

REVIEW

Impact of pre-existing mental health disorders on the receipt of guideline recommended cancer treatments: A systematic review

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Abstract

Objective: Disparities in cancer outcomes for individuals with pre-existing mental health disorders have already been identified, particularly for cancer screening and mortality. We aimed to systematically review the influence on the time from cancer diagnosis to cancer treatment, treatment adherence, and differences in receipt of guideline recommended cancer treatment.

Methods: We included international studies published in English from 1 January 1995 to 23 May 2022 by searching MEDLINE, Embase, and APA PsycInfo.

Results: This review identified 29 studies with 27 being published in the past decade. Most studies focused on breast, non-small cell lung and colorectal cancer and were of high or medium quality as assessed by the Newcastle Ottawa Scale. All studies were from high-income countries, and mostly included patients enrolled in national health insurance systems. Five assessed the impact on treatment delay or adherence, and 25 focused on the receipt of guideline recommended treatment. 20/25 studies demonstrated evidence that patients with pre-existing mental health disorders were less likely to receive guideline recommended therapies such as surgery or radiotherapy. In addition, there was a greater likelihood of receiving less intensive or modified treatment including systemic therapy.

Conclusions: Across different cancer types and treatment modalities there is evidence of a clear disparity in the receipt of guideline recommended cancer treatment for patients with pre-existing mental health disorders. The effect of pre-existing mental health disorders on treatment delay or adherence is under-researched. Future research needs to include low- and middle-income countries as well as qualitative investigations to understand the reasons for disparities in cancer treatment.

KEYWORDS

cancer, guideline treatment, mental health, oncology, psycho-oncology, time-to-treatment, treatment adherence and compliance

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1 | BACKGROUND

The burden of cancer is growing rapidly with the World Health Organization reporting 19 million new cancer cases and 9.9 million cancer deaths globally in 2020.¹ The management of co-existent diseases or health problems in people diagnosed with cancer is a major area of evaluation with mental health disorders increasingly recognized as being common in this population.² The prevalence of anxiety and/or depression is estimated to be between 20% and 25% amongst patients attending oncology clinics.³ This is highly relevant in the light of evidence that disparities in access to and outcomes from cancer care have been identified in individuals with a pre-existing Mental Health Disorder (PMHD).⁴ Previous research has demonstrated that cancer patients with these disorders are both less likely to undergo cancer screening and to have a higher risk of cancer mortality.^{4,5} One meta-analysis found that women with schizophrenia are less likely to receive mammographic screening compared with those without.⁵ A US study showed that patients with bipolar disorder, schizophrenia, or other psychotic disorder prior to a breast cancer diagnosis had higher all-cause mortality compared to those without.⁶ Another US study found a higher risk for all-cause, cancer-related, and non-cancer-related mortality after 5 years for patients with pre-existing depression compared to those without.⁷ In other words, individuals with PMHD have a lower life expectancy, especially those with severe PMHD.

It is known that good management of cancer care leads to a better outcome. However, a few studies including surveys of health professionals have found that the management of cancer care among individuals with PMHD is a challenge. For example, patients may experience diagnosis or treatment delays, have difficulties in adhering to or receipt of appropriate cancer treatment because of the symptoms of mental disorders.^{8,9} Poorer adherence could lead to those individuals with PMHD not being allocated to recommended treatment pathways. Therefore, the important questions about the management of cancer in the context of PMHD are to what extent patients experience treatment delays or receive different/less effective treatment regimens compared to those without PMHD. Such disparities are important to understand as they are likely to have an impact on mortality and morbidity from cancer.¹⁰ Equally, they may also be amenable to intervention if major disparities are evident.

Although some studies have explored the potential impact of PMHD on receipt of guideline recommended cancer treatment, this has not yet been investigated systematically. Furthermore, the impact of PMHD on the timely receipt of treatment or on treatment adherence remains unknown. The purpose of this review is therefore to synthesize the influence of PMHD on the time from cancer diagnosis to treatment, cancer treatment adherence, and differences in receipt of guideline recommended cancer treatment.

2 | METHODS/LITERATURE SEARCH

2.1 | Search strategy and selection criteria

This systematic review aims to investigate the influence of PMHD on (1) the time from a cancer diagnosis to receiving treatment, (2) adherence to cancer treatment and (3) differences in receipt of guideline recommended cancer treatment. PMHD was defined as a mental health-related diagnosis that had occurred and been diagnosed prior to a cancer diagnosis. This study focused on the most commonly diagnosed mental health/psychiatric disorders including schizophrenia spectrum and other psychotic disorders, depressive disorders, anxiety disorders, obsessive-compulsive disorders, bipolar and related disorders, such as mania.⁸ We also included trauma- and stressor-related disorders, dissociative disorders, feeding and eating disorders, substance-related and addictive disorders, and personality disorders.¹¹ However, mental health disorders caused by organic or neurological disorders, such as dementia and other cognitive disorders were excluded. The included and excluded mental disorders are listed in Table 1. All the mental health disorders in each study were determined using administrative health data which included outpatient or emergency department visits, hospital admissions, and physicians' notes (Table 2).

This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement¹² (Figure 1). Articles and abstracts published in English between 1 January 1995 and 23 May 2022 were searched for using MEDLINE, Embase, and APA PsycInfo. The search strategies are presented in supplement 1. Studies were excluded if: (1) they were not published in English; (2) they did not include a comparison group; (3) the mental disorder was diagnosed at or after a cancer diagnosis; (4) the mental disorders were defined by self-report questionnaire, or (5) they were case studies, review articles, editorials, qualitative studies, abstracts only or conference proceedings.

The included studies were assessed for quality using the Newcastle-Ottawa Scale (NOS) which consists of eight items with three subscales.¹³ The assessment of case-control studies includes case/control definition adequacy and representativeness, comparability of case and control, and ascertainment of exposure. The assessment of cohort studies includes representativeness of exposed/non-exposed cohorts, comparability of cohorts, and assessment of outcomes. The total maximum score is nine. A study scoring equal to or greater than seven is judged to demonstrate high quality and at a low risk of bias, and a study scoring equal to or less than four is low quality¹⁴ and at a high risk of bias.

The studies included were initially selected by YHW and EAD with AA checking them and agreeing the excluded studies. YHW and EAD then extracted data from each study, assessed its quality, and discussed any disagreement with AA to reach a consensus. RS reviewed the findings from the perspective of clinical psychiatry. All authors critically reviewed the manuscript and approved the final version.

TABLE 1 Mental disorders included and excluded from this review.

Included	Excluded
Schizophrenia spectrum and other psychotic disorders	Disruptive, impulse-control, and conduct disorders
Bipolar and related disorders	Somatic symptom and related disorders
Depressive disorders	Elimination disorders
Anxiety disorders	Sleep-wake disorders
Obsessive-compulsive and related disorders	Sexual dysfunctions
Trauma- and stressor-related disorders	Gender dysphoria
Dissociative disorders	Neurodevelopmental disorders
Feeding and eating disorders	Neurocognitive disorders
Substance-related and addictive disorders	Paraphilic disorders
Personality disorders	Other mental disorders
	Medication-induced movement disorders and other adverse effects of medication
	Other conditions that may be a focus of clinical attention

Table 2 shows the data extracted for each study. Descriptors include year of publication, period of analysis, study country, data sources analyzed, information on study subjects (cancer types and number of patients), mental health disorders (types, definition of PMHD, and duration prior to a cancer diagnosis), study design (measured items and adjusted variables), and main findings. Table 3 shows the NOS assessment for each of the eight items and the total score for each study. We also listed the factors used to adjust analyses in each study in Table 4. These included patients' demographic characteristics (age at the cancer diagnosis, sex, socioeconomic status, race/ethnicity, and geography of residence), disease characteristics (cancer stage, cancer diagnosis method, tumor size, and comorbidity), health coverage, and health provider information.

3 | RESULTS

We identified 7011 studies from our initial databases searches. Following application of our inclusion and exclusion criteria, 45 studies (35 studies and 10 additional studies identified by using the snowball method) were included for full text review. Of these, 16 studies were excluded because of (1) a definition of PMHD by self-report questionnaire, (2) without a comparison group, or (3) a diagnosis of mental health disorder at or after a cancer diagnosis. Of the 29 studies included in the final analysis, 26 studies were conducted during 2012–2022, with only three studies identified prior to this period.^{27,29,34} The main cancer types were breast ($n = 11$),^{15–25,43} non-small cell lung (NSCLC) ($n = 6$),^{30–34,43} colon ($n = 6$),^{27–29,41–43} and rectal cancers ($n = 6$).^{27,28,40–43} Other cancer types included head/neck ($n = 3$),^{36,42,43} prostate ($n = 3$),^{38,39,43} bladder ($n = 2$),^{15,43} cervical ($n = 2$),^{26,43} gastric ($n = 2$),^{41,43} esophageal ($n = 2$),^{35,43} pancreatic ($n = 2$),^{37,43} and urothelial

($n = 2$)^{42,43} cancers. The majority of studies were from the United States (US) ($n = 17$),^{15,19,22,24–26,29,31–35,37–40,42} Denmark ($n = 4$),^{20,23,28,30} and Japan ($n = 3$),^{16,21,41} with single studies identified from Australia,⁴³ Canada,²⁷ Finland,¹⁷ Germany,¹⁸ and Taiwan.³⁶

Of the 29 studies, only three investigated whether cancer patients with PMHD experienced any delays in the receipt of treatment following their diagnosis.^{15,22,42} Two studies focused on cancer treatment adherence.^{19,26} The rest explored differences in receipt of guideline recommended cancer treatment between cancer patients with PMHD and those without it.^{15–18,20,21,23–25,27–41,43}

3.1 | Time from cancer diagnosis to cancer treatments

Three studies, all from the US^{15,22,42} explored differences in time from cancer diagnosis to the receipt of cancer treatment between patients with and without PMHD. The first included 408 patients with an axis I mental health disorders (as defined by the Diagnostic and Statistical Manual of Mental Disorders IV, DSM-IV) at least 1 year prior to the diagnosis of colorectal, urothelial, and head/neck cancers.⁴² There was no significant difference in the time from diagnosis to initiation of treatment between patients with and without mental health disorders (median time: 43 vs. 44 days, $p = 0.2352$).⁴² By contrast, the second study focused on 16,636 women with breast cancer and found a positive association with PMHD and treatment delay of greater than or equal to 60 or 90 days. After controlling for patients' demographic characteristics and cancer stage, breast cancer patients with severe PMHD including bipolar disorder, schizophrenia, and other psychotic disorders had a 36% increased risk of a 60 days or greater delay in receiving their first treatment (surgery, chemotherapy, or radiation) following their initial

TABLE 2 Description of each study.

