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Association between preexisting mental illnesses and mortality among medicaid-insured women diagnosed with breast cancer

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Abstract

Background: We investigated the impact of preexisting mental illnesses on all-cause and cause-specific mortality among Medicaid-insured women diagnosed with breast cancer.

Methods: Data from the New York State Cancer Registry for 10,444 women diagnosed with breast cancer from 2004 to 2016 and aged <65 years at diagnosis were linked with Medicaid claims. Women were categorized as having depression or a severe mental illness (SMI) if they had at least three relevant diagnosis claims with at least one claim within three years prior to breast cancer diagnosis. SMI included schizophrenia, bipolar disorder, and other psychotic disorders. Estimated menopausal status was determined by age (premenopausal age <50; postmenopausal age ≥50). Hazard ratios (HR) and 95% confidence intervals (95%CI) were calculated with Cox proportional hazards regression, adjusting for potential confounders.

Results: Preexisting SMI was associated with greater all-cause (HR = 1.36; 95%CI 1.18, 1.57) and cancer-specific (HR = 1.21; 95%CI 1.03, 1.44) mortality compared to those with no mental illnesses. No association was observed between preexisting depression and mortality. Among racial/ethnic subgroups, the association between SMI and all-cause mortality was observed among

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Declaration of competing interest

None.

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Credit author statement

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.socscimed.2020.113643.

non-Hispanic white (HR = 1.47; 95%CI 1.19, 1.83) and non-Hispanic Asian/Pacific Islander (HR = 2.59; 95% 1.15, 5.87) women. Additionally, mortality hazards were greatest among women with preexisting SMI that were postmenopausal (HR = 1.49; 95%CI 1.25, 1.78), obese (HR = 1.58; 95%CI 1.26, 1.98), and had documented tobacco use (HR = 1.42; 95%CI 1.13, 1.78).

Conclusion: Women with preexisting SMI prior to breast cancer diagnosis have an elevated mortality hazard and should be monitored and treated by a coordinated cross-functional clinical team.

Keywords

Medicaid; Cancer registry; Mental illness; Depression; Schizophrenia; Bipolar disorder; Cardiovascular; Breast cancer

1. Introduction

In the United States (U.S.), mental illnesses and breast cancer are highly prevalent diseases. Among U.S. women, approximately 22% are living with mental illnesses and 12% will be diagnosed with breast cancer at some point in their life (Howlader et al., 2018; Substance Abuse and Mental Health Services Administration, 2018). Individuals with mental illnesses have higher age-adjusted mortality compared to the general population. Epidemiological studies have also reported a reduction in life expectancy of nearly two decades among individuals with severe mental illnesses (SMI), which includes behavioral, emotional, or mental disorder that considerably interferes or hinders life activities (Hjorthøj et al., 2017; Saha et al., 2007). SMI includes bipolar disorder, schizophrenia, major depressive disorder, and other psychotic disorders, as well as their related spectrum disorder (Correll et al., 2017; Das-Munshi et al., 2017; Iglay et al., 2017a). In 2019, an estimated forty thousand women died from breast cancer, making it the second leading cause of cancer death among U.S. women (Howlader et al., 2018). Prior studies have documented that mortality due to cancer is greater among patients with SMI in comparison to patients without mental illnesses, however, findings for non-major depression has not been widely reported (Cunningham et al., 2015; Goodwin et al., 2004; Kanani et al., 2016; Liang et al., 2017; Nordentoft et al., 2013; Tran et al., 2009).

Evidence from epidemiological studies indicates that mental illnesses are associated with elevated cancer risk and poorer cancer outcomes compared with the general population (Kanani et al., 2016; Liang et al., 2017; Musuuza et al., 2013; Ribe et al., 2016). Literature has suggested this disparity can be attributed to lower utilization of preventative care (e.g. cancer screening), behavioral factors (e.g. higher smoking rates), greater likelihood of not adhering to or delaying cancer treatment, higher prevalence of cardiovascular- and metabolic-related comorbidities, and inadequate patient-physician interaction (Chochinov et al., 2009; Chou et al., 2016; Iglay et al., 2017b; Irwin et al., 2014; Jensen et al., 2016; Kisely et al., 2016; Rummel-Kluge et al., 2010; Seeman and González-Rodríguez, 2018; Thornicroft et al., 2007; Weinstein et al., 2016). However, differences in survival and cause of death by severity of mental illnesses among women diagnosed with breast cancer remains poorly understood.

In the U.S., cancer and cardiovascular-related mortality account for a large proportion of deaths, both in the general population and among patients diagnosed with breast cancer or mental illnesses (Correll et al., 2017; Kirkham et al., 2019; Troeschel et al., 2019; Weinstein et al., 2016). Previous studies that assessed the relationship between mental illnesses and cancer outcomes focused primarily on overall mortality (Dalton et al., 2007; Kanani et al., 2016; Ribe et al., 2016). Among the limited studies that examined cause-specific mortality, the majority assessed breast-cancer-specific mortality (Cunningham et al., 2015; Dalton et al., 2018; Goodwin et al., 2004; Iglay et al., 2017a). The impact mental illnesses have on cardiovascular mortality among patients with breast cancer has not been widely reported. However, a large-scale meta-analysis reported that patients with SMI had over an eighty percent higher risk of cardiovascular disease mortality compared with the general population (Correll et al., 2017). For this reason, patients with comorbid mental illnesses and breast cancer are potentially a highly vulnerable population.

