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Systematic review of healthcare costs related to mental health conditions among cancer survivors

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Abstract

Introduction: This systematic review examines healthcare costs associated with mental health conditions among cancer survivors in the United States.

Areas covered: Ten published studies were identified. Studies varied substantially in terms of population, mental health conditions examined, data collection methods, and type of cost reported. Cancer survivors with mental health conditions incurred significantly higher total medical costs and costs of most service types compared to cancer survivors without a mental health condition. Additionally, the total healthcare expenditure related to mental health was higher among cancer survivors compared with people without history of cancer.

Expert commentary: Mental health conditions are associated with increased healthcare costs among cancer survivors. Future examination of other components of economic burden, including patient out-of-pocket costs, nonmedical costs, such as transportation, childcare, and productivity losses for patients and their caregivers, will be important. Additionally, evaluation of economic burden by cancer site, stage at diagnosis, duration of survivorship, and treatment(s) will increase understanding of the overall impact of mental health conditions on cancer survivors and on the healthcare system.

Keywords

| Cancer surv | ivors; mental | health; cost; e | conomic burd | len; systematic | c review | |
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Declaration of interest

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

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1. Introduction

Nearly one-third of cancer survivors, estimated at 15.5 million in the United States [1], are diagnosed with mental health conditions [2,3]. The most commonly occurring mental health disorders among cancer survivors, including those in active treatment and long-term survivors, are major depression, generalized anxiety disorder, adjustment disorder, panic disorder, or post-traumatic stress disorder [4]. Mental health conditions can worsen the health burden faced by cancer survivors. For example, studies have shown that mental health conditions are associated with decreased immune function among cancer survivors, resulting in more frequent infections [5–7] and in some cases, lower adherence to cancer treatments [8,9] which may increase their subsequent healthcare costs. The coexistence of cancer and mental health conditions could lead to higher likelihood of having other comorbidities such as diabetes, cardiovascular disease, and musculoskeletal conditions via multiple biochemical pathways [10,11].

Addressing mental health needs of the growing population of cancer survivors can lead to improved quality of life, mental and physical health outcomes, and may decrease economic burden on the healthcare system [12]. The National Academies of Sciences, Engineering, and Medicine (NASEM) (formerly Institute of Medicine) and other important oncology stakeholders such as the National Comprehensive Cancer Network (NCCN) and American College of Surgeons Commission on Cancer (ACoS) COC recommend distress management, including screening of patient's psychosocial health, be routinely incorporated into oncology care in order to provide effective clinical surveillance and management of mental health concerns [13,14]. The 2008 Institute of Medicine report, 'Cancer care for the whole patient: Meeting psychosocial health needs' states that full understanding of an individual's psychosocial problems is an essential precursor to ensuring the receipt of necessary psychosocial health services, the provision of good-quality healthcare, and improved health-related quality of life [13,15,16]. Routine screening for mental health conditions among cancer survivors and early treatment can reduce health service utilization [17].

In the general population, mental health conditions are associated with substantial economic burden to the health system as well as to individuals and their families. Studies have reported that in the United States, mental health disorders were associated with nearly \$193 billion in lost earnings each year [18] and the annual health spending on management of mental illness in the United States has been estimated to be \$201 billion [19]. Mental health conditions are responsible for the highest hospital, long-term care and ambulatory care costs compared to other chronic conditions among cancer survivors [20]. As such, understanding the economic burden of mental health conditions in this population can strengthen the case for early intervention [21,22]. In this study, we systematically review the evidence on the magnitude of healthcare costs specifically related to mental health conditions among cancer survivors. We synthesize findings from published literature on economic burden of mental health conditions among cancer survivors in the United States (1990–2017) to understand the potential benefits of early detection and treatment of mental health conditions and identify gaps and avenues for future research in this area.

2. Methods

This systematic literature review was conducted and described in accordance with the PRISMA guidelines [23].

2.1. Search strategy

A systematic search for published, English-language literature on cancer survivors' healthcare costs related to mental health conditions was conducted from 1 January 1990 to 31 December 2017. This search period was chosen because cancer mortality first fell in the 1990–2000 decade, thereby highlighting the issue of cancer survivorship [24]. This decade also witnessed the proliferation of research in the field of psycho-oncology [24]. Searches were executed in the following bibliographic databases: Medline (Ovid), EMBASE (Ovid), SCOPUS, CINAHL, EconLit, and Cochrane Library. Our search used a combination of keywords and controlled vocabulary for several concepts including cancer survivor and/or cancer patient, economic burden and costs, and mental health disorders, which were adapted for each database search. The term 'cancer survivor' refers to a person who has been diagnosed with cancer, from the time of diagnosis throughout his or her life [25]. Hence, our definition of cancer survivor includes patients undergoing cancer treatment, i.e. treatment phase which generally lasts for one year after cancer diagnosis, those who are in the followup phase, and those who are in their last year of life (terminal phase) [26]. Specific search terms regarding mental health disorders were derived from the most prevalent mental health conditions among cancer survivors [27] and key articles [28,29]. These search terms were consistent with the terminology used in the Diagnostic and Statistical Manual 5th edition (DSM-V) [30]. Terms to identify economic burden, including healthcare costs/expenditures were adapted from a summary of healthcare cost data sources [31]. The exact search strategy used in each of the electronic databases is reported in the Appendix. In addition, a manual search of article references was used to discover publications not identified in the database searches. The search results and study selection process are illustrated in Figure 1.