Authors, year (country)	Study subjects			Mental disorder			Design and findings		
	Data sources	Cancer site	No. of patients (year of diagnosis)	Type	Pre-existing	Definition of PMHD	Measured item	Adjusted variables	Outcome
Sathianathan et al., 2020 (US) ¹⁵	Surveillance, Epidemiology, and End Results (SEER) cancer registry data linked with Medicare claims files	Bladder cancer	66,476 (2004–2011)	1. Severe mental illness (SMI), consisting of bipolar disorder, schizophrenia, and other psychotic disorders, <i>n</i> = 726 2. Anxiety and depression (<i>n</i> = 430) 3. Anxiety (<i>n</i> = 1033) 4. Depression (<i>n</i> = 2279)	During the 3-year period prior to cancer diagnosis	Outpatient visits or hospital admissions with ICD-9 codes	Guideline-concordant treatment for patients with muscle-invasive bladder cancer: 1. Radical cystectomy (RC), 2. The time to cystectomy, 3. Neoadjuvant chemotherapy (NAC) in those undergoing RC 4. Curative therapy (RC or trimodally therapy (TMT))	Multivariable logistical regressions were used with adjustment for: 1. Year of diagnosis 2. Age 3. Gender 4. Race 5. Income level 6. Education level 7. Tumor grade 8. Charlson score	1. Compared with those without mental illness, patients with a SMI (OR = 0.67, 95% CI = 0.47–0.95), depression only (OR = 0.79, 95% CI = 0.66–0.95), and both anxiety and depression (OR = 0.57, 95% CI = 0.35–0.92) were significantly less likely to undergo RC. 2. The mean time to RC from the date of diagnosis was lower for patients with a SMI than those without (1.5 vs. 3.9 months, <i>p</i> < 0.001). 3. Compared with those without a mental illness, patients with a SMI (OR = 0.55, 95% CI = 0.37–0.81) and those with depression only (OR = 0.71, 95% CI = 0.58–0.88) were less likely to receive curative treatment.
Kaneshiro et al., 2022 (Japan) ¹⁶	St. Mary's Hospital medical records	Breast cancer	665 (01/2010–09/2020)	Schizophrenia (<i>n</i> = 55)	Yes, but unclear how long	Based on administrative health data with ICD-10 codes	Treatment 1. Radiation therapy 2. Hormone therapy 3. Chemotherapy 4. Recommended cancer treatment	Results were assessed by the chi-square test without adjustment for other variables.	1. 63.2% of the patients without schizophrenia had a mastectomy, while 84.2% of the schizophrenia group had a mastectomy (<i>p</i> = 0.0024). 2. Hormone therapy and anti-HER2 therapy were not significantly different between the two groups. 3. 56% of the patients with schizophrenia received radiation therapy, which was less than the 75% of patients without schizophrenia (<i>p</i> = 0.078). 4. 40% of the patients with schizophrenia received chemotherapy (<i>p</i> < 0.0001), and 61.8% received recommended cancer treatment (<i>p</i> = 0.0004); these values were lower than those without schizophrenia.
Ahgrén-Rimpiläinen et al., 2020 (Finland) ¹⁷	National Finnish Cancer Registry and Hospital Discharge Register	Breast cancer	80,671 (1990–2013)	1. Non-affective psychosis (NAPD, <i>n</i> = 2245) 2. Substance use disorder (SUD, <i>n</i> = 737) 3. Mood disorder (MD, <i>n</i> = 1855)	At least 1 year before cancer diagnosis	Hospital admissions with ICD-10 codes	Treatment 1. with surgery only, plus 2. radiotherapy, 3. chemotherapy/hormone therapy	Overall differences were assessed by Chi-square test without adjustment for other variables.	1. 48% of women without PMHD had received radiotherapy, compared to 38% of those with NAPD, 43% of those with SUD, and 43% with MD (<i>p</i> < 0.0001). 2. Differences for any treatment were significant for those with local but not significant for metastasized stage.

TABLE 2 (Continued)

Authors, year (country)	Study subjects		Pre-existing	Design and findings		Outcome
	Data sources	Cancer site		Measured item	Adjusted variables	
Groß et al., 2020 (Germany) ¹⁸	Survey of 87 hospitals by The Institute of Medical Sociology, Research and Rehabilitation Science, University of Cologne	Breast cancer	Yes, but unclear how long	Mastectomy versus breast conserving surgery	Two-level model was used with adjustment for: 1. Age 2. Educational level 3. Health insurance status 4. Cancer stage 5. Cancer diagnosis through mammography 6. Secondary diseases (cardiovascular disease, hypertension, diabetes, stroke, pulmonary disease, kidney disease, arthritis or rheumatism, overweight, other cancer diseases, or psychological illness)	Women with PMHD tend to receive a mastectomy (OR = 1.43, 95% CI = 0.79–2.60) rather than a breast conserving surgery (OR = 0.70, 95% CI = 0.42–1.17) but the odds were not significant ($p > 0.05$).
Haskins et al., 2019 (US) ¹⁷	SEER cancer registry data linked with Medicare claims files	Breast cancer	Within the 36 months prior to cancer diagnosis	Endocrine therapy: 1. Initiation 2. Discontinuation 3. Adherence	Cox regression/ Generalized estimating equations were used with adjustment for: 1. Race 2. Ethnicity 3. Age at diagnosis 4. Adjusted NCI comorbidity score 5. Year of cancer diagnosis	<ol style="list-style-type: none"> Patients with dementia or bipolar/psychotic/ schizophrenia disorders had lower adjusted initiation probabilities by year one of follow-up, versus those without these diagnoses 0.74 (95% CI = 0.73–0.74) and 0.73 (95% CI = 0.72–0.73) respectively, compared to the reference value of 0.76 (95% CI = 0.76–0.77). Patients with substance use or anxiety disorders less frequently continued endocrine therapy for at least 1 year, after adjustment: 0.85 (95% CI = 0.85–0.86) and 0.88 (95% CI = 0.87–0.88) respectively, compared to the reference value of 0.90 (95% CI = 0.89–0.90). Patients with substance use disorders significantly had 2.3% lower adherence rates.

(Continues)

TABLE 2 (Continued)

Authors, year (country)	Study subjects			Mental disorder	Design and findings			
	Data sources	Cancer site	No. of patients (year of diagnosis)		Type	Definition of PMHD	Measured item	Adjusted variables
Dalton et al., 2018 (Denmark) ²⁰	Danish Cancer Register and Danish Psychiatric Central Research Register	Breast cancer	56,152 (1995–2011)	Schizophrenia or related conditions (n = 499)	Based on administrative health data with ICD-8, ICD-9, and ICD-10 codes	Guideline treatment	Logistic regression was used with adjustment for: 1. Age at diagnosis 2. Calendar period 3. Level of education 4. Charlson comorbidity index score (CCI)	The OR for a woman with schizophrenia or related disorders not being allocated to guideline treatment for early-stage breast cancer as compared with patients without such a condition was 1.50 (95% CI = 1.15–1.94).
Shinden et al., 2017 (Japan) ²¹	Kagoshima University Hospital medical records	Breast cancer	773 (09/1992–01/2015)	1. Schizophrenia (n = 23) 2. Dementia (n = 16) 3. Intellectual disability (n = 10)	Based on administrative health data which included diagnosis by psychiatrists and received antipsychotic medication	Treatment	The results were assessed using the Pearson chi-square test without adjusting for other variables.	1. Patients with mental disorders underwent total mastectomy significantly more often than those without (78% vs. 59%, p = 0.011). 2. Significantly fewer patients with mental disorders also underwent postoperative adjuvant chemotherapy (0% vs. 19%, p = 0.0031) and radiation (2.2% vs. 18%, p = 0.0059).
Igley et al., 2017 (US) ²²	SEER cancer registry data linked with Medicare claims files	Breast cancer	16,636 (2005–2007)	1. Anxiety disorder (n = 1264) 2. Depression (n = 1381) 3. Anxiety disorder and depression (n = 848) 4. SMI (Consisting of bipolar disorder, schizophrenia, and other psychotic disorder; n = 482)	During the 3-year period prior to breast cancer diagnosis	Treatment (surgery, adjuvant chemotherapy, and adjuvant radiation therapy) delays of ≥60 and ≥90 days	Multivariable binomial regression was used with adjustment for: 1. Age 2. Income 3. CCI 4. Race 5. Ethnicity 6. SEER registry location 7. Marital status 8. Cancer stage	1. Patients with SMI had an increased risk for initial treatment delay of ≥60 days from diagnosis (RR = 1.36, 95% CI = 1.06–1.74). 2. Patients with any mental illness experienced an increased risk for adjuvant chemotherapy delay of ≥90 days from the last operation (RR = 1.13, 95% CI = 1.01–1.26), and each category of mental illness, except depression, showed a non-significant trend for this association.
Suppli et al., 2017 (Denmark) ²³	Danish Cancer Register and Danish Psychiatric Central Research Register	Breast cancer	45,325 (04/1998–12/2011)	Depression (n = 6812; 6068 had previously received anti-depressants and 744 had a previous hospital contact for depression)	Outpatient visits and hospital admissions with ICD-9 codes	Guideline Adjuvant Systemic Therapy	Multivariable logistic regression was used with adjustment for: 1. Age and menopausal status 2. Educational level 3. Cohabiting status 4. CCI 5. Calendar year at diagnosis 6. Tumor size 7. No. of tumor-positive axillary lymph node 8. Estrogen-receptor status	1. An increased OR for women who had used antidepressants not to be allocated to guideline breast cancer treatment (OR = 1.14, 95% CI = 1.03–1.27). 2. Women with a previous hospital contact for depression had elevated ORs for not being allocated to guideline breast cancer treatment (OR = 1.32, 95% CI = 0.99–1.77).