In the U.S., Medicaid provides health insurance to economically disadvantaged individuals and is the single largest payer for mental health-related services (Centers for Medicare and Medicaid Services, n. d.). The present study investigated the association between preexisting mental illnesses and overall and cause-specific mortality among New York State (NYS) Medicaid-insured women diagnosed with breast cancer. More specifically, this study aimed to (1) examine the impact of preexisting SMI and depression on all-cause, cancer-specific, and cardiovascular-specific mortality among women diagnosed with breast cancer; and (2) evaluate differences in all-cause mortality hazard by demographic and clinical characteristics.

2. Methods

2.1. Study design and data sources

A retrospective cohort study was conducted utilizing linked data from the NYS Department of Health Cancer Registry and Medicaid. The Cancer Registry-Medicaid linkage allows for assessment of cancer stage, vital status, Medicaid enrollment, and medical care utilization. Detailed information on the Cancer Registry-Medicaid linkage methodology was previously published (Boscoe et al., 2011). Briefly, individuals were linked to Medicaid enrollment, eligibility, encounter, and claims data by a unique Medicaid identification number. Women were eligible for this study if they were ≤64 years of age at breast cancer diagnosis (as 65 years of age is largely when U.S. adults become Medicare-insured), had a known year of breast cancer diagnosis, and had histologically confirmed, first primary, invasive breast cancer (Surveillance, Epidemiology, and End Results [SEER] site recode 26,000) diagnosed between 2004 and 2016. In the event where day of breast cancer diagnosis was not recorded, we imputed the day that corresponds to the approximate middle of the month. Additionally, if month of diagnosis was missing, then June was imputed. The distribution of breast cancer date of diagnosis was similar between the middle of the month with all other days in that month, and for month of diagnosis we observed less than a 2% increased diagnosis for June compared with all other months. This indicates that missing day or month of diagnosis likely had a minimal impact. No women included in this study had both day and month of diagnosis missing. Women were excluded if they were not enrolled in Medicaid

before breast cancer diagnosis or were not enrolled for at least eleven out of twelve months following breast cancer diagnosis.

2.2. Study population and covariates

In the present study the primary focus for mental illnesses were depression and SMI. We defined mental illnesses based on the presence of at least three relevant claims for mental illnesses with at least one claim within three years before breast cancer diagnosis, as determined by International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9CM) or Tenth Revision (ICD-10) codes for depression or SMI. The Centers for Medicare and Medicaid Services General Equivalence Mappings were used to convert between ICD-9CM and ICD-10 (Roth, 2016). SMI included bipolar disorder, schizophrenia, major depressive disorder, and other psychotic disorders (Correll et al., 2017; Iglay et al., 2017a). The ICD-9CM and ICD-10 codes for depression and SMI are shown in Supplemental Table 1. If an individual was classified as having depression along with SMI, they were grouped as SMI.

Women with mental illnesses were excluded if they did not have at least three diagnosis claims for mental illnesses ($n = 1332$). We also excluded women who were diagnosed with mental illnesses after breast cancer, did not have at least one claim within three years before breast cancer diagnosis, or had a diagnosis for dementia or personality disorder before breast cancer diagnosis ($n = 3620$). We excluded women diagnosed with dementia or personality disorder before diagnosis of breast cancer as these disorders are distinct and different from other types of mental illnesses considered in this analysis (Das-Munshi et al., 2017; Iglay et al., 2017a; Kivipelto et al., 2018). Supplemental Figure 1 presents the inclusion criteria for the study cohort. Women were categorized as not having a mental illness if they had no ICD-9CM or ICD-10 codes indicating depression or SMI. Comorbidities were also determined by ICD-9CM and ICD-10 codes and included chronic kidney disease, type 2 diabetes mellitus, chronic obstructive pulmonary disease (COPD), obesity, coronary heart disease, stroke, and hypertension.

Demographic and other individual-level characteristics included age at diagnosis (continuous), race/ethnicity (Non-Hispanic Black, Non-Hispanic white, Non-Hispanic Asian/Pacific Islander, Non-Hispanic other, Hispanic), marital status at breast cancer diagnosis (Single, Married/Domestic partner, Divorced/Separated, Widowed, Unknown), documented tobacco use (yes/no), and date of death or date of last contact (continuous). Since there was no information on menopausal status, age was used as a proxy estimate (premenopausal <50 years of age and postmenopausal ≥50 years of age) (Morabia and Flandre, 1992; Phipps et al., 2010; Shao et al., 2018; Thomas et al., 2001).

Breast cancer characteristics included SEER Summary Stage (local, regional, distant, unknown), tumor grade (Grades I-IV, and unknown), and hormone receptor status (estrogen receptor [ER], progesterone receptor, [PR], and unknown). We categorized breast cancer hormone receptor status as hormone receptor positive (ER positive and/or PR positive) and hormone receptor negative (ER negative and PR negative).

Breast cancer treatment variables included hormone therapy, surgery, radiation, and chemotherapy, and were dichotomized (yes/no) for documented receipt of treatment. Sequence number was used to determine whether the patient's breast cancer was the only cancer diagnosis or the first of multiple reportable cancer diagnoses. Cause-specific mortality was determined by ICD-10 codes for cardiovascular (I00–I99) and cancer (C00–C97) mortality, while all-cause mortality was determined by vital status (alive or dead).