2.2. Study selection

All references were uploaded in Covidence systematic review software (https://covidence.org) and duplicates were removed. Two reviewers (JK, JQ) conducted a dual review of the titles and abstracts. Articles were excluded if the abstract did not contain some indication of 'cost/expenditure,' 'mental health disorders' and 'cancer.' Studies conducted outside the United States were excluded because of differences in healthcare systems. Cost-effectiveness studies of interventions addressing mental health conditions among cancer survivors were included for full-text review.

Two reviewers (JK, JQ) conducted full-text reviews of all potentially relevant articles to further assess eligibility. The two reviewers agreed on more than 95% of all articles reviewed. Any disagreements between reviewers were resolved by consensus. Articles were included if they described costs or expenditures associated with mental health disorders among cancer survivors. Cost-effectiveness or cost-utility analysis of treatment interventions for mental health disorders were selected for extraction only if they reported the cost of usual care (in absence of any intervention) for cancer survivors with mental health

conditions. We excluded studies that examined cost-effectiveness of broader interventions to improve quality of life or psychosocial status among cancer survivors, but did not focus on treatment of specific mental health conditions. Articles were excluded if they did not report indirect costs such as work productivity in monetary terms. Further, articles were also excluded if the comparison group was other than cancer survivors without a mental health condition or individuals without a cancer history but with a mental health condition in order to ensure comparability of results across the studies. Trial protocols, pilot studies, reviews, overviews, commentaries, conference abstracts, and gray literature were also excluded during the selection process.

2.3. Data extraction

The following information was extracted using a standardized data collection form: author and publication year, data source and time period of the study, geographic setting, number of cancer survivors, comparison group, cancer site, phase of care, mental health condition/s reported, method for identifying mental health condition, prevalence of mental health condition/s among cancer survivors, other clinical and sociodemographic variables controlled for in the study (in matching or in multivariable analyses), type of cost estimates, including service type (e.g. inpatient, outpatient, office-visit, drug prescription) and source of payment (e.g. Medicare, Medicaid, Military, out-of-pocket), reference year for costs and time frame of costs, unadjusted and adjusted additional costs per person estimate for cancer survivors associated with mental health conditions. The additional costs due to mental health conditions were reported as total costs and by service type (e.g. inpatient, outpatient, and prescription drugs) and source of payment. Cost estimates were not adjusted to a single reference year, nor was a quantitative synthesis of cost estimates performed due to the heterogeneity in mental health conditions reported, cancer survivor populations, time periods of data collection, care settings, cost estimates reported, and other differences in methodology [32].

3. Results

3.1. Study characteristics

The characteristics of the 10 studies included in the systematic review are presented in Table 1. Although we searched for studies published during the past 28 years, all the eligible studies on healthcare costs related to mental health conditions among cancer survivors were published between 2010 and 2016. Three studies examined costs associated with substance use among cancer survivors [4,33,34], three studies examined depression [26,35,36], one study examined serious psychological distress (SPD) [28], and four studies examined a broader range of mental health conditions [4,29,37,38]. None of the studies offered a rationale or conceptual framework for examining the specific mental health conditions among cancer survivors. Prevalence of depression among cancer survivors ranged from 8.5% to 14%, SPD was estimated to be 8.2% and substance use ranged from 7.4% to 12.4% depending on the population studied. Prevalence of other mental health conditions (definitions vary by study and are presented in footnotes to Table 1) ranged from 3.9% to 26.7%.

Five out of the 10 studies included all cancer sites, three were restricted to prostate cancer [26,33,34] and two to breast cancer [4,38]. Most studies presented costs by phase of care. For most studies, the treatment phase referred to the first year after diagnosis whereas follow-up phase referred to the period after the initial year and the duration varied across studies [26,33]. However, in Zhang et al. [38], hospital admissions with breast cancer as the primary diagnosis were considered to be in the treatment phase whereas hospital admissions with breast cancer as a secondary diagnosis were considered to be in the follow-up phase [38]. Eight of the 10 studies presented total costs for all inpatient and out-patient care and prescription drugs, 3 out of these 8 studies presented a breakdown by service type. The remaining two studies presented inpatient costs only.