TABLE 2 (Continued)

Authors, year (country)	Study subjects		Mental disorder		Design and findings				
	Data sources	Cancer site	No. of patients (year of diagnosis)	Type	Pre-existing	Definition of PMHD	Measured item	Adjusted variables	Outcome
Mahabaleshwarar et al., 2015 (US) ²⁴	Medicaid analytic extract including data for 39 of 51 US States	Breast cancer	2142 (2007)	1. Mood disorders 2. Psychotic disorders 3. Substance abuse and dependence disorders 4. Other mental disorders (Total n = 806)	During 12 months prior to the date of breast cancer diagnosis	Hospital admissions with ICD-9 codes and other therapy files	Guideline-Consistent Breast Cancer Treatment	Hierarchical logistic regression was used with adjustment for: 1. Age at diagnosis 2. Race 3. Type of reimbursement system 4. Cancer stage 5. CCI 6. Location of residence 7. State of residence 8. No. of outpatient visits	Women with any pre-existing mental illness were less likely to receive guideline-consistent breast cancer treatment compared to those without any pre-existing mental illness (OR = 0.79, 95% CI = 0.65–0.97).
Goodwin et al., 2004 (US) ²⁵	SEER cancer registry data linked with Medicare claims files	Breast cancer	24,696 (1993–1996)	Depression (n = 1841)	Within the 24 months before diagnosis of breast cancer	Outpatient visits and hospital admissions with ICD-9 codes	Definitive treatment	Logistic regression was used with adjustment for: 1. Age 2. Ethnicity 3. CCI 4. Marital status 5. No. of doctor visits 6. SEER registry location	1. Women with depression were less likely to receive treatment considered definitive (59.7% vs. 66.2%, p < 0.05). 2. A prior diagnosis of depression was associated with an increased odds of receiving less-than-definitive therapy (OR = 1.19, 95% CI = 1.06–1.33).
Rubinsak et al., 2019 (US) ²⁶	Virginia Common-wealth University Health System	Cervical cancer	129 (2005–2006)	Substance use disorders (SUD, n = 14)	Past and current	Chart review, and defined PMHD by DSM-5 guidelines	1. Treatment adherence: Time to complete radiation therapy (RT) from the first date of treatment 2. Total radiation dose received	Results were assessed by student t-test without adjustment for other variables.	1. No differences in the mean number of days to complete RT in the SUD group compared to those without SUD (62.7 ± 24.8 vs. 57.2 ± 21.4, p = 0.818). 2. Radiation dose was similar between groups; patients with SUD receiving a mean dose of 82.2 ± 19 Gy, and patients without SUD receiving 81.1 ± 16.8 Gy (p = 0.596).
Mahar et al., 2020 (Canada) ²⁷	Ontario Cancer Registry	Colorectal cancer (CRC)	24,507 (04/2007–12/2012)	Severe psychiatric illness (SPI, consisting of major depression, bipolar disorder, schizophrenia, and other non-organic psychotic illnesses, n = 740)	Six months to 5 years preceding the cancer diagnosis	Based on administrative health data which included hospitalizations, psychiatric visits, and emergency department visits	Guideline recommended treatment: 1. Surgical resection (for stage II and III) 2. Adjuvant treatment (for stage III colon cancer and stage II/III rectal cancer)	Logistic regression and modified Poisson regression with robust error variance were used with adjustment for: 1. Age 2. Sex 3. Primary tumor location 4. Stage at diagnosis 5. Rurality of residence, 6. Year of diagnosis	1. Individuals with a SPI were significantly less likely to receive either cancer treatment. 2. CRC patients with an inpatient SPI history were 2.15 times (95% CI = 1.07–4.33) more likely to not receive potentially curative surgery and 2.07 times (95% CI = 1.72–2.50) more likely to not receive adjuvant treatment following resection. 3. CRC patients with an outpatient SPI history were 1.51 times (95% CI = 0.88–2.59) more likely to not

(Continues)

TABLE 2 (Continued)

Authors, year (country)	Study subjects		Mental disorder	Design and findings				
	Data sources	No. of patients (year of diagnosis)		Type	Pre-existing	Definition of PMHD	Measured item	Adjusted variables
Kaerlev et al., 2018 (Denmark) ²⁸	National Danish Colorectal Cancer Group database and National Patient Registry	25,194 (2007–2013)	Psychiatric disorders (Consisting of schizophrenia, schizotypal and delusional disorder, and mood affective disorders, $n = 422$)	10 years to 120 days prior to the date of the operation	Hospital admissions with ICD-10 codes	Treatment (palliative vs. an intended curative operative treatment)	Logistic regression was used with adjustment for: <ol style="list-style-type: none"> Age Sex CCI Cancer stage at the time of operation Educational level Socio-economic position 	<ol style="list-style-type: none"> Colon cancer patients with psychiatric disorders had decreased adjusted OR for having an oncological treatment (OR = 0.55, 95% CI = 0.40–0.76). For patients with rectal cancer, no difference was seen.
Baillargeon et al., 2011 (US) ²⁹	SEER cancer registry data linked with Medicare claims files	80,670 (1993–2005)	<ol style="list-style-type: none"> Mood disorder ($n = 8261$) Psychotic disorder ($n = 3576$) Substance use disorder ($n = 3443$) Dementia ($n = 7267$) Other mental disorder ($n = 9322$) 	During the 2-year period before cancer diagnosis	Outpatient visits and hospital admissions with ICD-9 codes and physicians claims	Treatment (surgery, radiotherapy, and chemotherapy)	Logistic regression was used with adjustment for: <ol style="list-style-type: none"> Age Race and ethnicity Sex Marital status SEER region Income CCI Year of diagnosis Cancer stage (for no-treatment model only) 	Patients surviving 6 months found those with mental disorders were more likely to have received no treatment (RR = 2.09, 95% CI = 1.86–2.35); and more likely to have received no chemotherapy for Stage III cancer (RR = 1.63, 95% CI = 1.49–1.79).
Iachina et al., 2017 (Denmark) ³⁰	Danish Lung Cancer and Depression Register Database.	27,234 (2009–2011)	Depression ($n = 508$)	From 10 years before the start of the lung cancer diagnostics process	Outpatient visits and hospital admissions with ICD-10 codes	Treatment, surgery, and oncological treatment	Logistic regression was used with adjustment for: <ol style="list-style-type: none"> Age Sex Cancer Stage Modified Charleston Comorbidity Index 	<ol style="list-style-type: none"> Patients with depression had a lower ratio for treatment (Hazard Ratio, HR = 0.79, 95% CI = 0.64–0.96). Patients with recurrent depression had a lowest treatment ratio (HR = 0.66, 95% CI = 0.51–0.85). No statistically significant effect of depression on the ratio of surgical treatment. Patients with depression had a lower ratio for oncological treatment (HR = 0.76, 95% CI = 0.64–0.91); Patients with a recurrent depressive disorder had the lowest oncological treatment ratio as well (HR = 0.65, 95% CI = 0.52–0.83).

TABLE 2 (Continued)