2.3. Statistical analysis

Continuous variables were reported as the mean ± standard deviation, and for categorical variables relative frequencies were calculated. Contingency tables and χ^2 tests were used to estimate the relationships between categorical variables. Diagnosis of a mental illness prior to breast cancer was dichotomized (yes/no) and identified by comparing breast cancer date of diagnosis with either first depression or SMI diagnosis claim date. Cox proportional hazards regression models were fit to assess the association between mental illnesses and all-cause and cause-specific mortality, while adjusting for confounders. Potential confounders were determined based on being associated with both mental illnesses and survival, and could not be an intervening variable between mental illnesses and survival. Backward selection was utilized to determine the structure of the final statistical model. Covariates were included in the model only if they changed the estimates for the association between mental illnesses and mortality by greater than 10%. Variables removed from the final model included estimated menopausal status, radiation treatment, tumor grade, hypertension, and subsequent cancers, and were consistent for all three outcomes. In our final model, we adjusted for age at breast cancer diagnosis, race/ethnicity, breast cancer date of diagnosis, marital status at diagnosis, obesity, chronic kidney disease, type 2 diabetes mellitus, stroke, hormone receptor status, chemotherapy, surgery, hormone therapy, SEER summary stage, and documented tobacco use.

Cox proportional hazards models were repeated with stratification by race/ethnicity, estimated menopausal status, obesity status, tobacco use, SEER summary stage, hormone receptor status, and subsequent cancer diagnosis to assess whether the relationship between mental illnesses and overall mortality differed across these study population characteristics. For overall survival, we performed likelihood ratio tests to compare models with and without an interaction term between the exposure (SMI or depression) and demographic or clinical characteristics (reported as P for interaction). Likelihood ratio tests were calculated by taking the difference between −2 log likelihoods for models with and without the interaction terms between SMI or depression and the covariate of interest, with the degrees of freedom equal to the difference between the number of parameters in the two models. Additionally, we created covariate-adjusted survival curves derived from adjusted hazard functions for overall and cause-specific survival, and compared via score test, which also approximates the log-rank test (Kim et al., 2006).

Though few covariates had missing data, we performed multiple imputation methodology to account for uncertainty due to missing values (percent missing values for all variables ranged from 0.7% to 8.1%) (Sidi and Harel, 2018; White et al., 2011). We created equations to impute the missing values and included all values in the final adjusted models (White

et al., 2011). Date of breast cancer diagnosis was used as the time point to estimate adjusted hazard ratios (HR) and 95% confidence intervals (95% CI), starting with diagnoses occurring on or after January 1, 2004 until the date of death or date of last contact for surviving patients. Women without recent follow-up who were not known to be deceased were considered alive as of the censoring date (December 31, 2016). All statistical tests were two-tailed and p-value ≤0.05 was considered statistically significant. Analyses were performed using SAS software version 9.4.

3. Results

3.1. Study population characteristics

This study included 10,444 women with breast cancer. Of these individuals, 3203 had a diagnosis of preexisting mental illnesses, with 1430 diagnosed with SMI and 1773 diagnosed with depression. Table 1 presents the distribution by demographic and clinical characteristics. There were differences in prevalence of mental illnesses across race/ethnicity, marital status at diagnosis, and estimated menopausal status categories (all *p*s < 0.0001). Additionally, women with SMI were on average older, more likely to be obese, and more likely to have documented tobacco use (all $p < 0.0001$). Most women were diagnosed with local stage disease. In addition, chronic kidney disease, COPD, coronary heart disease, type 2 diabetes mellitus, stroke, and hypertension were more common among women with mental illnesses compared to women without mental illnesses (all $p < 0.0001$) (Supplemental Table 2).

3.2. All-cause and cause-specific mortality

Table 2 presents the regression analyses for all-cause and cause-specific mortality by exposure status (no mental illnesses, SMI, or depression). After adjusting for potential confounders, women with SMI had an increased all-cause (HR = 1.36; 95% CI 1.18, 1.57) and cancer-specific (HR = 1.21; 95% CI 1.03, 1.44) mortality hazard, but was not associated with cardiovascular-specific mortality. When examining by preexisting depression, no associations were observed for all-cause and cause-specific mortality. Fig. 1 displays adjusted survival curves by presence of mental illnesses. The adjusted ten-year overall survival among women with SMI was ~3.8% lower than for women with depression (76.9%) and ~5.2% lower compared to women with no mental illnesses (78.3%). Supplemental Figures 2 and 3 present the adjusted survival curves for cancer-specific and cardiovascular-specific survival, respectively. The adjusted ten-year cancer-specific survival among women with SMI was ~2.1% and ~2.8% lower compared to women with depression (80.0%) and those with no mental illnesses (80.7%), respectively. Finally, the adjusted ten-year cardiovascular-specific survival among women with SMI was ~0.7% lower compared to women with depression (97.6%) and ~0.8% lower than women with no mental illnesses (97.7%).