Five of the 10 studies used nationally representative data sets such as the Medical Expenditure Panel Survey (MEPS) and the Nationwide Inpatient Sample (NIS). Diagnoses of mental health conditions in studies using national surveys (e.g. MEPS) were based on self-reported diagnoses, mental health visits or prescription drugs. MEPS (three studies) and NIS (two studies) include information on out-of-pocket direct medical cost by the patient/ family along with third-party payer cost. MEPS includes costs by service type while NIS is restricted to inpatient costs only. Claims data provide payment information, whereas NIS provides information on hospital charges. Of the two studies that use NIS, Fox et al. [4] used converted charges into costs using the Agency for Healthcare Research and Quality (AHRQ) cost-to-charge ratio files, whereas Zhang et al. [38] did not convert charges to costs. Of the five studies that did not use nationally representative data, three studies used the Surveillance, Epidemiology and End Results (SEER) cancer registry data linked to Medicare claims data (SEER-Medicare), one study used cancer registry data from three states (Georgia, Illinois and Maine) linked to that states' Medicaid claims data [37], and the other study used Military Health System claims data [36]. Although five of these studies used claims data, none used commercial insurance claims data and were restricted to direct medical costs by third-party payer only.

3.2. Additional costs of mental health conditions among cancer survivors

Nine of the 10 studies included in the review compared costs for cancer survivors with mental health conditions to survivors without mental health conditions (cancer controls), whereas one study compared costs of mental health services spent by cancer survivors with costs of mental health services spent by individuals without a cancer history. The results of these studies are presented in Table 2. Costs are presented by the mental health condition studied, phase of care and service type. Results are presented as unadjusted and/or adjusted additional costs per person due to mental health conditions or associated with mental health conditions among cancer survivors. Six out of the 10 studies presented annual costs, one presented semiannual costs, two presented total costs over the period of the study, and one presented costs per inpatient encounter. Due to the heterogeneity in the data, no particular reference year was used for cost adjustment [39].

None of the studies identified in our review addressed other components of economic burden in cancer survivors, such as costs associated with patient time or transportation costs, nor did they address indirect costs, such as work productivity loss.

3.2.1. Unadjusted costs—Pan and Sambamoorthi [35] reported the additional annual unadjusted mean total costs for depression per cancer survivor compared to cancer survivors without depression as \$6,310 in 2009 dollars using MEPS data whereas Jeffery and Linton [36] reported it as \$8484 in 2009 dollars in their study of military health system beneficiaries. Fox et al. [4] reported the additional unadjusted mean inpatient costs for a psychiatric diagnosis among women in the treatment phase for breast cancer as \$1283 and for substance use as \$1711 in 2008 dollars compared to women in the treatment phase for breast cancer without mental health conditions. All of these estimated differences were significant at *p*-value < 0.05. Four other studies also presented unadjusted differences in cost between cancer survivors with and without mental health conditions. However, they did not test the statistical significance of these differences.

3.2.2. Adjusted costs—Regression analyses were conducted in four studies to derive the additional adjusted per person costs associated with mental health conditions among cancer survivors. Sociodemographic and clinical factors included in the multivariable regression analysis in these studies are presented in Table 1. In all four studies, mental health diagnoses were significantly associated with higher total costs among cancer survivors, ranging from \$2213 in 2009 dollars to \$11,009 in 2003 dollars.

Pan and Sambamoorthi [35] reported the additional adjusted per person total cost due to depression among cancer survivors as \$2,213 in 2009 dollars compared to cancer survivors without depression. They also reported that depression is associated with higher costs for inpatient services, prescription drugs and emergency department services but not for outpatient services. Han et al. [28] found that the adjusted additional per person total cost associated with SPD among cancer survivors was \$5,482 in 2010 dollars compared to cancer survivors without SPD. By service type, the study also found that cancer survivors with SPD had significantly higher office-based (\$1108), inpatient (\$1768), emergency department (\$144), and prescription (\$1033) expenditures. Among Medicaid-insured cancer survivors in the treatment phase, Subramanian et al. [37] reported higher semiannual total costs (\$11,009 in 2003 dollars), inpatient costs (\$6,883), prescription drugs costs (\$715), ambulatory service costs (\$1,198), and long-term care costs (\$2,214) associated with mental health diagnoses in the treatment phase compared to cancer survivors without mental health conditions in Georgia, Maine, and Illinois.

Among the two studies that reported inpatient costs only, Fox et al. [4] found that psychiatric diagnosis or substance use among breast cancer survivors is associated with higher inpatient costs per admission during treatment phase compared to cancer survivors without mental health conditions. Fox et al. [4] reported the adjusted additional per person inpatient cost among breast cancer survivors associated with substance use in the treatment phase is \$727 in 2008 dollars. Additional adjusted costs by service type are presented in Table 2.

3.3. Mental health costs of cancer survivors compared to individuals without a cancer history

Three of the 10 studies compared healthcare costs between cancer survivors with a mental health condition and individuals without a cancer history with a mental health condition.

Jayadevappa et al. [26] found higher unadjusted total costs among Medicare-insured cancer survivors with substance use disorders compared to those without a cancer history. Li et al. [29] found lower out-of-pocket cost and lower prescription drug cost in the treatment phase and lower total costs in the follow-up phase among young cancer survivors as compared to those without a cancer history. Li et al. [29] examined cost spent for mental health services specifically, while all the rest examined cost for all services by service type and/or payer type. Subramanian et al. [37] found higher adjusted total (\$4,299 in 2003 dollars), inpatient (\$4,235) and long-term care (\$1,325) semiannual costs, and lower adjusted ambulatory service (\$937) costs among Medicaid-insured cancer survivors with mental health conditions in the treatment phase compared to those without a cancer history.