Authors, year (country)	Study subjects		Mental disorder		Design and findings				
	Data sources	Cancer site	No. of patients (year of diagnosis)	Type	Pre-existing	Definition of PMHD	Measured item	Adjusted variables	Outcome
Lin et al., 2016 (US) ³¹	Department of Defence Central Cancer Registry and the Military Health System Data Repository	NSCLC	5054 (1998–2007)	<ol style="list-style-type: none"> Any mental disorder Psychotic disorder Dementia Mood disorder Substance abuse disorder Anxiety disorder Other mental health disorder (Total $n = 18,858$)	During the 2-year period before NSCLC diagnosis	Based on administrative health data with ICD-9 codes	Receipt of any cancer treatments	Multivariate Cox proportional hazards regression was used with adjustment for: <ol style="list-style-type: none"> Age Sex Race Marital status Sponsor service branch Active-duty status Tobacco use Comorbidity index Tumor stage Grade Histology Recurrence Specific mental disorders 	<ol style="list-style-type: none"> No significant differences in receiving any cancer treatment between the groups by mental health disorder status. No association was observed between other specific mental health disorders and receipt of any cancer treatment. Further analyses on receipt of surgery (stages I and II patients only), chemotherapy (stages III and IV patients only), and radiation therapy (stages III and IV patients only) did not reveal differences between patients with and without mental health disorders.
Sullivan et al., 2014 (US) ³²	Veterans Integrated Service Network 20 and Veterans Affairs Central Cancer Registry	NSCLC	1966 (1995–2010)	Depression ($n = 265$)	Within 2 years prior to lung cancer diagnosis	Outpatient visits and hospital admissions with ICD-9 codes	First-line chemotherapy	Logistic regression was used with adjustment for: <ol style="list-style-type: none"> Age Race/ethnicity Tobacco use Cancer stage Year of diagnosis Distance to nearest VAMC CCI 	No significant differences in chemotherapy receipt between all advanced stage patients with and without a diagnosis of depression.
Bergamo et al., 2014 (US) ³³	SEER cancer registry data linked with Medicare claims files	NSCLC	96,702 (1992–2007)	Schizophrenia ($n = 1303$)	Yes, but unclear	Outpatient visits and hospital admissions with ICD-9 codes	Stage-appropriate treatment	Logistic regression was used with adjustment for: <ol style="list-style-type: none"> Age Sex Marital status Race/ethnicity Income Histology Comorbidity status 	<ol style="list-style-type: none"> Patients with schizophrenia aged 66 years and over presented with earlier stage disease were less likely to receive stage appropriate treatment. They were significantly less likely to undergo surgery for stage I–IIA disease (OR = 0.82, 95% CI = 0.68–0.98), receive combined radiation and chemotherapy for stage IIIB (OR = 0.39, 95% CI = 0.26–0.58) or to receive chemotherapy for stage IV disease (OR = 0.39, 95% CI = 0.30–0.50). Among patients with a pre-existing diagnosis of schizophrenia and stage I–II NSCLC, those who were not treated with surgical resection were less frequently treated with radiation therapy (OR = 0.62, 95% CI = 0.45–0.85).

(Continues)

TABLE 2 (Continued)

Authors, year (country)	Study subjects		Mental disorder	Design and findings					
	Data sources	Cancer site		No. of patients (year of diagnosis)	Type	Definition of PMHD	Measured item	Adjusted variables	Outcome
Sullivan et al., 2014 (US) ³⁴	Veterans Integrated Service Network 20 and oncology registry. VISN20 (Alaska, Idaho, Oregon, and Washington).	NSCLC	3869 (1995–2010)	Depression (n = 549)	Within 2 years before lung cancer diagnosis	Outpatient visits and hospital admissions with ICD-9 codes	1. Radiation receipt (for stage III and IV) 2. Surgical resection (for stage I and II) 3. Chemotherapy receipt (for stage II, III and IV)	Logistic regression was used with adjustment for: 1. Age 2. Year of diagnosis 3. CCI 4. Race/ethnicity 5. Tobacco use 6. Lung cancer stage 7. Histology 8. Distance to the Veterans Affairs tertiary facility	There was no association between depression diagnosis with surgery among stage I and II patients, chemotherapy receipt among stage II-IV patients, or radiation receipt among stage III-IV disease.
O'Rourke et al., 2008 (US) ³⁵	Portland Veterans Administration Hospital records	Esophageal cancer	160 (1989–2003)	1. Psychiatric illness (n = 52) 2. Depression (n = 41) 3. Post-traumatic stress disorder (n = 10) 4. Anxiety disorder (n = 8) 5. Dementia (n = 7) 6. Schizophrenia (n = 6) 7. Personality Disorder (n = 2)	Yes, but unclear	Based on administrative health data, but unclear what information was used	Surgery	The results were assessed by Chi-square test without adjustment for other variables.	38% of patients with psychiatric illness received surgical therapy, compared to 59% of patients without (p = 0.031).
Chang et al., 2013 (Taiwan) ³⁶	Taiwan's National Health Insurance Database	Oral cancer	16,687 (2002–2006)	Non-specific mental health disorders (Consisting of schizophrenia, major affective disorder, and other mental illness, n = 206)	Yes, but unclear	Hospital admissions with ICD-9 codes	Surgery and adjuvant treatment	Logistic regression was used with adjustment for: 1. Age 2. Sex 3. CCI 4. Geographic region 5. Urbanization level 6. Enrolled category 7. Hospital ownership and accreditation level	Patients with mental health disorders were less likely to receive surgery with or without adjuvant therapy (OR = 0.47, 95% CI = 0.34–0.65).
Boyd et al., 2012 (US) ³⁷	SEER cancer registry data linked with Medicare claims files	Pancreatic cancer	23,745 (1992–2005)	Depression (n = 1868)	In the 3–27 months before the diagnosis of pancreas cancer	Based on administrative health data with ICD-9 codes	Definitive treatment: 1. Surgery or visit with a surgeon (for locoregional disease) 2. Chemotherapy or visit with medical oncologist (for distant disease)	Logistic regression was used with adjustment for: 1. Age 2. Sex 3. Race 4. Marital status 5. SEER region 6. Comorbidities	1. Patients with depression and locoregional disease had 37% lower odds of undergoing surgical resection compared to patients without depression (OR = 0.63, 95% CI = 0.52–0.76). 2. Patients with depression and distant disease had 21% lower odds of receiving chemotherapy compared to patients without depression (OR = 0.79, 95% CI = 0.70–0.90).

TABLE 2 (Continued)

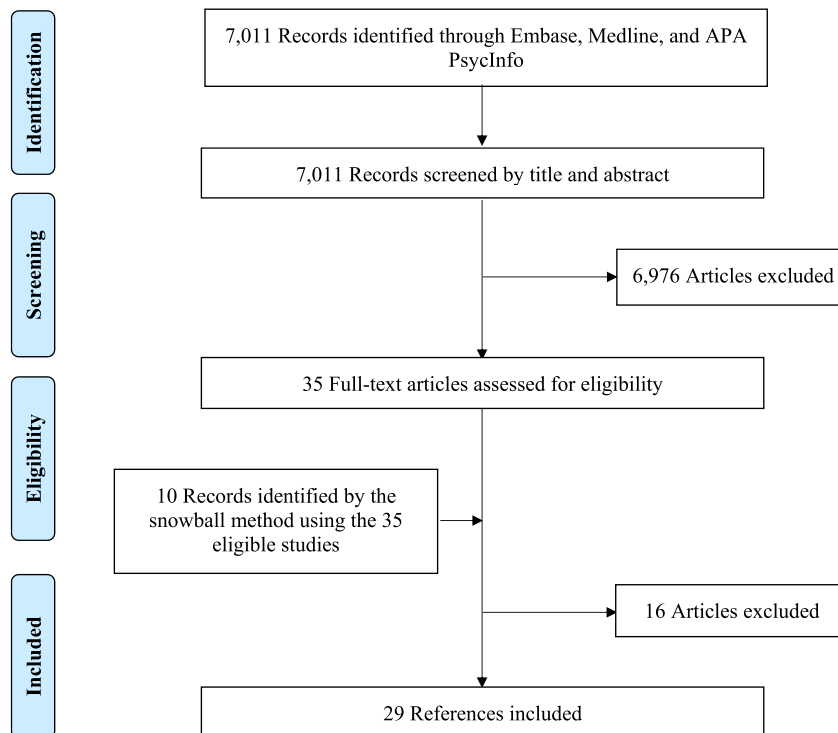
Authors, year (country)	Study subjects		Mental disorder		Design and findings			
	Data sources	No. of patients (year of diagnosis)	Type	Pre-existing	Definition of PMHD	Measured item	Adjusted variables	Outcome
Fried et al., 2019 (US) ³⁸	SEER cancer registry data linked with Medicare claims files	49,985 (2006–2013)	SMI (Consisting of bipolar disorder, schizophrenia, and other psychotic disorder, <i>n</i> = 523)	Within the 2 years prior to prostate cancer diagnosis	Outpatient visits and hospital admissions with ICD-9 codes	1. Surgery 2. Radiation concurrent with hormone therapy	Logistic regression was used with adjustment for: 1. Year of diagnosis 2. Age at diagnosis 3. CCI 4. Race/ethnicity 5. Marital status 6. Census tract median income 7. Census Tract % below poverty level 8. Census Tract % above high school 9. Urban/Rural status 10. Geographic region 11. Cancer stage	Among patients with high-grade localized prostate cancer, those with SMI had 34% (OR = 0.66, 95% CI = 0.49–0.89), and 19% (OR = 0.81, 95% CI = 0.67–0.98) lower odds of receiving surgery or radiation concurrent with hormone therapy, respectively, within 1 year from cancer diagnosis.
Prasad et al., 2014 (US) ³⁹	SEER cancer registry data linked with Medicare claims files	41,275 (2004–2007)	Depression (<i>n</i> = 1894)	Within the 2 years before prostate cancer diagnosis	Outpatient visits and hospital admissions with ICD-9 codes and carriers claims files	Definitive therapy (surgery or radiation) for localized disease	Logistic regression was used with adjustment for: 1. Year of diagnosis 2. Age at diagnosis 3. CCI 4. Race 5. Marital status 6. SEER region 7. Census measurements of median household income and education 8. Residence in a metropolitan area 9. Grade of tumor 10. NCCN risk category	1. Men with depression were less likely to select radiation for low-risk (OR = 0.76, 95% CI = 0.63–0.92) or high-risk disease (OR = 0.82, 95% CI = 0.68–0.98). 2. They were also less likely to choose surgery for intermediate risk disease (OR = 0.72, 95% CI = 0.58–0.91). 3. Overall, they were significantly less likely to undergo definitive therapy (surgery or radiation) across all risk strata.
Wiegand et al., 2015 (US) ⁴⁰	National Inpatient Sample database. An all-payer US inpatient care database, based on a 20% stratified sample of non-federal hospital admissions	23,890 (2004–2011)	1. Anxiety disorders 2. Mood disorders 3. Schizophrenia and other psychotic disorders 4. Substance use disorders (Total <i>n</i> = 4863)	Yes, but unclear	Based on administrative health data with ICD-9 codes	Sphincter-sparing surgery	Logistic regression was used with adjustment for: 1. Age 2. Sex 3. Race 4. Income 5. CCI 6. Insurance payer type 7. Year 8. Hospital volume/location/teaching status	1. Patients with any psychiatric diagnosis were less likely to have sphincter-sparing surgery (OR = 0.77, 95% CI = 0.72–0.83). 2. Odds were also lower for patients with mood disorder (OR = 0.70, 95% CI = 0.60–0.81), schizophrenia/psychotic conditions (OR = 0.64, 95% CI = 0.42–0.98) and substance use disorder (OR = 0.81, 95% CI = 0.74–0.90).

