific survival was compared for recent psychiatric service users and nonusers.	Adult aged 18-64 Breast and Colorectal Cancer registrations between 2006 and 2010. Mental illness was defined as mental illness that has been disruptive enough to lead to contact with adult secondary mental health services in the 5 years prior to cancer diagnosis. Schizophrenia, schizoaffective disorder, bipolar affective disorder, or other nonorganic psychosis
Ribe, Laurberg, Laursen et al [25]	2016 Denmark	Women with breast cancer alone, women with SMI alone, women with SMI and breast cancer and women with neither condition	All women who were born in Denmark, at least 25 years of age and alive at some point during follow-up between 1980 and 2012. SMI defined by all inpatient and outpatient contacts to a psychiatric hospital
Igley, Santorelli, Hirshfield et al [26]	2017 USA	5 year follow up of elderly women with breast cancer and SMI compared to those without SMI	Breast cancer in elderly women aged 68 and over SMI is defined in the study by ICD codes for bipolar disorder, schizophrenia or other psychotic disorder on one inpatient or two outpatient claims within 3 years of diagnosis of breast cancer.

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Fried, Sadeghi-Nejad, Gu et al [31]	2018 USA	5 year survival data for older patients with locoregional high grade nonmetastatic prostate cancer with and without coexisting SMI	Locoregional high grade non metastatic prostate cancer in males aged 67 or over, diagnosed between 2006 and 2013 SMI defined by a recorded diagnosis in 2 years prior to cancer diagnosis
Baillargeon et al [28]	2011 USA	Individuals aged 67 or over with a diagnosis of colon cancer comparing stage at diagnosis, receipt of cancer treatment and cancer specific mortality with and without a pre-existing mental disorder	79079 with a diagnosis of colon cancer aged 67 or over between 1993 and 2005 Mental disorder defined by ICD codes recorded during 2 years before diagnosis including all mood disorders, all psychotic disorders, dementia, substance abuse and dependence disorder and other mental disorders not classified
Kisely et al [18]	2008 Canada	Individuals in contact with primary care or specialist mental health services during 1995 to 2001 in Nova Scotia linked to cancer registrations and death records	All cancer diagnoses. Mental disorders defined by ICD 10 codes Dementia and other organic conditions, schizophrenia, other nonaffective psychoses, alcohol and/or drug disorders, mood disorders (affective psychoses and/or depression, neuroses, personality disorders, adjustment reactions, and other mental disorders
Kisely et al [17]	2013 Australia	All cancer registrations between 1988 –2007. Linked with death records and mental health records in Western Australia.	6586 new cancers in psychiatric patients. All cancer types and psychiatric disorder defined by ICD codes with first contact with services occurring between 1988 and 2007. Psychiatric disorder includes dementia.
Chang et al [19]	2014 England	43 746 cancer cases were identified from records, of these 15166 did not have stage at diagnosis confirmed. After removal of those with missing data, 8477 cases remained. 125 of these had received an SMI diagnosis.	Mental health categorised into the following groupings (ICD codes):dementia, substance use disorders, schizophrenia, schizoaffective disorder, bipolar disorder, depressive disorders, anxiety disorders and personality disorders. SMI was defined as a diagnosis of schizophrenia, schizoaffective disorder or bipolar disorder
Crump et al [22]	2013 Sweden	National cohort study of 6587036 Swedish adults, including 6618 with bipolar disorder 2003 - 2009	Bipolar disorder only and study outcomes including the following specific comorbidities, identified by any primary or secondary diagnosis in the Swedish Outpatient Registry or the Swedish Hospital Registry and classified according to ICD-10codes: cardiovascular disease subclassified as hypertension, ischemic heart disease, and stroke; any cancer; diabetes mellitus; lipid disorders; influenza or pneumonia; and chronic obstructive pulmonary disease.
Batty et al [21]	2012 Sweden	Comparing cancer mortality in men with and without psychiatric admissions	All male cancer, all psychiatric admissions.
Hemmington et al [20]	2019 NZ	1652 patients diagnosed with cancer in the period 1 January 2016 to 31 December 2016.	Mental health split into three groups: nonmental health, moderate mental health, and serious mental health defined as:
John et al [2]	2018 UK	3.9 million individuals in Wales, 2004–2013, was included in the study.	SMI divided into three groups based on the diagnostic categories ICD 10 and Read Codes version 2: 1) schizophrenia, schizotypal and delusional disorders; 2) bipolar disorder and other mood related disorders 3) other severe mental illness
Dalton et al [34]	2018 Denmark	1995-2011. Overall survival of women with early stage breast cancer alone compared to those with early stage breast cancer and schizophrenia or related disorders. Median follow up of 5.5 years in breast cancer and schizophrenia population and 5.9 years in breast cancer alone.	Breast cancer (early stage) and schizophrenia, paranoid states, other psychoses; excluding, reactive depressive psychosis; reactive excitation and unspecified psychosis.