4. Discussion

4.1. Summary of results

The objective of this study was to systematically review the evidence on healthcare costs related to mental health conditions among cancer survivors during the past 28 years. Despite the high prevalence of mental health conditions among cancer survivors and the associated health burden, very few studies have examined the costs associated with mental health among cancer survivors. The studies included in this systematic review were heterogeneous in terms of the cancer sites, data sources used, mental health conditions examined, and costs components reported. Thus, quantitative synthesis of the results from the reviewed literature was difficult to report. However, there are a number of common findings from the systematic review of literature in this study. Mental health conditions are associated with increased healthcare costs among cancer survivors across all service types (e.g. inpatient, outpatient, prescription drugs) and all phases of care. Total healthcare costs due to mental health conditions are lower in the treatment phase (i.e. within 1 year after cancer diagnosis) compared to the follow-up phase, whereas inpatient costs are higher in the treatment phase than in the follow-up phase [26,38]. Costs associated with mental health conditions remained significantly high even among patients who were in a terminal phase and died during the study period as a result of cancer-related complications [26].

Compared to individuals without a cancer history, individuals aged 18–64 years within 1 year of cancer diagnosis and with mental health conditions incurred higher total costs. Li et al. [29] also reported that cancer survivors aged 18–64 years diagnosed with cancer incurred lower prescription drug costs and lower out-of-pocket costs for mental health conditions in the treatment phase compared to individuals without cancer history. This could be due to cancer patients forgoing mental healthcare during the complex and intensive cancer treatment stage. Lower out-of-pocket costs could be a result of meeting maximum out-of-pocket spending limits due to cancer treatment. Inpatient costs were the largest contributor to increased total costs for mental health conditions among cancer survivors compared to individuals without a cancer history.

4.2. Implications

Our findings highlight the economic burden of mental health conditions among cancer survivors. These findings support the need for tailored interventions addressing early

detection and treatment of mental health conditions among cancer survivors. They highlight the paucity of studies at the intersection of cancer, mental health and cost of care, and underscore the need for continued efforts in evaluating the economic burden of cancer survivorship over time. The studies also draw attention to the patient populations and treatment phases wherein interventions are most likely to reduce costs associated with mental health.

4.3. Future research

There are significant gaps in literature related to healthcare expenditures associated with mental health conditions among cancer survivors. While most studies focus on breast and prostate cancers, studies examining lung, head and neck, and other cancers with possible associations to mental health conditions and resulting expenditures are lacking [40]. Subsequently, more research is needed to understand the burden of mental health conditions across cancer sites. None of the studies included in the review examine out-of-pocket costs separately for cancer survivors with mental health conditions compared to cancer survivors without mental health conditions. With increasing cost-sharing, cancer survivors have to bear a higher proportion of the economic burden of mental health conditions [41]. Cancer survivors were significantly more likely than those without a cancer history to forgo mental healthcare due to financial reasons [42]. In addition, increased financial burden among cancer survivors further exacerbates distress and other mental health conditions, and reduces quality of life [43]. Thus, it is vital to examine out-of-pocket costs for mental health conditions among the financially vulnerable cancer survivor populations [42].

Another significant gap in the literature is the lack of cost estimates specific to management of mental health conditions among cancer survivors rather than total healthcare costs incurred by cancer survivors with mental health conditions. In this review, only Li et al. [29] reported costs specific to treatment of mental health services. A study by Alwhaibi et al. [44] examined the costs of treating depression using psychotherapy, antidepressants, and a combination of both for cancer survivors diagnosed with depression. Compared to cancer survivors with depression who received no treatment, additional annual direct medical costs incurred by Medicare for those receiving antidepressants alone, psychotherapy alone, and a combination of both were \$3,871, \$8,694, and \$12,789, respectively [44]. It is important to examine the costs of treating specific mental health services among cancer survivors in order to provide better inputs for evaluation of interventions addressing management of mental health conditions among cancer survivors.

An important gap in the literature is the lack of studies reporting the indirect costs of mental health conditions among cancer survivors. Mental health conditions are associated with lost productivity [45,46]. Only one study by Cleeland et al. computed the percentage work impairment due to high emotional distress among cancer survivors [47]. However, they did not provide a monetary value of lost productivity. Productivity losses and limitations in employment may lead to reduced income. Most working-age cancer survivors who receive their health insurance through their employers, and limitations in ability to work may also jeopardize insurance coverage and increase risk of financial hardship. Thus, the indirect costs of mental health conditions may be substantial. Mortality and morbidity costs are other

indirect costs that are not well reported in literature on mental health conditions among cancer survivors. Mental health conditions have been associated with increased mortality risks through biochemical and behavioral mechanisms [48]. Additionally, certain mental health conditions among cancer survivors may be associated with higher suicidal ideation, and even suicide rates [49,50]. Examining these indirect costs of mortality related to mental health conditions among cancer survivors will result in a better understanding of the economic burden.