(Continues)

TABLE 2 (Continued)

Authors, year (country)	Study subjects		Mental disorder		Design and findings				
	Data sources	Cancer site	No. of patients (year of diagnosis)	Type	Pre-existing	Definition of PMHD	Measured item	Adjusted variables	Outcome
Ishikawa et al., 2016 (Japan) ⁴¹	The Japanese Diagnosis Procedure Combination database. A national inpatient database	Colorectal and gastric cancers	12,475 (2010–2013)	Schizophrenia (n = 2495)	Yes, but unclear	Based on administrative health data with ICD-10 codes	Invasive treatment (receipt surgical or endoscopic treatment)	Logistic regression was used with adjustment for: 1. Age 2. Sex 3. CCI 4. Smoking status 5. Site of cancer 6. Average income per capita 7. Cancer stage	Patients with schizophrenia had lower odds of invasive treatment (OR = 0.77, 95% CI = 0.69–0.85).
Wadia et al., 2015 (US) ⁴²	Veterans Affairs Connecticut Health Care System	Colorectal, head/neck, and urothelial cancers	408 (2008–2011)	Mental health comorbidities (MHC, DSM-IV Axis I mental disorders, n = 151)	At least 1 year prior to cancer diagnosis	Outpatient visits and hospital admissions with ICD-9 codes and healthcare provider notes	Time from diagnosis to treatment	The results were shown by median (days) without adjustment for other variables.	No significant differences in the time from diagnosis to initiation of treatment between patients with and without MHC (43 vs. 44 days, p = 0.2352).
Kisely et al., 2013 (Australia) ⁴³	The population-based data sets of Western Australian include the Hospital Morbidity Data System, Registrar General's Death Registration Data, Mental Health Information System, and Western Australian Cancer Registry	Mixed	135,442 (1988–2007)	Non-specific mental health disorders (n = 6586)	Yes, but unclear	Based on administrative health data, but unclear what information was used	Treatment with surgery, chemotherapy, and radiotherapy	Cox proportional hazards regression was used with adjustment for: 1. Presence of metastases 2. Patient demographic characteristics 3. Clinical features	1. Psychiatric patients had a reduced likelihood of surgery (HR = 0.81, 95% CI = 0.76–0.86); for resection of colorectal (males HR, 0.82, females HR = 0.68), breast (HR = 0.74), and cervical cancer (HR = 0.73). 2. They received significantly less radiotherapy for breast (2.6% vs. 4.1%), colorectal (1.6% vs. 3.9%), and uterine cancers (13% vs. 21.1%) and fewer chemotherapy sessions (10.3 vs. 12.1 sessions).

FIGURE 1 PRISMA diagram.



diagnosis compared to breast cancer patients without PMHD (adjusted risk ratio [RR] = 1.36, 95% confidence interval [CI] = 1.06–1.74).²² Breast cancer patients with PMHD had a 13% increased risk of a delay of 90 days or more from their last operation to adjuvant chemotherapy (adjusted RR = 1.13, 95% CI = 1.01–1.26) (Table 2).²² The third study compared the time duration from a bladder cancer diagnosis to radical cystectomy between individuals with severe PMHD including bipolar disorder, schizophrenia, or other psychotic disorders ($n = 726$) to those without.¹⁵ It found that the mean time to radical cystectomy was significantly lower for bladder cancer patients with severe PMHD compared to those without (1.5 vs. 3.9 months, $p < 0.001$).¹⁵

3.2 | Cancer treatment adherence

Two studies from Denmark were concerned with adherence to cancer treatment.^{19,26} Rubinsak et al.²⁶ investigated the time taken to complete radiation therapy by 129 cervical cancer patients. They found no difference in the mean number of days to complete radiation therapy in patients with substance use disorders compared to those without (62.7 vs. 57.2 days, $p = 0.818$). Haskins et al.¹⁹ focused on endocrine therapy for women with breast cancer. They found that compared to women with breast cancer but without PMHD, those with substance use disorders (hazard ratio (HR) = 0.85, 95% CI = 0.85–0.86) or anxiety disorders (HR = 0.88, 95% CI = 0.87–0.88) were less compliant with their endocrine therapy for at least 1 year after controlling for cancer stage, race/ethnicity, age, comorbidity, and year of cancer diagnosis (Table 2).

3.3 | Differences in receipt of guideline recommended cancer treatments

Our review identified a total of 25 studies that focused on the treatment of nine main cancer types: breast, prostate, colon, rectum, NSCLC, bladder, head/neck, esophageal and pancreatic cancers (Table 2).

3.4 | Breast cancer

There were eight studies of women with breast cancer conducted across Finland,¹⁵ Germany,¹⁸ the US ($n = 2$),^{24,25} Denmark ($n = 2$),^{20,23} and Japan ($n = 2$).^{16,21} Three studies found that breast cancer patients with schizophrenia,²⁰ depression²³ and any mental health illness²⁴ were less likely to be allocated to guideline recommended cancer treatment. These studies showed consistently that people with PMHD were more likely to be allocated to non-guideline treatment [OR] (OR = 1.50, 95% CI = 1.15–1.94)²⁰ (OR = 1.14, 95% CI = 1.03–1.27,²³ or less likely to receive guideline recommended cancer treatment (OR = 0.79, 95% CI = 0.65–0.97)²⁴ but did not specify the type of treatment in the analysis. One study from Japan showed that women with PMHD underwent total mastectomy significantly more often (89% vs. 78%, $p = 0.011$) and underwent postoperative adjuvant chemotherapy (0% vs. 19%, $p = 0.0031$) and radiation therapy (2.2% vs. 18%, $p = 0.0059$) less often, compared with those women without PMHD.²¹ Another study from Japan showed that women with a pre-existing diagnosis of schizophrenia were significantly more likely to undergo mastectomy (84.3% vs.

TABLE 3 NOS scale.

Author, year	Selection		Comparability		Outcome		Adequacy of follow-up of Quality score	
	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at the start of the study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome		Follow-up long enough for an outcome to occur
Sathianathan et al., 2020 ¹⁵	*	*	*	*	*	*	*	8
Kaneshiro et al., 2022 ¹⁶	*	*	*	*	*	*	*	8
Ahlgren-Rimpläinen et al., 2020 ¹⁷	*	*	*	*	*	*	*	4
Groß et al., 2020 ¹⁸	*	*	*	*	*	*	*	6
Haskins et al., 2019 ¹⁹	*	*	*	*	*	*	*	7
Dalton et al., 2018 ²⁰	*	*	*	*	*	*	*	7
Shinden et al., 2017 ²¹	*	*	*	*	*	*	*	3
Iglay et al., 2017 ²²	*	*	*	*	*	*	*	8
Suppli et al., 2017 ²³	*	*	*	*	*	*	*	6
Mahabaleshwarar et al., 2015 ²⁴	*	*	*	*	*	*	*	7
Goodwin et al., 2004 ²⁵	*	*	*	*	*	*	*	7
Rubinsak et al., 2019 ²⁶	*	*	*	*	*	*	*	7
Mahar et al., 2020 ²⁷	*	*	*	*	*	*	*	8
Kaerlev et al., 2018 ²⁸	*	*	*	*	*	*	*	6

TABLE 3 (Continued)

Author, year	Selection		Comparability		Outcome		Quality score	
	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at the start of the study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome		Follow-up long enough for an outcome to occur
Baillargeon et al., 2011 ²⁹	*	*	*	*	*	*	*	7
Iachina et al., 2017 ³⁰	*	*	*	*	*	*	*	6
Lin et al., 2016 ³¹	*	*	*	*	*	*	*	6
Sullivan et al., 2014 ³²	*	*	*	*	*	*	*	8
Bergamo et al., 2014 ³³	*	*	*	*	*	*	*	7
Sullivan et al., 2014 ³⁴	*	*	*	*	*	*	*	7
O'Rourke et al., 2008 ³⁵	*	*	*	*	*	*	*	5
Chang et al., 2013 ³⁶	*	*	*	*	*	*	*	6
Boyd et al., 2012 ³⁷	*	*	*	*	*	*	*	8
Fried et al., 2019 ³⁸	*	*	*	*	*	*	*	8
Prasad et al., 2014 ³⁹	*	*	*	*	*	*	*	7
Wiegand et al., 2015 ⁴⁰	*	*	*	*	*	*	*	5
Wadia et al., 2015 ⁴²	*	*	*	*	*	*	*	6
Kisely et al., 2013 ⁴³	*	*	*	*	*	*	*	6
Author, year	Selection		Comparability		Exposure		Quality score	
	Is the case definition adequate	Representativeness of the cases	Selection of controls	Definition of controls	Comparability of cases and controls on the basis of the design or analysis	Ascertainment of exposure		Same method of ascertainment for cases and controls
Ishikawa et al., 2016 ⁴¹	*	*	*	*	*	*	*	7

TABLE 4 Adjustment for other variables carried out in each study.