3.3. All-cause mortality by demographic and clinical characteristics

Table 3 presents stratified multivariable-adjusted analyses assessing all-cause mortality by preexisting mental illnesses. Increased all-cause mortality hazard was observed for preexisting SMI versus no mental illnesses among non-Hispanic white (HR = 1.47; 95%

CI 1.19, 1.83) and non-Hispanic Asian/Pacific Islander (HR = 2.59; 95% CI 1.15, 5.87) populations, but was not statistically significant among non-Hispanic Black and Hispanic women ($P = 0.13$ for interaction). Additionally, the strongest associations were observed among postmenopausal women (HR = 1.49; 95% CI 1.25, 1.78; $P = 0.03$ for interaction), obese individuals (HR = 1.58; 95% CI 1.26, 1.98; $P = 0.13$ for interaction), and documented tobacco use (HR = 1.42; 95% CI 1.13,1.78; $P = 0.84$ for interaction). When examining associations by breast cancer characteristics, the greatest mortality hazard was observed for localized stage at diagnosis (HR = 1.53; 95% CI 1.19, 1.96; $P < 0.01$ for interaction) and hormone receptor-negative tumors (HR = 1.56; 95% CI 1.22, 1.99; $P = 0.24$ for interaction). Further, for subsequent diagnosis of one or more reportable neoplasms, only women with one lifetime primary malignancy had an elevated mortality hazard for SMI (HR = 1.43; 95% CI 1.22, 1.67; $P = 0.03$ for interaction).

We further examined demographic and clinical characteristics on all-cause mortality among women with preexisting depression. When examining by race/ethnicity we only observed elevated all-cause mortality hazard among non-Hispanic Black women with preexisting depression compared to non-Hispanic Black women with no mental illnesses (HR = 1.32; 95% CI 1.01, 1.73; $P = 0.84$ for interaction). Additionally, associated increased mortality hazard were observed for no documented tobacco use (HR = 1.20; 95% CI 1.00, 1.45; $P = 0.20$ for interaction) and one lifetime primary malignancy (HR = 1.18; 95% CI 1.00, 1.38; $p = 0.84$ for interaction).

4. Discussion

Medicaid-insured women with preexisting SMI at breast cancer diagnosis had an elevated all-cause mortality hazard compared to those without mental illnesses. This was also observable for cancer-specific mortality, where women with SMI had a 21% increased mortality hazards. Earlier studies reported elevated mortality among women with SMI diagnosed with breast cancer, aligning with our findings (Iglay et al., 2017a; Musuuza et al., 2013; Ribe et al., 2016). In a retrospective cohort study among women ≥68 years of age diagnosed with breast cancer, women with preexisting SMI had greater than a twofold increased overall mortality hazard compared to women without mental illnesses (Iglay et al., 2017a). A nationwide cohort study among women diagnosed with breast cancer reported that women with schizophrenia had greater overall mortality hazard than women without schizophrenia (Dalton et al., 2007). In analyses of cause-specific mortality, we also observed that preexisting SMI was associated with cancer mortality. However, limited prior studies have examined cause-specific mortality. Of these studies, the majority examined breast cancer-specific mortality, where results indicated either no significant association (Dalton et al., 2007; Iglay et al., 2017a) or a borderline statistically significant association (Cunningham et al., 2015; Dalton et al., 2018). The differences between the current results and some prior studies are potentially attributable to differences in study population characteristics such as age and socioeconomic status. For instance, the present study included nonelderly economically disadvantaged women while prior studies included either elderly women only, examined schizophrenia exclusively, or included women at all levels of income. Additionally, to the best of our knowledge, this is the first study to report cardiovascular-specific mortality among women with preexisting mental illnesses diagnosed

with breast cancer. We observed women with SMI diagnosed with breast cancer had a 38% increased cardiovascular-specific mortality, though the hazard ratio was not statistically significant. Our findings of elevated cardiovascular-specific mortality hazard were similar to prior literature including a meta-analysis that reported higher cardiovascular-related mortality among women with schizophrenia and other psychotic disorders compared with the general population, (Correll et al., 2017; Olfson et al., 2015).

We observed no statistically significant association between depression and mortality among women with breast cancer, contrasting with some previous epidemiological studies (Goodwin et al., 2004; Kanani et al., 2016). These differences are likely due to (1) differences in defining depression (i.e. grouping of major depression and non-major depression); (2) duration of preexisting depression; and (3) timing of depression in relation to breast cancer diagnosis (before or after breast cancer diagnosis). In a large prospective cohort study, women with newly developed depression (within three years) before breast cancer diagnosis had higher all-cause mortality compared to individuals without depression, while no association was observed for women with depression at study baseline (Liang et al., 2017). These findings suggest that the impact duration of preexisting depression on mortality among women with breast cancer may be influenced by ability to manage this mood disorder. Those with depression for longer periods may have better treatment strategies or established coping mechanisms than individuals newly diagnosed, where onset could have resulted from illness or changes in life circumstances, all potentially influencing physical health, changes in behavior (e.g. tobacco use, alcohol consumption), and breast cancer treatment adherence (Fluharty et al., 2017; Goodwin et al., 2004; Iglay et al., 2017b; Liang et al., 2017; Ménard et al., 2016).