Early detection and indicated treatment of mental health conditions among cancer survivors can reduce their utilization of health services [17]. Despite the high economic burden and high out-of-pocket expenses associated with mental health conditions among cancer survivors, there are few studies that quantify the cost savings derived from early detection and treatment of mental health conditions, specifically among cancer survivors [51,52]. A systematic review of randomized controlled trials and nonrandomized studies by Mitchell provide evidence for the role of psychological distress screening in improving levels of distress, anxiety, and depression and improving overall quality of life [53]. The NCCN recommends routing distress screening for all cancer patients [54]. The ACoS COC has set psychosocial distress screening as a patient care standard since 2015. The standard requires ACoS COC-accredited cancer centers to integrate and monitor distress screening and, when needed, refer patients to psychosocial healthcare services [55]. Despite these recommendations, the prevalence of distress screening among cancer survivors remains low [54]. Literature is scarce on clinical effectiveness and cost-effectiveness of interventions aiming to improve distress screening rates, and of models of care that integrate psychological services with cancer, especially in the United States. There are a number of studies that examined cost-effectiveness of web-based or phone-based modalities for management of distress in this population [56,57]. However, there is a need to synthesize the evidence from these diverse studies in order to guide practice and policy decisions [58].

Other limitations in the literature reviewed include the inability to determine whether mental health conditions among cancer survivors were preexisting illnesses or were diagnosed during the course of cancer treatment or in the continuing phase. Additionally, although the reviewed studies include some socio-demographic determinants in their analyses, there is a need to incorporate social and economic determinants related to material hardship such as food and housing insecurity that may be associated with mental health [59]. Future research can address these limitations in the current literature.

5. Expert commentary

A recent report from NASEM stated that the purpose of healthcare is to 'continuously reduce the impact and burden of illness, injury, and disability, and improve health and functioning' [60]. In order to achieve this, there is a need to draw attention to and monitor patients' psychosocial concerns and provide services, when indicated, to enable better management of mental health concerns and any underlying illness. With a rapidly aging population, increasing number of cancer survivors, and rising prevalence of mental health conditions among cancer survivors, it will be important to provide appropriate and timely diagnostic and treatment services for mental health conditions among cancer survivors [13].

Given the substantial economic burden of mental health conditions among cancer survivors and the significant gaps in this literature, further research on different type of cancers, treatment modalities, and measures of economic burden (i.e. lost productivity, years of potential life lost, quality-adjusted and disability-adjusted life years) are needed. All of the studies in this systematic review were conducted using data prior to the implementation of the ACoS COC standards regarding distress management [55]. These standards may increase mental health service use related to diagnosis and treatment in the short term. It will be important to monitor how this early mental health service use offsets later costs related to mental health conditions among cancer survivors. Similarly, the studies may not reflect the full impact of anticipated changes in the health insurance landscape following passage of the Patient Protection and Affordable Care Act (ACA) given the differing implementation dates for various ACA provisions, including inclusion of mental and behavioral health services as an essential health benefit, annual and lifetime coverage limitations, the elimination of preexisting condition exclusions, the expansion of Medicaid, and the availability of costsharing subsidies [61]. The data collection period for these studies also predates the final regulations effective on 13 January 2014, regarding the implementation of the Mental Health Parity and Addiction Equity Act (MHPAEA) of 2008 which requires parity between mental health or substance use disorder benefits and medical/surgical benefits with respect to financial requirements and treatment limitations under group health plans and group and individual health insurance coverage [62]. Thus, economic studies that include longer term trends of economic burden among cancer survivors with mental health conditions are needed.

6. Five-year view

The NASEM's 2017 workshop on 'Long-Term Survivorship Care After Cancer Treatment: A Workshop,' examined the state of science and practice for early integration of psychosocial support in survivorship care and provided recommendations for the near future [63]. Proceedings from this meeting suggest that the next 5 years will likely see implementation of interventions focused on improving distress screening that raise patient and provider awareness. At the health system level, presence of mental health professionals in the cancer care team and holistic integration of cancer care across the cancer treatment spectrum will be imperative in the next 5 years. Additionally, it will be important to link distress management standards and related interventions to quality metrics and value-based payments in order to ensure accountability.

In addition to distress screening, there is a need for evaluation of evidence-based, low-cost psychosocial interventions such as self-management and e-Health for management of distress with resource-intensive interventions being reserved for those most in need [64]. Future research in this area over the next 5 years is vital. While interventions and best practices exist, increased evaluation, dissemination, and implementation is needed with cancers survivors from diverse socioeconomic and demographic background [58], and those who have increased needs based on severity of mental health presentation. Evaluating the cost-effectiveness of interventions will also be important next steps.