Author, year	Cancer types	Mental health disorder	Country	Health coverage	Age	Stage	Other cancer info.	Comorbidity/Health condition	Sex	Year	SES	Race/ethnicity	Other socio-economic	Geography	Hospital info.
Sathianathan et al., 2020 ¹⁵	Bladder	Anxiety disorder, depression, bipolar disorder, schizophrenia, and other psychotic disorders	US	All covered by Medicare	X	-	X; Tumor grade	X; CCI	X	X	X	X	X; Educational level	-	-
Kaneshiro et al., 2022 ¹⁶	Breast	Schizophrenia	Japan	All covered by National Health Insurance	-	-	-	-	-	-	-	-	-	-	-
Ahigrén-Rimpiläinen et al., 2020 ¹⁷	Breast	Non-affective psychosis, substance use disorder, mood disorder	Finland	All covered by National Health Insurance	-	-	-	-	-	-	-	-	-	-	-
Groß et al., 2020 ¹⁸	Breast	Non-specific mental health illness	Germany	-	X	X	X; Cancer diagnosis method	X; Secondary diseases	-	-	-	-	X; Educational level	-	-
Haskins et al., 2019 ¹⁹	Breast	Depression, anxiety disorder, adjustment disorder, delirium, dementia, personality disorder, bipolar disorder, schizophrenia, non-schizophrenia psychosis, substance use	US	All covered by Medicare	X	X	-	X; Adjusted NCI comorbidity score	-	X	-	X	-	-	-
Dalton et al., 2018 ²⁰	Breast	Schizophrenia or related conditions	Denmark	All covered by National Health Insurance	X	-	-	X; CCI	-	X	-	-	X; Educational level	-	-
Shinden et al., 2017 ²¹	Breast	Schizophrenia, dementia, intellectual disability	Japan	All covered by National Health Insurance	-	-	-	-	-	-	-	-	-	-	-
Iglay et al., 2017 ²²	Breast	Anxiety disorder, depression, bipolar disorder, schizophrenia, and other psychotic disorder	US	All covered by Medicare	X	X	-	X; CCI	-	-	X	X	X; Marital status	X	-
Suppli et al., 2017 ²³	Breast	Depression	Denmark	All covered by National Health Insurance	X	-	X; Tumor size, No. of tumor-positive axillary lymph node, estrogen-receptor status	X; CCI	-	X	-	-	X; Educational level, cohabiting	-	-
Mahabaleshwarar et al., 2015 ²⁴	Breast	Mood disorder, psychotic disorder	US	All covered by Medicaid	X	X	-	X; CCI, No. of outpatient visits	-	-	-	X	-	X	-
Goodwin et al., 2004 ²⁵	Breast	Depression	US	All covered by Medicare	X	-	-	X; CCI, No. of doctor visits	-	-	-	X	X; Marital status	X	-

TABLE 4 (Continued)

Author, year	Cancer types	Mental health disorder	Country	Health coverage	Age	Stage	Other cancer info.	Comorbidity/Health condition	Sex	Year	SES	Race/ethnicity	Other socio-economic	Geography	Hospital info.
Rubinsak et al., 2019 ²⁶	Cervical	Substance use disorder	US	-	-	-	-	-	-	-	-	-	-	-	-
Mahar et al., 2020 ²⁷	Colorectal	Depression, bipolar disorder, schizophrenia, and other non-organic psychotic illnesses	Canada	All covered by Universal Health-care system	X	X	X; Primary tumors location	-	X	X	-	-	-	X	-
Kaerlev et al., 2018 ²⁸	Colorectal	Schizophrenia, schizotypal and delusional disorder, mood affective disorder	Denmark	All covered by National Health Insurance	X	X	-	X; CCI	X	-	X	-	X; Educational level	-	-
Baillargeon et al., 2011 ²⁹	Colon	Mood disorder, psychotic disorder, substance use disorder, dementia, other mental disorder	US	All covered by Medicare	X	X	-	X; CCI	X	X	X	X	X; Marital status	X	-
Iachina et al., 2017 ³⁰	Non-small cell lung cancer	Depression	Denmark	All covered by National Health Insurance	X	X	-	X; CCI	X	-	-	-	-	-	-
Lin et al., 2016 ³¹	Non-small cell lung cancer	Any mental disorder	US	All covered by Military Health System	X	X	X; Tumor grade, histology, recurrence	X; Comorbidity index, specific mental disorder, tobacco use	X	-	-	X	X; Marital status	-	-
Sullivan et al., 2014 ³²	Non-small cell lung cancer	Depression	US	Data were obtained from Veterans Affairs	X	X	-	X; CCI, tobacco use	-	X	-	X	-	X	-
Bergamo et al., 2014 ³³	Non-small cell lung cancer	Schizophrenia	US	All covered by Medicare	X	-	X; Histology	X; Comorbidity index	X	-	X	-	X; Marital status	-	-
Sullivan et al., 2014 ³⁴	Non-small cell lung cancer	Depression	US	Data were obtained from Veterans Affairs	X	X	X; Histology	X; CCI, tobacco use	-	X	-	-	-	X	-
O'Rourke et al., 2008 ³⁵	Esophageal cancer	Psychiatric illness, depression, post-traumatic stress disorder, anxiety disorder, dementia, schizophrenia, personality disorder	US	Data were obtained from a Veterans Affairs hospital	-	-	-	-	-	-	-	-	-	-	-
Chang et al., 2013 ³⁶	Oral	Schizophrenia, major affective disorder, other mental illness	Taiwan	All covered by National Health Insurance	X	-	-	X; CCI	X	-	-	-	-	X	X; Hospital ownership, accreditation level
Boyd et al., 2012 ³⁷	Pancreatic	Depression	US	All covered by Medicare	X	-	-	X; Comorbidity	X	-	-	X	X; Marital status	X	-
Fried et al., 2019 ³⁸	Prostate	Bipolar disorder, schizophrenia, other psychotic disorder	US	All covered by Medicare	X	X	-	X; CCI	-	X	X	X	X; Marital status, poverty level, education level	X	-
Prasad et al., 2014 ³⁹	Prostate	Depression	US	All covered by Medicare	X	-	X; Grade of tumors, NCCN risk category	X; CCI	-	X	X	X	X; Marital status, education level	X	--

(Continues)

TABLE 4 (Continued)

Author, year	Cancer types	Mental health disorder	Country	Health coverage	Age	Stage	Other cancer info.	Comorbidity/Health condition	Sex	Year	SES	Race/ethnicity	Other socio-economic	Geography	Hospital info.
Wiegand et al., 2015 ⁴⁰	Rectal	Anxiety disorder, mood disorder, schizophrenia and other psychotic disorder, substance use disorder	US	-	X	-	-	X; CCI	X	X	X	X	-	-	X; Hospital volume/location/teaching status
Ishikawa et al., 2016 ⁴¹	Gastric, colorectal	Schizophrenia	Japan	All covered by National Health Insurance	X	X	X; Site of cancer	X; CCI, tobacco use	-	X	X	-	-	-	-
Wadia et al., 2015 ⁴²	Colorectal, urothelial, head/neck	DSM IV Axis I mental disorders	US	Data were obtained from Veterans Affairs	-	-	-	-	-	-	-	-	-	-	-
Kisely et al., 2013 ⁴³	Mixed	Non-specific mental health disorder	Australia	All covered by Medicare	X	-	X; Metastases	X; Length of stay in inpatient care	X	-	X	-	-	-	-

63.2%, $p = 0.0024$) and less often received chemotherapy (40% vs. 88.7%, $p < 0.0001$), and guideline recommended cancer treatment (61.8% vs. 79.1%, $p = 0.0004$), compared with those women without schizophrenia.¹⁶ However, there was no significant difference on radiation therapy (56.2% vs. 75.9%, $p = 0.078$), hormone therapy (84.2% vs. 90.6%, $p = 0.20$) and anti-HER2 therapy (50% vs. 81.5%, $p = 0.35$) between the two groups in that study.¹⁶ Furthermore, one US study showed that women with a pre-existing diagnosis of depression were less likely to receive treatment with curative intent (59.7% vs. 66.2%, $p < 0.05$).²⁵ The study from Finland demonstrated that 48% of women without PMHD had received radiotherapy, in contrast to 38% of those with a history of non-affective psychosis, 43% of those with substance use disorder, and 43% of those with a history of mood disorder ($p < 0.001$).¹⁷ However, one study from Germany showed that women with PMHD tended to receive a mastectomy (OR = 1.43, 95% CI = 0.79–2.60) rather than a breast conserving surgery (OR = 0.70, 95% CI = 0.42–1.17) but the odds were not significant after controlling for age, education, cancer stage, health condition, and health insurance.¹⁸

3.5 | Prostate cancer

Two studies from the US focused on men with prostate cancer and reported consistent findings. Men defined as having a pre-existing diagnosis of depression ($p < 0.006$) or severe PMHD including bipolar disorder, schizophrenia, and other psychotic disorder were less likely to undergo either surgery or radiation therapy with curative intent.^{38,39} Men with severe PMHD were less likely to receive surgery (OR = 0.66, 95% CI = 0.49–0.89) and radiation therapy with hormone therapy (OR = 0.81, 95% CI = 0.67–0.98).³⁸

3.6 | Colon and rectal cancers

The three studies evaluating the impact of PMHD in patients diagnosed with colon cancer all found an impact on the likelihood of receiving a guideline recommended therapy.^{28,29,41} A Danish study found that patients with schizophrenia, schizotypal and delusional disorder, or mood affective disorders were less likely to receive oncological treatment (chemotherapy or radiotherapy, by cancer site) compared to patients without PMHD (OR = 0.55, 95% CI = 0.40–0.76).²⁸ A study from the US of colon cancer patients with PMHD surviving 6 months from diagnosis found they were more likely not to be allocated to any treatment (RR = 2.09, 95% CI = 1.86–2.35) or adjuvant chemotherapy for colon cancer with Stage III (RR = 1.63, 95% CI = 1.49–1.79).²⁹