In analyses stratified by demographic and clinical characteristics, we observed that the association between SMI and increased mortality hazard among women with breast cancer tended to be stronger in specific subgroups. When stratified by race/ethnicity, a statistically significant association between preexisting SMI and overall mortality was observed among non-Hispanic white women, aligning with previous findings of excess mortality among this group with SMI compared with the general population (Chang et al., 2010; Das-Munshi et al., 2017; Druss et al., 2011). We also observed elevated mortality hazard among non-Hispanic Asian/Pacific Islander women and though not statistically significant among Hispanic women. Previous literature on health outcomes among non-Hispanic Asian/Pacific Islander and Hispanic women with mental illnesses remains inconsistent, where studies suggest that the severity of psychiatric morbidity is influenced by a combination of country of birth and stress related to degree of social assimilation (Alarcón et al., 2016; Salas-Wright et al., 2015). Among women with preexisting depression, an increased mortality hazard was only observed among non-Hispanic Black women. Elevated mortality among this group might be explained by racial disparities in mental illness treatment, where prior studies reported that in the U.S, non-Hispanic Black adults with clinically diagnosed depression were more likely to be under-treated for depression compared to non-Hispanic white adults (Akincigil et al., 2012; Vyas et al., 2020). This disparity in treatment may contribute to lower cancer screening rates and treatment adherence, especially among this economically disadvantaged study population (Bickell et al., 2008; Daly and Olopade, 2015; Jannat-Khah et al., 2020; Liang et al., 2017; Vyas et al., 2020). In analyses stratified by estimated

menopausal status, we observed postmenopausal women with SMI had a 49% increased all-cause mortality hazard compared with women without mental illnesses. Menopause is the period when schizophrenia symptoms often worsen and become most resistant to treatment (McGregor et al., 2017; Seeman and González-Rodríguez, 2018), which is also when delusional disorders often begin (Seeman and González-Rodríguez, 2018). During this same time period, estrogen levels are declining, often requiring postmenopausal women to increase their dosage of antipsychotic medication to maintain control of symptoms (Crawford and DeLisi, 2016; McGregor et al., 2017; Searles et al., 2018). However, antipsychotic drugs and other SMI treatment may adversely interact with cancer therapy, and prior studies have reported that although alterations in the recommended treatment regimen for SMI often occur, these changes can contribute to poorer survival compared to individuals without mental illnesses (Crump et al., 2013; Seeman and González-Rodríguez, 2018; Weinstein et al., 2016). We also observed that although SMI was associated with increased mortality regardless of obesity status, the strongest association was observed among obese women. Previous studies have observed that the cardiac side-effects caused by some antipsychotics drugs may contribute to elevated mortality risk among obese compared with nonobese individuals (Howell et al., 2019), which may help to explain this association. Additionally, we observed that among women with documented tobacco use, SMI was associated with higher mortality hazard than those without mental illnesses. Prior studies documented that individuals with SMI have greater nicotine dependence, smoke more heavily, and have lower rates of smoking cessation than the general population (Tsoi et al., 2013). When examined by hormone receptor status, hormone receptor negative women with SMI had a substantially greater mortality hazard compared to hormone receptor negative women without mental illnesses. The elevated mortality hazard among women with SMI could be due to lower likelihood of adhering to tailored treatment (Goodwin et al., 2004; Iglay et al., 2017b; Johnson, 2012; Weinstein et al., 2016). In addition, we observed a relationship between preexisting SMI and depression on elevated mortality hazard among women with only one lifetime primary malignancy. No statistically significant associations were observed among women with two or more primary cancers, although power was limited by the small number of women with more than one malignant primary.

Increased mortality among women with preexisting SMI who are subsequently diagnosed with breast cancer can potentially be attributed to lower continuity of care than in the general population, or greater risk of healthcare system failures where the physician and patient may agree on specific cancer therapy, but care did not ensue (Bickell et al., 2008; Bickell and Young, 2001; Chou et al., 2016; Irwin et al., 2014). Women with mental illnesses may also be less inclined to utilize cancer screening programs thus contributing to challenges in early breast cancer detection (Chochinov et al., 2009; Chou et al, 2011, 2016; Jensen et al., 2016; Kisely et al., 2016). Previous studies documented that elevated mortality could be the result of individuals with mental illness being less likely to receive stage-appropriate treatment or more likely to delay initiating treatment, especially among those with SMI(Anuk et al., 2019; Goodwin et al., 2004; Haskins et al., 2019; Iglay et al., 2017a, 2017b; Johnson, 2012; Weinstein et al., 2016). Prior studies also reported that patients with mental illnesses have more comorbidities and greater likelihood of engaging more frequently in behavior that contributes to poor cancer survivorship (e.g. tobacco use)

than those without mental illnesses, as observed in the present study (Chou et al, 2011, 2016; Irwin et al., 2014). Poor patient-physician interaction is another potential contributor to poor cancer survivorship. Patients with mental illnesses often experience diagnostic overshadowing, where clinicians may attribute physical symptoms indicating cancer or an adverse reaction to cancer treatment as a manifestation of a mental disorder (Iglay et al., 2017a; Shefer et al., 2014; Thornicroft et al., 2007). Diagnostic overshadowing can lead to poor patient-physician interaction and misdiagnosis, ultimately discouraging patients with mental illnesses from seeking timely medical care (Chou et al., 2016; Shefer et al., 2014). Delays in initiating cancer treatment and nonadherence to treatment regimens can also occur as a result of mental disorders such as psychoses and/or cognitive dysfunction (Goodwin et al., 2004; Iglay et al., 2017a, 2017b; Johnson, 2012). Patients who delay initiating and/or are nonadherent to treatment may not perceive the importance of timely cancer diagnosis and treatment, contributing to poorer survival. Moreover, elevated cardiovascular-specific mortality hazard among women with SMI may not only be caused by their higher cardiometabolic disorder risk profile (e.g. obesity, smoking, sedentary lifestyle), but also antipsychotic medications prescribed for schizophrenia may have metabolic side effects that can contribute to cardiovascular-related death (Howell et al., 2019; Laursen et al., 2014; Rummel-Kluge et al., 2010).