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Appendix

| Database searched | Search terms |
|--------------------------|---|
| Medline(Ovid) | (Cancer* or neoplasm*) and (survivor* or patient* or history) AND Cost* or economic* or financ* or expenditure* or income or out-of-pocket or (lost adj2 productivity) or (loss adj2 productivity) AND exp Mental Disorders/ or exp Mental Health/ or exp Mental Health Services/ or exp Depression/ or exp Depressive Disorder/ or exp Stress Disorders, Post-Traumatic/ or exp Stress, Psychological/ or Memory Disorders/ or Memory/ or Neurocognitive Disorders/ or Dementia/ or Delirium/ or Cognition Disorders/ or Cognitive Dysfunction/ or (mental adj2 (illness* or disorder* or problem* concerns or conditions)).mp. or ((psychological or psychosocial) adj1 (illness* or disorder* or distress or problem* or issues or concerns)).mp. or (emotional adj1 (illness* or disorder* or distress or problem* or issues or oncerns.mp. or mental health concerns.mp. or depressive symptoms.mp. or emotional concerns.mp. or PTSD.mp. or post-traumatic stress.mp. or psychological disability. mp. or Attention Deficit Hyperactivity Disorder.mp. or Attention Deficit Disorder.mp. or neurocognitive dysfunction.mp. or cognitive.mp. or neurocognitive.mp. or memory.mp. |
| Embase (Ovid) | Cancer survivor/ or cancer patient/ or ((Cancer* or neoplasm*) and (survivor* or patient* or history)).ti,ab. AND (Cost* or economic* or financ* or expenditure* or income or out-of-pocket or (lost adj2 productivity) or (loss adj2 productivity)).ti,ab. AND exp mental disease/ or exp mental health/ or exp mental health service/ or exp depression/ or exp posttraumatic stress disorder/ or exp stress/ or exp memory disorder/ or exp memory/ or exp 'disorders of higher cerebral function'/ or exp cognitive defect/ or ((mental adj2 (illness* or disorder* or problem* concerns or conditions)) or ((psychological or psychosocial) adj1 (illness* or disorder* or distress or problem* or issues or concerns)) or (emotional adj1 (illness* or disorder* or distress or problem* or issues)) or mental health concerns or depression or emotional concerns or PTSD or post-traumatic stress or psychological disability or Attention Deficit Hyperactivity Disorder or Attention Deficit Disorder or neurocognitive dysfunction or cognitive or neurocognitive or memory).ti,ab. |
| CINAHL (EBSCO) | ((Cancer* OR neoplasm*) AND (survivor* OR patient* OR history)) AND Cost* OR economic* OR financ* OR expenditure* OR income OR 'loss of productivity' OR 'lost productivity' OR 'productivity loss' OR 'loss in productivity' AND (MH 'Mental Disorders'+) OR (MH 'Mental Health') OR (MH "Mental Health Services) or (MH Depression) OR (MH Stress Disorders, Post-Traumatic) OR (MH 'Stress, Physiological') or (MH 'Memory Disorders') OR (MH Memory) OR (MH 'Cognition Disorders'+) OR (mental N3 (illness* OR disorder* OR problem* OR concerns OR conditions)) OR ((psychological OR psychosocial) N3 (illness* OR disorder* OR distress OR problem* OR issues OR concerns)) OR (emotional N3 (illness* OR disorder* OR distress OR problem* OR issues)) OR mental health concerns OR depression OR emotional concerns OR PTSD OR post-traumatic stress OR psychological disability OR Attention Deficit Hyperactivity Disorder OR Attention Deficit Disorder OR neurocognitive dysfunction OR cognitive OR neurocognitive OR memory |
| EconLit (EBSCO) | ((Cancer* OR neoplasm*) AND (survivor* OR patient* OR history)) AND Cost* OR economic* OR financ* OR expenditure* OR income OR 'loss of productivity' OR 'lost productivity' OR 'productivity loss' OR 'loss in productivity' AND 'mental health' OR 'mental illness' OR 'mental disorder' OR ((psychological OR psychosocial) AND (illness* OR disorder* OR distress OR problem* OR concerns OR issues)) OR ((emotional) AND (illness* OR disorder* OR distress OR problem* OR concerns OR issues)) OR depression OR 'depressive symptoms' OR PTSD OR posttraumatic stress OR 'psychological disability' OR Attention Deficit Hyperactivity Disorder OR Attention Deficit Disorder OR neurocognitive dysfunction OR cognitive OR neurocognitive OR memory |
| Cochrane Library (Wiley) | ((Cancer* OR neoplasm*) AND (survivor* OR patient* OR history)) AND Cost* OR economic* OR financ* OR expenditure* OR income OR 'loss of productivity' OR 'lost productivity' OR 'productivity loss' OR 'loss in productivity' AND [mh 'Mental Disorders'] OR [mh 'Mental Health'] OR [mh 'Mental Health Services'] OR [mh 'Depression'] OR [mh 'Stress, Psychological'] OR [mh 'Memory Disorders'] OR [mh 'Memory'] OR [mh 'Memory'] OR [mh 'Attention Deficit Disorder with Hyperactivity'] OR (mental health concerns or depressive symptoms or emotional concerns or PTSD or post-traumatic stress or psychological disability or Attention Deficit Hyperactivity Disorder or Attention Deficit Disorder or neurocognitive or memory or (mental near/3 (illness* or disorder* or problem* or distress or issues or concerns)) or (emotional near/3 (illness* or disorder* or problem* or distress |