By contrast, the results from studies of rectal cancer were inconsistent.^{28,40} One study from Denmark found no difference in the type of treatment received for patients with PMHD and those without (OR = 0.72, 95% CI = 0.46–1.11).²⁸ However, one US study found patients with any PMHD were less likely to have sphincter-sparing rectal cancer surgery (OR = 0.77, 95% CI = 0.72–0.83),

especially those with a pre-existing diagnosis of mood disorder (OR = 0.70, 95% CI = 0.60–0.81), schizophrenia/psychotic conditions (OR = 0.64, 95% CI = 0.42–0.98), and substance use disorder (OR = 0.81, 95% CI = 0.74–0.90).⁴⁰

One study from Japan demonstrated that patients with colorectal or gastric cancers and pre-existing schizophrenia were less likely to receive invasive treatment (surgical or endoscopic treatment) (OR = 0.77, 95% CI = 0.69–0.85).⁴¹ Another study from Canada compared the differences in receipt of guideline recommended cancer treatment between individuals with severe PMHD including major depression, bipolar disorder, schizophrenia, and other non-organic psychotic illnesses and those without. This study showed that patients with colorectal cancer and severe PMHD hospital admissions were more likely not to be allocated to curative surgery (RR = 2.15, 95% CI = 1.04–4.33). In addition, patients with severe PMHD either for outpatient visits (RR = 1.22, 95% CI = 1.00–1.49) or hospital admissions (RR = 2.07, 95% CI = 1.72–2.50) were more likely not to be allocated to adjuvant chemotherapy following resection.²⁷

3.7 | Non-small cell lung cancer

The five studies of patients with NSCLC found inconsistent results.^{30–34} One study from Denmark demonstrated that patients with depression were less likely to receive oncological treatment (surgical resection, chemo +/- radiotherapy, targeted or immunomodulating drug therapies) (HR = 0.76, 95% CI = 0.64–0.91).³⁰ A US study found that older patients with schizophrenia were less likely to receive stage appropriate treatment compared to those older patients without schizophrenia. For example, surgery for stage I–IIIA NSCLC (OR = 0.82, 95% CI = 0.68–0.98); chemoradiotherapy for stage IIIB NSCLC (OR = 0.39, 95% CI = 0.26–0.58); or chemotherapy for stage IV disease (OR = 0.39, 95% CI = 0.30–0.50). Among patients with a pre-existing diagnosis of schizophrenia and stage I–II NSCLC, those who were not treated with surgical resection were less frequently treated with radiation therapy (OR = 0.62, 95% CI = 0.45–0.85).³³ However, the US study also showed no difference in receiving adjuvant chemotherapy for resected stage II–IIIA disease ($p = 0.52$).³³ Another US study found no difference in the cancer treatment received by patients with PMHD compared to those without (HR = 1.00, 95% CI = 0.94–1.07).³¹ Similar results were also reported in two further US studies which focused on lung cancer patients with a pre-existing diagnosis of depression.^{32,34} One showed no significant differences in chemotherapy receipt for patients with advanced stage disease irrespective of a pre-existing diagnosis of depression ($p = 0.88$).³² The other study demonstrated that a diagnosis of depression did not influence receipt of surgery among stage I–II patients ($p = 0.34$), receipt of chemotherapy among stage II, III, and IV patients ($p = 0.47, 0.29, \text{ and } 0.21$, respectively), or receipt of radiation therapy for patients with stage III ($p = 0.15$) or stage IV ($p = 0.74$).³⁴

3.8 | Other cancers (bladder, head/neck, esophageal, and pancreatic cancers)

Four studies investigated differences in the receipt of guideline recommended cancer treatment between individuals with and without PMHD before a diagnosis of bladder,¹⁵ head/neck,³⁶ esophageal,³⁵ and pancreatic³⁷ cancers respectively. The first study from the US¹⁵ showed that bladder cancer patients with severe PMHD including bipolar disorder, schizophrenia, or other psychotic disorders (OR = 0.67, 95% CI = 0.47–0.95), depression only (OR = 0.79, 95% CI = 0.66–0.95), or both anxiety and depression (OR = 0.57, 95% CI = 0.35–0.92) were significantly less likely to undergo radical cystectomy. In addition, patients with severe PMHD (OR = 0.55, 95% CI = 0.37–0.81) and those with depression only (OR = 0.71, 95% CI = 0.58–0.88) were less likely to receive curative treatment.¹⁵ The second study from Taiwan found that patients with oral cancer and PMHD were less likely to receive surgery with or without adjuvant therapy (OR = 0.47, 95% CI = 0.34–0.65).³⁶ The third study from the US showed a similar result finding that patients with esophageal cancer and PMHD less often underwent surgical resection than those without (38% vs. 59%, $p = 0.031$).³⁵ The last study from the US focused on pancreatic cancer and showed that patients with depression had 37% (OR = 0.63, 95% CI = 0.52–0.76) lower odds of undergoing surgical resection and 21% (OR = 0.79, 95% CI = 0.70–0.90) lower odds of receiving chemotherapy compared to patients without depression.³⁷

In summary, the impact on receipt of cancer treatment by PMHD varied for different cancer types, types of mental health disorders, or types of cancer treatment. However, the majority of studies showed that individuals with PMHD were less likely to be allocated to guideline recommended cancer treatment. This was the case for 7/8 studies for breast cancer,^{16,17,19,21,23–25} 2/2 studies for prostate cancer,^{38,39} 3/3 studies for colon cancer,^{28,29,41} 1/2 studies for rectal cancer,⁴⁰ 2/2 for colorectal cancer,^{27,41} 2/5 for NSCLC,^{30,33} and one study of bladder, head/neck, esophageal, and pancreatic cancers.^{15,35–37}

3.9 | Results robustness

We assessed the quality of studies included in the review using the NOS (See methods). 17/29 of the studies were judged to be of high quality,^{15,16,19,20,22,24–27,29,32–34,37–39,41} 10/29 of medium quality,^{18,23,28,30,31,35,36,40,42,43} and 2/29 of low quality (Table 3).^{17,21} Most studies adjusted for patients' demographic characteristics (age, sex, socio-economic status, and race/ethnicity) and disease characteristics (cancer stage, cancer diagnosis method, tumor size, and comorbidity). In addition, most of the study subjects were enrolled in national health insurance programs or were Medicare beneficiaries in the US. Fewer studies reported results that were adjusted for hospital level characteristics (hospital ownership, accreditation level and teaching hospital status) or geographical residence (Table 4).

3.10 | Findings categorized by cancer types and mental health disorders

We also looked at the implications on receipt of treatment by PMHD and then subdivided according to tumor types (supplement 2) and mental health disorder (supplement 3). Individuals with bladder, breast cancer, and non-small cell lung cancer were investigated for more different types of PMHD compared to those with cervical, colon, rectal, esophageal, oral, pancreatic, or prostate cancers (supplement 2). Furthermore, many studies focused on depression, schizophrenia, and psychiatric disorders or non-specific PMHD. A few studies explored the differences in receipt of guideline recommended cancer treatment among pre-existing substance use disorder or severe mental illnesses (supplement 3).

The influences of different types of PMHD on treatment among breast cancer and NSCLC were inconsistent. Women with breast cancer and pre-existing depression were more likely not to be allocated to guideline treatment (OR = 1.14, 95% CI = 1.03–1.27),²³ while those with schizophrenia and psychiatric disorders (61.8% vs. 79.1%, $p = 0.0004$ ¹⁶; OR = 1.50, 95% CI = 1.15–1.94),²⁰ or non-specific PMHD (OR = 0.79, 95% CI = 0.65–0.97)²⁴ were less likely to receive guideline treatment. This was especially so for women with depression who were more likely not to be allocated to curative intent (OR = 1.19, 95% CI = 1.06–1.33)²⁵ and women with schizophrenia who less often underwent chemotherapy (40.0% vs. 88.7%, $p < 0.0001$).¹⁶ In addition, women with non-specific PMHD received less postoperative adjuvant chemotherapy (0% vs. 19%, $p = 0.0031$) and radiation therapy (2.2% vs. 18%, $p = 0.0059$) but underwent more mastectomies (78% vs. 59%, $p = 0.011$).²¹ However, one study showed no significant difference in surgery between women with and without non-specific PMHD (mastectomy: OR = 1.43, $p > 0.05$; conserving surgery: OR = 0.70, $p > 0.05$).¹⁸ Another study found no significant difference in hormone therapy ($p = 0.20$) and anti-HER2 therapy ($p = 0.35$) between women with and without schizophrenia.¹⁶ One study showed that individuals with NSCLC and pre-existing non-specific PMHD had no differences in surgery ($p = 0.845$), chemotherapy ($p = 0.706$), or radiation therapy ($p = 0.269$) compared to those without pre-existing non-specific PMHD.³¹ There were also no differences for people with NSCLC and pre-existing depression in surgery ($p = 0.053$ ³⁰; OR = 0.83, $p = 0.34$)³⁴ or chemotherapy (OR = 0.98, $p = 0.88$),³² especially for those with cancer stage II, III and IV (OR = 0.76, $p = 0.47$; OR = 1.28, $p = 0.29$; OR = 0.78, $p = 0.21$, respectively).³⁴ In addition, compared to those NSCLC patients without pre-existing depression, there were no differences in radiation therapy for those with pre-existing depression and cancer stage III (OR = 1.38, $p = 0.15$) or cancer stage IV (OR = 0.94, $p = 0.74$).³⁴ But NSCLC patients with pre-existing schizophrenia and psychiatric disorders showed different outcomes. They were less likely to receive surgery for NSCLC stage I-IIIA (OR = 0.82, 95% CI = 0.68–0.98), chemotherapy for stage IV (OR = 0.39, 95% CI = 0.26–0.58), and combined radiation and chemotherapy for stage IIIB (OR = 0.39, 95%

CI = 0.30–0.50).³³ However, the sample size of studies was too small to draw any clear conclusions.