4.1. Limitations and strengths

Although our study provides new insight on the relationship between preexisting mental illnesses and mortality among women with breast cancer, several limitations must be noted. First, we did not consider specifics of breast cancer treatments (i.e. type of chemotherapy), psychiatric medication, and other types of substance use (e.g. illicit drugs), which may have impacted mortality. Second, age was used as a proxy for menopausal status, and therefore we were unable to account for the potential effects of individual-level factors such as obesity and smoking on timing of menopause (Tao et al., 2015; Whitcomb et al., 2018). Third, there is a chance of under-adjusting due to missing information on potential behavioral confounding factors such as physical activity and dietary habits, all of which have been previously reported to influence mental health and cancer survivorship (Huang et al., 2018; Johnston et al., 2018; Picon-Ruiz et al., 2017). Fourth, the present study was unable to account for duration of SMI and depression, which has been shown in prior studies to potentially influence health outcomes (Liang et al., 2017). Fifth, the study did not account for length of time enrolled in Medicaid and continuity of enrollment before breast cancer diagnosis, which may influence quality of care and possibly cancer prognosis. This limitation may also impact the ability to accurately categorize mental illness status. Sixth, we were unable to account for human epidermal growth factor receptor 2 (HER2)/neu receptor status, which influences breast cancer treatment plan because a large proportion of women were missing this information, where those diagnosed at earlier years in the study were more likely to not have this reported. Seventh, we were unable to account for the influence functional impairment due to SMI has on daily life activities (i.e. ability to work, health seeking behavior) contributed to mortality. Finally, it may be that tobacco use was not consistently reported, resulting in misclassification.

Our study limitations are offset by notable strengths including a large, racially and ethnically diverse population enrolled in Medicaid, the largest sole payer for mental health services in NYS. This study utilized objective data potentially avoiding recall bias for comorbid conditions (e.g. type 2 diabetes mellitus). Additionally, obesity status was determined by clinical measurement instead of self-report, where individuals tend to overestimate height and underreport weight (Gorber et al., 2007). Finally, there is no gold standard for identification of mental illnesses through claims data. For this reason, we utilized a conservative approach for identification of mental illnesses (three relevant diagnosis claims for SMI or depression with at least one claim within three years before breast cancer diagnosis). By utilizing this approach, we lessen the probability of misdiagnosis of mental illnesses, thus providing greater certainty of a patient's SMI or depression diagnosis.

5. Conclusions

In conclusion, the present study suggests that Medicaid-insured women with preexisting SMI at breast cancer diagnosis have a greater mortality hazard than women without preexisting mental illnesses. These results highlight the importance of collaboration between oncologists, psychiatrists, and other health care providers to establish a coordinated care plan for breast cancer patients with preexisting SMI. Further research is needed on the optimal medical care model for integrating breast cancer treatment and SMI care.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data statement

Data from this study are unavailable as we do not have approval from the New York State Department of Health and other related governmental organizations to share data.

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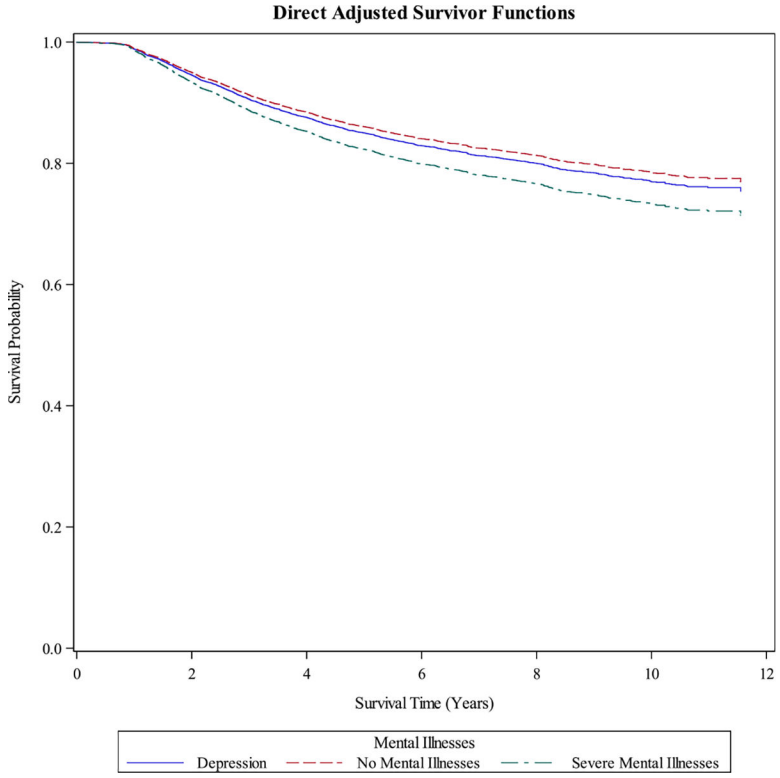

Fig. 1.

Adjusted survival curves for overall survival by preexisting mental disorder among Medicaid-insured women diagnosed with breast cancer in New York State, 2004–2016.

Note. Adjusted for age at breast cancer diagnosis, race/ethnicity, breast cancer date of diagnosis in days, marital status at diagnosis, obesity, chronic kidney disease, type 2 diabetes mellitus, stroke, hormone receptor status, chemotherapy, surgery, hormone therapy, SEER Summary Staging, and documented tobacco use.