Farasatpour et al [37]	2013 USA	Breast cancer and schizophrenia or schizoaffective disorder. 56 patients (across 34 facilities). Control group of 478.	Breast cancer and schizophrenia or schizoaffective disorder between 1999 and 2005.

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Sharma et al [36]	2010 UK	Breast cancer Schizophrenia treatment, trial participation, informed consent compared to non schizophrenia population	Breast cancer and schizophrenia Jan 1993 – March 2009.
Wieghard et al [42]	2015 USA	Rectal cancer and psychiatric disease	23,914 patients who underwent surgery for rectal cancer 2004 to 2011 identified. ICD-9 codes used to identify psychiatric diagnoses. Psychiatric diagnoses; anxiety disorders, mood disorders, schizophrenia and other psychotic disorders, and substance abuse and dependence disorders.
Irwin et al [35]	2017 USA	Breast cancer and schizophrenia 1993-2015.	95 patients from a single institution with Schizophrenia and breast cancer. Delays to diagnosis or treatment, deviations from stage-appropriate treatment, and interruptions in treatment in schizophrenia and non schizophrenia breast cancer population. Schizophrenia diagnosed at least 1 year prior to breast cancer diagnosis.
Fond et al [39]	2019 France	Advanced cancer (patients aged 15 years or older with a diagnosis of brain cancer, liver cancer, or any metastatic solid cancer,) and schizophrenia. Jan 2013 and Dec 2016.	Individuals with advanced cancer and schizophrenia compared to individuals without schizophrenia. 2481 patients with schizophrenia and 222477 controls.
Viprey et al [40]	2020 France	Individuals aged 15 and older who died from terminal lung cancer in hospital in France (2014–2016). 633 schizophrenia patients and 66,469 controls	Individuals with schizophrenia and lung cancer death compared to those with lung cancer death but without schizophrenia for indicators of palliative and end of life care.
Mateen et al [41]	2008 USA	Lung cancer and schizophrenia	Pre-existing schizophrenia and potentially curative lung cancer made between 1980 and 2004. Total of 29 patients included. Single centre.
Hwang et al [38]	2012 USA	Breast cancer and schizophrenia	55 individuals. schizophrenia or schizoaffective disorder and breast cancer using ICD codes between 1999 and 2005.

References

- [1] National Health Service Digital. Excess under 75 mortality rates in adults with serious mental illness - 2016 to 2018. (Cited 2021 August 30). Available from: <https://www.gov.uk/government/statistics/excess-under-75-mortality-rates-in-adults-with-serious-mental-illness-2016-to-2018>
- [2] John A, McGregor J, Jones I, Lee SC, Walters JTR, Owen MJ, et al. Premature mortality among people with severe mental illness - new evidence from linked primary care data. *Schizophr Res*. 2018 September 01;199:154–162.
- [3] Chesney E, Goodwin GM, Fazel S. Risks of all-cause and suicide mortality in mental disorders: a meta-review. *World Psychiatry*. 2014 June 01;13(2):153–160.
- [4] McManus S, Bebbington P, Jenkins R, Brugha T. Mental health and wellbeing in England: adult psychiatric morbidity survey 2014. *Leeds: NHS Digital*. 2016. [webarchive.nationalarchives.gov.uk/ukgwa/20171010183932tfl. http://content.digital.nhs.uk/catalogue/PUB21748/apms-2014-full-rpt.pdf](http://webarchive.nationalarchives.gov.uk/ukgwa/20171010183932tfl/http://content.digital.nhs.uk/catalogue/PUB21748/apms-2014-full-rpt.pdf).
- [5] Cancer Research UK. Worldwide cancer statistics. (Cited 2021 August 30). Available from: <https://www.cancerresearchuk.org/health-professional/cancer-statistics/worldwidecancer#heading-Zero>
- [6] Carney CP, Jones L, Woolson RF. Medical comorbidity in women and men with schizophrenia: a population-based controlled study. *J Gen Intern Med*. 2006 November 01;21(11):1133–1137.
- [7] Wender RC, Brawley OW, Fedewa SA, Gansler T, Smith RA. A blueprint for cancer screening and early detection: Advancing screening's contribution to cancer control. *CA Cancer J Clin*. 2019 January 01;69(1):50–79.
- [8] DE Hert M, Correll CU, Bobes J, Cetkovich-Bakmas M, Cohen D, Asai I, et al. Physical illness in patients with severe mental disorders. I. Prevalence, impact of medications and disparities in health care. *World Psychiatry*. 2011 February 01;10(1):52–77.