Based on supplement 3, individuals who suffered from different types of PMHD showed inconsistent disparities in receipt of guideline recommended cancer treatment. More than one half of the studies demonstrated that people with depression prior to a diagnosis of cancer were less likely to undertake surgery, radiation therapy, and unspecified guideline recommended treatment (3/5, 2/3, and 1/1 studies, respectively).^{15,23,25,37,39} The number of studies for substance use disorder was only two and with different types of cancer treatment. The findings showed that individuals with a pre-existing substance use disorder were less likely to receive sphincter-sparing surgery for rectal cancer,⁴⁰ and no difference on radiation dose for cervical cancer.²⁶ For individuals with schizophrenia and/or psychiatric disorders prior to a cancer diagnosis, more than half of studies showed that they were less likely to be allocated to surgery, chemotherapy, and unspecified guideline recommended treatment (4/5, 3/4, and 2/2 studies, respectively).^{16,20,28,33,35,40,41} Despite the included mental health disorders of severe PMHD in each study being inconsistent, the findings of disparities in receipt of guideline recommended cancer treatment were similar. People who suffered from severe PMHD were less likely to receive surgery, chemotherapy, and radiation therapy.^{15,27,38}

4 | DISCUSSION

This systematic review identified 29 studies published internationally between 1995 and 2022, which assessed the impact of PMHD on three critical aspects of the cancer care pathway: access to guideline recommended cancer treatment, treatment delay and treatment compliance. Nearly all were conducted in the last decade (2012–2022) and all studies were from high-income countries, such as the US, Denmark, and Japan. They also mostly included patient groups or populations enrolled in national health insurance systems or the US Medicare, Veterans Affairs and Military Health systems, where fewer barriers in accessing treatment might be expected. The majority of studies focused on breast cancer, non-small cell lung cancer, and colorectal cancer, with approximately one half of included studies being assessed as high quality.

From the studies included in this review, only five aimed to establish the impact of PMHD on treatment delay or adherence, and their findings are inconsistent. The remaining 25 studies explored differences in receipt of guideline recommended cancer treatment between cancer patients with and without PMHD. Most studies focused on bladder, breast and non-small cell lung cancer with depression and schizophrenia being the commonest mental health disorders considered. However, a significant proportion of studies (15/29) did not differentiate the type of mental health disorder evaluated. Broadly across all cancer types and modalities of treatment (surgery, radiotherapy, or systemic therapy), there is evidence of a clear disparity in the receipt of guideline recommended

treatment. Disparities in cancer care for individuals with PMHD have already been identified, especially in relation to cancer screening⁵ uptake and cancer mortality.^{6,7} However, to our knowledge, there has been no previous systematic review which has considered the influence across the spectrum of diverse PMHD on these key aspects of the cancer treatment pathway. Given the prevalence of mental health disorders and increasing incidence of cancer, this review highlights an area of unmet need that requires further empirical evaluation.

Patient-level, health care provider-level, and systems-level factors may all contribute to disparities in delay, receipt of, and adherence to cancer treatment.⁴⁴ For example, individuals with severe mental health disorders may be socially isolated, and have poorer recall of medical recommendations, which may lead to self-neglect, difficulty with communicating symptoms, paranoid and inappropriate behavior, and non-adherence to treatment and appointments.^{44–46} Symptoms such as paranoia, disorganized thoughts, and decreased sensitivity to pain, may all contribute to delayed health-seeking, misunderstanding of cancer, and discontinued treatment.^{47,48} Problems with communication between physicians and patients may also lead to inappropriate treatments,⁴⁸ especially for patients who suffer from paranoia symptoms, which could lead them to fear and distrust their treating physicians.⁴⁸ Mental health disorders might also complicate cancer treatment procedures, for example, the administration of radiotherapy. Patients need to be alone in the treatment room to receive ionizing radiation and to follow instructions from an automated voice during treatment sessions. Patients with a tendency for paranoia, auditory hallucinations, or severe anxiety may be too distressed to follow this treatment, and the multidisciplinary team may therefore decide that radiotherapy is not appropriate.⁴⁹ Besides, individuals with severe mental health disorders are more likely to suffer from low function or dysfunctions which may affect their independent decision-making capacity. In this situation, primary caregivers, such as family, friends, or neighbors, may assume responsibilities of monitoring medication or improving compliance.^{50,51} Therefore, the primary caregivers may influence patients' cancer treatment pathway as well. Physicians also need to consider potential drug interactions in developing individual cancer treatment plans. Many psychotropic drugs including clomipramine, duloxetine, haloperidol, paroxetine, sertraline, and fluoxetine can interact with cancer treatments,^{50,52} and lead, for example, to increased side-effects for tamoxifen, docetaxel, paclitaxel, and cyclophosphamide.⁵³ Patients' comorbidities, for instance, obesity, diabetes, and cardiovascular disease can also complicate cancer treatment and lead to poorer outcomes.^{44,49,54} In addition, financial burdens are associated with worse cancer treatment adherence.⁵⁵

Separate care pathways for primary care, oncology, and mental health services may also result in the disparities identified in our review. This may be improved by better integration of multidisciplinary care pathways.^{47,56–58} For example, the cancer care team should involve or have easy access to mental health professionals with expertise in establishing trust and clear communication in language that is tailored to individuals with different types of

PMHD.⁵⁶ Furthermore optimizing active mental health disorders and improving control of mental health symptoms prior to cancer treatment and establishing a person-centered care program could ultimately ensure appropriate access to guideline recommended therapies, compliance and ultimately improvements in survival outcomes. For example, Irwin et al.⁵⁹ developed an intervention called 'Bridge' for patients with schizophrenia, bipolar disorder, and severe major depression. Bridge entailed person-centered care from a psychiatrist and case manager, and in collaboration with an oncologist, enabled patients to initiate and complete cancer treatment.

4.1 | Study limitations

This review includes only studies published in English and those which defined both cancer and mental health disorder using data held within electronic medical records. Variable definitions for type of mental health disorder and the use of different types of electronic medical records may make it challenging to establish the degree of severity. The adjustment for confounders used across these studies varied considerably and the definitions of guideline recommended cancer treatment are defined in each study dependent on the clinical database available. It is therefore possible that bias may exist in the assessment of the impact of PMHD on cancer treatment. In addition, although DSM and ICD commonly define mental disorders as those having an influence on a persons' function and social interaction, illnesses are heterogeneous. In the absence of an adjustment for the severity of mental disorders, it is still unclear whether poorer adherence and less recommended cancer treatment are driven by health providers' opinions, patients' preferences, communication barriers, or health system structural deficiencies.

There are a number of implications of this research that are clinically and policy relevant, in particular that there are major gaps in the current evidence base. First, we note that the impact of PMHD on cancer treatment delay and adherence is a hugely under-researched topic (only five studies were identified) and this is an area that requires urgent evaluation to provide evidence and guidance to support management. Second, there is little evidence of the impact of PMHD on access to treatment for complex cancer types such as Central Nervous Systems tumors as well as other common cancer such as skin cancer and haematological malignancies. Third, the disparities in cancer care for individuals with many other types of PMHD, such as anxiety disorder, personality disorders, or obsessive-compulsive disorders, are still unclear. Fourth, the present study has explored quantitative studies, but to further supplement this work qualitative studies are required to better understand patients' and professionals' perspectives in different health systems and the underlying reasons for disparities in cancer treatments for PMHD patients with differing severity. Finally, the research studies all derived from high income settings and the implications in terms of access to care for patients with a cancer diagnosis and PMHD in low-to-middle-income countries settings remains unknown.

4.2 | Clinical implications

Across a broad range of cancer types and modalities of care, there is evidence of a clear disparity in the receipt of guideline recommended cancer treatment for patients with PMHD. However, the possible influence on treatment delay and treatment adherence is still under-researched. We suggest future research should focus on the impact of PMHD on treatment delay or adherence, develop research in middle-income and low-income countries, and establish more qualitative studies to better understand the reasons for disparities in cancer treatments for PMHD patients with different illness severity. Furthermore, integrated health care systems providing a person-centered approach to care should be improved to address disparities in cancer care for individuals with cancer who also have PMHD.

5 | CONCLUSION

This study reveals evidence of a clear disparity in the receipt of guideline recommended cancer treatment for individuals with PMHD across different cancer types. To reduce the disparity and improve the outcomes of cancer care for patients with PMHD, a person-centered approach involving multidisciplinary professionals should be provided.

AUTHOR CONTRIBUTIONS

The studies included in this systematic review were initially selected by Yueh-Hsin Wang and Elizabeth A. Davies with Ajay Aggarwal checking them and agreeing the excluded studies. Yueh-Hsin Wang and Elizabeth A. Davies then extracted data from each study, assessed its quality, and discussed any disagreement with Ajay Aggarwal to reach a consensus. Robert Stewart reviewed the findings from the perspective of clinical psychiatry. All authors critically reviewed the manuscript and approved the final version.

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CONFLICT OF INTEREST

RS declares research support received in the last 36 months from Janssen, GSK and Takeda.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

REGISTRATION AND PROTOCOL

This review was not registered, and a protocol was not prepared.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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