Table 1

Demographic and health characteristics of 10,444 Medicaid-insured women diagnosed with breast cancer from 2004 to 2016 in New York State, by presence of mental illnesses.

Variables	Severe Mental Illnesses (*n* = 1430) *n* (%)	Depression (*n* = 1773) *n* (%)	No Preexisting Mental Illnesses (*n* = 7241) *n* (%)	Total (*n* = 10,444) *n* (%)	*P* value[b]
Age at diagnosis, mean years (SD)	52.8 (7.7)	50.9 (8.5)	50.4 (9.2)	50.8 (8.9)	<0.0001
Race/Ethnicity					<0.0001
Non-Hispanic Black	349 (24.4)	352 (19.9)	1845 (25.5)	2546 (24.4)	
Non-Hispanic White	659 (46.1)	810 (45.7)	2131 (29.4)	3600 (34.5)	
Non-Hispanic Asian/Pacific Islander	50 (3.4)	68 (3.8)	1396 (19.3)	1514 (14.5)	
Non-Hispanic Other	5 (0.4)	12 (0.7)	67 (0.9)	84 (0.8)	
Hispanic	367 (25.7)	531 (29.9)	1802 (24.9)	2700 (25.8)	<0.0001
Marital Status					
Single (never married)	731 (51.1)	757 (42.7)	2512 (34.7)	4000 (38.3)	
Married or Domestic Partner	262 (18.3)	466 (26.3)	3058 (42.2)	3786 (36.2)	
Divorced or Separated	312 (21.8)	406 (22.9)	1047 (14.5)	1765 (16.9)	
Widowed	75 (5.3)	99 (5.6)	365 (5.0)	539 (5.2)	
Unknown	50 (3.5)	45 (2.5)	259 (3.6)	354 (3.4)	
Estimated Menopausal Status[a]					<0.0001
Postmenopausal	961 (67.2)	1068 (60.2)	4025 (55.6)	6054 (58.0)	
Premenopausal	469 (32.8)	705 (39.8)	3216 (44.4)	4390 (42.0)	<0.0001
Documented Tobacco Use					
Yes	615 (43.0)	739 (41.7)	975 (13.5)	2329 (22.3)	
No	815 (57.0)	1034 (58.3)	6266 (86.5)	8115 (77.7)	
Obese					<0.0001
Yes	794 (55.5)	938 (52.9)	2053 (28.3)	3785 (36.2)	
No	636 (44.5)	835 (47.1)	5188 (71.7)	6659 (63.8)	
Hormone Therapy					<0.0001
Yes	617 (43.1)	865 (48.8)	3003 (41.4)	4485 (42.9)	
No	753 (52.7)	845 (47.7)	3936 (54.4)	5534 (53.0)	
Unknown	60 (4.2)	63 (3.5)	302 (4.2)	425 (4.1)	

Variables	Severe Mental Illnesses (*n* = 1430) *n* (%)	Depression (*n* = 1773) *n* (%)	No Preexisting Mental Illnesses (*n* = 7241) *n* (%)	Total (*n* = 10,444) *n* (%)	*P* value[b]
Surgery					0.0005
Yes	1289 (90.1)	1632 (92.0)	6520 (90.0)	9441 (90.4)	
No	127 (8.9)	134 (7.6)	670 (9.3)	931 (8.9)	
Unknown	14 (1.0)	7 (0.4)	51 (0.7)	72 (0.7)	0.3352
Radiation					
Yes	1331 (93.1)	1675 (94.5)	6772 (93.5)	9778 (93.6)	
No	31 (2.2)	31 (1.7)	126 (1.8)	188 (1.8)	
Unknown	68 (4.7)	67 (3.8)	343 (4.7)	478 (4.6)	
Chemotherapy					<0.0001
Yes	697 (48.7)	996 (56.2)	4181 (57.7)	5874 (56.2)	
No	709 (49.6)	740 (41.7)	2894 (40.0)	4343 (41.6)	
Unknown	24 (1.7)	37 (2.1)	166 (2.3)	227 (2.2)	
Hormone receptor status[c]					<0.0001
Hormone receptor positive	1070 (74.8)	1335 (75.3)	5038 (69.6)	7443 (71.3)	
Hormone receptor negative	274 (19.2)	340 (19.2)	1659 (22.9)	2273 (21.7)	
Unknown	86 (6.0)	98 (5.5)	544 (7.5)	728 (7.0)	
SEER Summary Staging					<0.0001
Localized	823 (57.6)	1034 (58.3)	3918 (54.1)	5775 (55.3)	
Regional	492 (34.4)	633 (35.7)	2734 (37.8)	3859 (37.0)	
Distant	75 (5.2)	83 (4.7)	462 (6.4)	620 (5.9)	
Unknown	40 (2.8)	23 (1.3)	127 (1.7)	190 (1.8)	<0.0001
Tumor Grade					
Grade I	220 (15.4)	251 (14.2)	761 (10.5)	1232 (11.8)	
Grade II	566 (39.6)	672 (37.9)	2814 (38.9)	4052 (38.8)	
Grade III	507 (35.5)	716 (40.4)	3058 (42.2)	4281 (41.0)	
Grade IV	2 (0.1)	4 (0.2)	27 (0.4)	33 (0.3)	
Unknown	135 (9.4)	130 (7.3)	581 (8.0)	846 (8.1)	
Subsequent cancers					0.0003
One lifetime primary malignancy	1253 (87.6)	1580 (89.1)	6582 (90.9)	9415 (90.1)	
First of two or more malignant primaries	177 (12.4)	193 (10.9)	659 (9.1)	1029 (9.9)	
Age at death, mean years (SD)	57.2 (8.2)	54.6 (9.4)	53.8 (10.0)	54.5 (9.7)	<0.0001

Variables	Severe Mental Illnesses (*n* = 1430) *n* (%)	Depression (*n* = 1773) *n* (%)	No Preexisting Mental Illnesses (*n* = 7241) *n* (%)	Total (*n* = 10,444) *n* (%)	*P* value[b]
Documented death	293 (20.5)	249 (14.0)	1053 (14.5)	1595 (15.3)	<0.0001

Note: p ≤ 0.05 was considered statistically significant.