- [9] Naylor C, Parsonage M, McDaid D, Knapp M, Fossey M and Galea A. Long-term conditions and mental health. The cost of comorbidities. 2012 https://www.kingsfund.org.uk/sites/default/files/field/field_publication_file/long-termconditions-mental-health-cost-comorbidities-naylor-feb12.pdf
- [10] Thornicroft G. Physical health disparities and mental illness: the scandal of premature mortality. *Br J Psychiatry*. 2011 December 01;199(6):441–442.
- [11] Naughton MJ, Weaver KE. Physical and mental health among cancer survivors: considerations for long-term care and quality of life. *N C Med J*. 2014 August 01;75(4):283–286.
- [12] Grant MJ, Booth A. A typology of reviews: an analysis of 14 review types and associated methodologies. *Health Info Libr J*. 2009 June 01;26(2):91–108.
- [13] Arskey H, O'Malley L. Scoping studies: towards a methodological framework. *Int J Soc Res Methodol*. 2005;8(1):19–32.
- [14] Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med*. 2009;6(7).
- [15] Critical Appraisal Skills Programme UK. CASP checklists. (Cited 2021 August 30). Available from: <https://casp-uk.net/casp-tools-checklists/>
- [16] QSR International Pty Ltd. (2020) NVivo (released in March 2020), <https://www.qsrinternational.com/nvivo-qualitative-data-analysis-software/home>
- [17] Kisely S, Crowe E, Lawrence D. Cancer-related mortality in people with mental illness. *JAMA Psychiatry*. 2013 February 01;70(2):209–217.
- [18] Kisely S, Sadek J, MacKenzie A, Lawrence D, Campbell LA. Excess cancer mortality in psychiatric patients. *Can J Psychiatry*. 2008 November 01;53(11):753–761.
- [19] Chang CK, Hayes RD, Broadbent MT, Hotopf M, Davies E, Moller H, et al. A cohort study on mental disorders, stage of cancer at diagnosis and subsequent survival. *BMJ Open*. 2014 January 29;4(1) e004295-004295.

- [20] Hemmington A, Huang D, Coomarasamy C, Young MJ, Consedine NS, Reynolds LM. When mental illness and cancer collide: An investigation of the predictors of outcomes for cancer patients with a history of mental health problems. *Psychooncology*. 2020 March 01;29(3):525–531.
- [21] Batty GD, Whitley E, Gale CR, Osborn D, Tynelius P, Rasmussen F. Impact of mental health problems on case fatality in male cancer patients. *Br J Cancer*. 2012 May 22;106(11):1842–1845.
- [22] Crump C, Sundquist K, Winkleby MA, Sundquist J. Comorbidities and mortality in bipolar disorder: a Swedish national cohort study. *JAMA Psychiatry*. 2013 September 01;70(9):931–939.
- [23] Ahlgren-Rimpilainen AJ, Arffman M, Suvisaari J, Manderbacka K, Lumme S, Keskimäki I, et al. Excess mortality from breast cancer in female breast cancer patients with severe mental illness. *Psychiatry Res*. 2020 April 01;286:112801.
- [24] Cunningham R, Sarfati D, Stanley J, Peterson D, Collings S. Cancer survival in the context of mental illness: a national cohort study. *Gen Hosp Psychiatry*. 2015 December 01;37(6):501–506.
- [25] Ribe AR, Laurberg T, Laursen TM, Charles M, Vedsted P, Vestergaard M. Ten-year mortality after a breast cancer diagnosis in women with severe mental illness: A Danish population-based cohort study. *PLoS One*. 2016 July 27;11(7):e0158013.
- [26] Iglay K, Santorelli ML, Hirshfield KM, Williams JM, Rhoads GG, Lin Y, et al. Impact of preexisting mental illness on all-cause and breast cancer-specific mortality in elderly patients with breast cancer. *J Clin Oncol*. 2017 December 20;35(36):4012–4018.
- [27] Manderbacka K, Arffman M, Lumme S, Suvisaari J, Keskimäki I, Ahlgren-Rimpilainen A, et al. The effect of history of severe mental illness on mortality in colorectal cancer cases: a register-based cohort study. *Acta Oncol*. 2018 June 01;57(6):759–764.
- [28] Baillargeon J, Kuo YF, Lin YL, Raji MA, Singh A, Goodwin JS. Effect of mental disorders on diagnosis, treatment, and survival of older adults with colon cancer. *J Am Geriatr Soc*. 2011 July 01;59(7):1268–1273.