| Database searched | Search terms |
|-------------------|--|
| | or issues or concerns)) or ((psychological or psychosocial) near/3 (illness* or disorder* or problem* or distress or issues or concerns))) |
| Scopus | (TITLE-ABS-KEY (((cancer* OR neoplasm*) AND (patient* OR history OR survivor*)) AND (cost* OR economic* OR financ* OR expenditure* OR income OR (loss W/2 productivity) OR (lost W/2 productivity)))) AND (((TITLE-ABS-KEY (mental AND health AND concerns OR depression AND symptoms OR emotional AND concerns OR ptsd OR post-traumatic AND stress OR psychological AND disability OR attention AND deficit AND hyperactivity AND disorder OR attention AND deficit AND disorder OR neurocognitive OR cognitive) OR TITLE-ABS-KEY ((mental W/2 (illness* OR disorder* OR problem* OR distress OR issues OR concerns)) OR (emotional W/2 (illness* OR disorder* OR problem* OR distress OR issues OR concerns))) OR TITLE-ABS-KEY (((psychological OR psychosocial) W/2 (illness* OR disorder* OR problem* OR distress OR issues OR concerns))))) OR (INDEXTERMS ('Mental Health' OR psychological OR psychosocial OR 'Mental Disorders' OR 'Mental Health' OR 'Mental Health Services' OR depression OR 'Depressive Disorder' OR 'Stress Disorders, Post-Traumatic' OR 'Stress, Psychological' OR 'Memory Disorders' OR 'Memory' OR 'Neurocognitive Disorders' OR 'Dementia' OR 'Delirium' OR 'Cognition Disorders' OR 'Cognitive Dysfunction'))) AND (not INDEX (medline) AND NOT INDEX (embase)) |

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Key issues

- Mental health conditions are associated with increased healthcare costs among cancer survivors across all phases of care and all service types.
- There is a lack of published studies that examine out-of-pocket costs, indirect productivity costs, and mortality costs for cancer survivors with mental health conditions compared to cancer survivors without mental health conditions.
- Early detection and treatment of mental health conditions, especially among cancer survivor populations at higher risk of mental health conditions, may lead to lower healthcare utilization and lower costs.

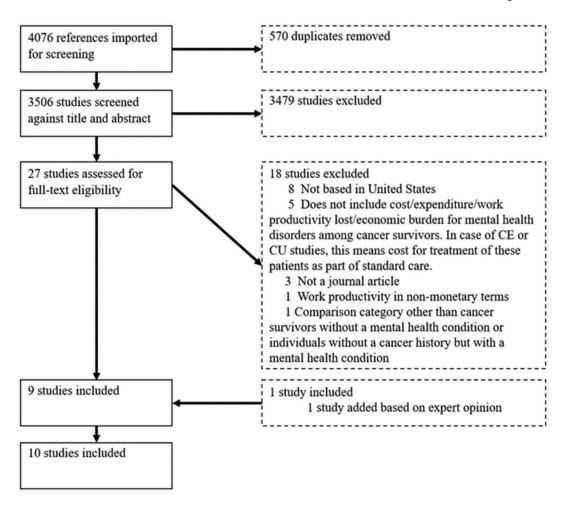


Figure 1. Flowchart illustrating the study selection

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Table 1.

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Study characteristics.