[a]Estimated menopausal status defined as: Premenopausal <50 years of age and Postmenopausal ≥50 years of age.

[b]Significant difference between groups determined by X^2 test (all categorical variables) or *t*-test (age at diagnosis and age at death).

[c]Hormone receptor positive, estrogen receptor positive and/or progesterone receptor positive; Hormone receptor negative, estrogen receptor negative and progesterone receptor negative.

Table 2

Multivariable-adjusted analysis for preexisting mental illnesses in relation to mortality among 10,444 Medicaid-insured women diagnosed with breast cancer from 2004 to 2016 in New York State.

Variables	Presence of Mental Illnesses HR (95% CI)[a]		
	No Mental Illnesses	Severe Mental Illnesses	Depression
All-cause Mortality	Referent	1.36 (1.18, 1.57)	1.10 (0.95, 1.27)
Cancer Mortality	Referent	1.21 (1.03, 1.44)	1.05 (0.89, 1.25)
Cardiovascular Mortality	Referent	1.38 (0.90, 2.12)	1.06 (0.65, 1.72)

Abbreviations: HR, Hazard Ratio 95% CI, 95% confidence interval.

[a]Adjusted for age at breast cancer diagnosis, race/ethnicity, breast cancer date of diagnosis in days, marital status at diagnosis, obesity, chronic kidney disease, type 2 diabetes mellitus, stroke, hormone receptor status, chemotherapy, surgery, hormone therapy, SEER Summary Staging, and documented tobacco use.

Table 3

Multivariable-adjusted analysis assessing the impact of preexisting mental illnesses on all-cause mortality among 10,444 Medicaid-insured women with breast cancer by demographic and clinical subgroup characteristics in New York State, 2004–2016.

Variables	Presence of Mental Illnesses versus No Mental Illnesses[a]			
	Severe Mental Illnesses (*n* = 1430)		Depression (*n* = 1773)	
	HR (95%CI)	LR test *p*-value[c]	HR (95% CI)	LR test *p*-value[c]
Race/Ethnicity		0.13		0.84
Non-Hispanic White	1.47 (1.19, 1.83)		0.92 (0.73, 1.17)	
Non-Hispanic Black	1.24 (0.96, 1.60)		1.32 (1.01, 1.73)	
Non-Hispanic Asian/Pacific Islander	2.59 (1.15, 5.87)		1.03 (0.37, 2.88)	
Non-Hispanic Other	–		–	
Hispanic	1.19 (0.86,1.65)		1.13 (0.85, 1.51)	
Menopause Status[b]		0.03		0.09
Postmenopausal	1.49 (1.25, 1.78)		1.13 (0.93, 1.37)	
Premenopausal	1.20 (0.93, 1.53)		1.05 (0.83, 1.33)	
Obese		0.13		0.48
Yes	1.58 (1.26, 1.98)		1.21 (0.96, 1.53)	
No	1.25 (1.04, 1.51)		1.02 (0.84, 1.24)	
Documented Tobacco use		0.84		0.20
Yes	1.42 (1.13, 1.78)		0.99 (0.77, 1.26)	
No	1.31 (1.09, 1.57)		1.20 (1.00, 1.45)	
SEER Summary Staging		<0.01		0.01
Localized	1.53 (1.19, 1.96)		1.22 (0.94, 1.59)	
Regional	1.42 (1.15, 1.76)		1.17 (0.93, 1.46)	
Distant	1.12 (0.81, 1.54)		0.89 (0.65, 1.22)	
Hormone receptor status[c]		0.24		0.60
Hormone receptor positive	1.27 (1.07, 1.51)		1.06 (0.88, 1.27)	
Hormone receptor negative	1.56 (1.22, 1.99)		1.15 (0.89, 1.48)	
Subsequent cancers		0.03		0.84
One lifetime primary malignancy	1.43 (1.22, 1.67)		1.18 (1.00, 1.38)	
First of two or more malignant primaries	1.03 (0.72, 1.47)		0.78 (0.51, 1.17)	

Abbreviations: HR, Hazard Ratio; 95%CI, 95% confidence interval; LR test, likelihood ratio test; ER, estrogen receptor; PR, progesterone receptor.

Note: "—"indicates not calculable.

[a] Adjusted for age at breast cancer diagnosis, race/ethnicity, breast cancer date of diagnosis in days, marital status at diagnosis, obesity, chronic kidney disease, type 2 diabetes mellitus, stroke, hormone receptor status, chemotherapy, surgery, hormone therapy, SEER Summary Staging, and documented tobacco use.

[b] Estimated menopausal status defined as: Premenopausal <50 years of age and Postmenopausal ≥50 years of age.

[c] *p*-values from likelihood ratio test for each parameter group.