- [29] Arffman M, Manderbacka K, Suvisaari J, Koivunen J, Lumme S, Keskimäki I, et al. The impact of severe mental illness on lung cancer mortality of patients with lung cancer in Finland in 1990–2013: a register-based cohort study. *Eur J Cancer*. 2019 September 01;118:105–111.
- [30] 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 April 01;76(3):215–220.
- [31] Fried DA, Sadeghi-Nejad H, Gu D, Zhou S, He W, Giordano SH, et al. Impact of serious mental illness on the treatment and mortality of older patients with locoregional high-grade (nonmetastatic) prostate cancer: retrospective cohort analysis of 49 985 SEER-Medicare patients diagnosed between 2006 and 2013. *Cancer Med*. 2019 May 01;8(5):2612–2622.
- [32] Manderbacka K, Arffman M, Suvisaari J, Ahlgren-Rimpilainen A, Lumme S, Keskimäki I, et al. Effect of stage, comorbidities and treatment on survival among cancer patients with or without mental illness. *Br J Psychiatry*. 2017 November 01;211(5):304–309.
- [33] Toender A, Munk-Olsen T, Vestergaard M, Larsen JT, Suppli NP, Dalton SO, et al. Impact of severe mental illness on cancer stage at diagnosis and subsequent mortality: a populationbased register study. *Schizophr Res*. 2018 November 01;201:62–69.
- [34] Dalton SO, Suppli NP, Ewertz M, Kroman N, Grassi L, Johansen C. Impact of schizophrenia and related disorders on mortality from breast cancer: A population-based cohort study in Denmark, 1995–2011. *Breast*. 2018 August 01;40:170–176.
- [35] Irwin KE, Park ER, Shin JA, Fields LE, Jacobs JM, Greer JA, et al. Predictors of disruptions in breast cancer care for individuals with schizophrenia. *Oncologist*. 2017 November 01;22(11):1374–1382.
- [36] Sharma A, Ngan S, Nandoskar A, Lowdell C, Lewis JS, Hogben K, et al. Schizophrenia does not adversely affect the treatment of women with breast cancer: a cohort study. *Breast*. 2010 October 01;19(5):410–412.
- [37] Farasatpour M, Janardhan R, Williams CD, Margenthaler JA, Virgo KS, Johnson FE. Breast cancer in patients with schizophrenia. *Am J Surg*. 2013 November 01;206(5):798–804.
- [38] Hwang M, Farasatpour M, Williams CD, Margenthaler JA, Virgo KS, Johnson FE. Adjuvant chemotherapy for breast cancer in patients with schizophrenia. *Oncol Lett*. 2012 April 01;3(4):845–850.
- [39] Fond G, Salas S, Pauly V, Baumstarck K, Bernard C, Orleans V, et al. End-of-life care among patients with schizophrenia and cancer: a population-based cohort study from the French national hospital database. *Lancet Public Health*. 2019 November 01;4(11):e583–e591.
- [40] Viprey M, Pauly V, Salas S, Baumstarck K, Orleans V, Llorca PM, et al. Palliative and high-intensity end-of-life care in schizophrenia patients with lung cancer: results from a French national population-based study. *Eur Arch Psychiatry Clin Neurosci*. 2020 September 02.
- [41] Mateen FJ, Jatoti A, Lineberry TW, Aranguren D, Creagan ET, Croghan GA, et al. Do patients with schizophrenia receive state-of-the-art lung cancer therapy? A brief report. *Psychooncology*. 2008 July 01;17(7):721–725.
- [42] Wiegand NE, Hart KD, Herzig DO, Lu KC, Tsikitis VL. Psychiatric Illness is a Disparity in the Surgical Management of Rectal Cancer. *Ann Surg Oncol*. 2015 December 01;22(3):573 Suppl.
- [43] Public Health England. Health Matters Smoking and Mental Health. 2021. <https://www.gov.uk/government/publications/health-matters-smoking-and-mentalhealth/health-matters-smoking-and-mental-health>.
- [44] Scott D, Happell B. The high prevalence of poor physical health and unhealthy lifestyle behaviours in individuals with severe mental illness. *Issues Ment Health Nurs*. 2011;32(9):589–597.
- [45] Chen A, Chen L, Vaughan A, Sreeraman R, Farwell D, Luu Q, et al. Tobacco smoking during radiation therapy for head-and-neck cancer is associated with unfavorable outcome. *Int J Radiat Oncol Biol Phys*. 2011;79:414–419.
- [46] Steinberger E, Kollmeier M, McBride S, Novak C, Pei X, Zelefsky M. Cigarette smoking during external beam radiation therapy for prostate cancer is associated with an increased risk of prostate cancer-specific mortality and treatment-related toxicity. *BJU Int*. 2015;116:596–603.