| First author, year | Data source/setting | Cancer survivor population | Comparison group | Cancer site | Mental health condition/s reported | Identification of mental health condition | Prevalence of condition among survivors | Clinical and sociodemographic control variables | Costs reported |
|--------------------|--|---|---|-------------------|---|---|--|--|---|
| Chhatre, 2014 | 2000–2009 SEER-Medicare/ multiple cities and states | 14,277 men 66 years | Cancer survivors without condition | Advanced Prostate | Substance use | ICD 9 diagnosis codes in claims data | 10.6% | Age, race, sex, marital status, mrality, area-level income, health insurance, cancer treatment, cancer stage, number of comorbid conditions | Direct medical costs paid by Medicare |
| Fox, 2013 | 2005–2008 Nationwide Inpatient Sample/National | 40,202 women 18 years undergoing nastectomy for breast cancer | Cancer survivors without condition | Breast | (a) Psychiatric diagnosis b (b) Substance use (alcohol or drug abuse) | Hospital Discharge Records | 4.5% | Age, race, sex, income, health insurance coverage, cancer treatment and complications, cancer stage, number of comorbid conditions, hospital factors | Direct medical costs paid by third party and patient |
| Han, 2015 | 2008–2010 MEPS/National | 4326 cancer survivors 18 years | a) Cancer survivors without condition (b) Individuals without a cancer history with and without condition | All sites | Serious psychological distress | Kessler 6 screener, self-report | 8.2% | Age, race, sex, marital status, poverty status, health insurance coverage, number of comorbid conditions, risk factors (BMI, smoking, physical activity) | Direct medical costs paid by third party and patient |
| Jayadevappa, 2012 | 1995–2003 SEER-Medicare/ multiple cities and states | 50,147 men 66 years | Cancer survivors without condition | Prostate Cancer | Depression | ICD 9 diagnosis codes in claims data | 8.5% | Age, race, sex, marital status, rurality, income, health insurance, cancer treatment, cancer stage and grade, number of comorbid conditions | Direct medical costs paid by Medicare |
| Jayadevappa, 2016 | 2000–2009 SEER-Medicare/ multiple cities and states | 8484 men between 66–74 years 5763 men 75 years | Cancer survivors without condition | Advanced Prostate | Substance use | ICD 9 diagnosis codes in claims data | Age 66–74: 12.4% 75 years: 7.4% | Age, race, sex, marital status, rurality, income, health insurance, cancer treatment, cancer stage, number of comorbid conditions | Direct medical costs paid by Medicare |
| Jeffery, 2012 | 2006–2010 Military data repository/active military | 11,074 military health beneficiary cancer survivors 18–64 years | Cancer survivors without condition | All sites | Depression | ICD 9 diagnosis codes in claims data | 12.6% | No covariates evaluated | Direct medical cost paid by Military Health System |
| Li, 2015 | 2008-2011 MEPS/National | 5944 cancer survivors 18 years | 76,887 Individuals without cancer history | All sites | Treated mental health conditions | Self-reported mental health service use | Reported by year since dx, and age group | Age, race, sex, marital status, education, income, health insurance coverage, usual source of care, years since diagnosis, number of comorbid conditions, risk factors (BMI, smoking) | Direct medical costs paid by third party and patient |
| Pan, 2015 | 2006–2009 MEPS/National | 4766 cancer survivors 21 years old | Cancer survivors without condition | All sites | Depression | Self-reported mental health service use | 14% | Age, race, sex, rurality, education, income, health insurance coverage, perceived physical and mental health, cardiovascular disease, anxiety, number of comorbid conditions, risk factors (BMI, smoking), year of observation | Direct medical costs paid by third party and patient |
| Subramanian, 2012 | 2000–2003 Medicaid claims linked cancer registry/Georgia, Maine, and Illinois only | 4628 cancer survivors between age 21 and 64 | Cancer survivors without condition | All sites | Mental health conditions d | ICD 9 diagnosis codes in Claims data | 14.3% | Age, race, sex, income, region, cancer site, number of comorbid conditions | Direct medical costs paid by Medicaid |
| Zhang, 2010 | 2006 Nationwide Inpatient Sample/ National | 16,161 breast cancer survivors 18 years old | Cancer survivors without condition | Breast | Mental health conditions | Hospital discharge records | 26.7% | Age, race, sex, perceived physical and mental health, cancer treatment, other comorbid conditions, admission type | Direct medical costs paid by third party and patient |

SEER: Surveillance, Epidemiology, and End Results; MEPS: Medical Expenditure Panel Survey; ICD: International Classification of Diseases; BMI: body mass index.

 $^{^{2}}$ ubstance use includes drug psychoses, alcohol dependence, and nondependent use of drugs

b Psychiatric diagnoses include major depression, generalized anxiety disorder, adjustment disorder, panic disorder, or post-traumatic stress disorder.

 $^{^{}C}$ Mental health conditions include mood disorders, anxiety disorders, psychotic disorders, substance use disorders, and sleep disorders.

dental health conditions include schizophrenic disorders, episodic mood disorders, delusional disorders, anxiety/personality disorders, and depressive disorders.

Rental health conditions include dementia, substance use, alcoholic and drug psychoses, delirium, schizophrenia, episodic mood disorders, paranoid states, other psychoses, generalized anxiety disorders, personality disorders, psychosexual disorders, depressive disorder, other adult onset mental conditions

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Table 2.

Additional per person expenditure associated with mental health conditions among cancer survivors.

| First author, year | | | | | Unadjusted | Adjusted additional | Cost time frame/ |
|-----------------------------|--------------------------------------|---|---------------------|-------------------------|------------------------------|-----------------------|--|
| | Condition | Comparator | Phase of care | Service type | costs in \$ | confidence intervals) | reference year |
| Chhatre, 2014 ^{ad} | Drug Psychoses | Cancer survivors without condition | All phases combined | Total | 32,309 | NA | Total costs over 6 years |
| | Alcohol Dependence Syndrome | | | | 21,075 | NA | |
| | Nondependent use of drugs | | | | 29,038 | NA | |
| Han, 2015 | Serious psychological distress (SPD) | Cancer survivors without condition | NA | Total | NA | 5482*(3379, 7584) | Annual/2010 |
| | | | | Office-based Outpatient | NA | 1108*(294, 1922) | |
| | | | | Hospital outpatient | NA | I | |
| | | | | Inpatient | NA | 1768 (545, 2291) | |
| | | | | Emergency Department | NA | 144*(58, 2291) | |
| | | | | Prescription drugs | NA | 1033*(441, 1605) | |
| Fox, 2013 ^d | Psychiatric diagnosis | Cancer survivors without condition | Treatment | Inpatient | 1284 * | , [*] | Cost per inpatient mastectomy encounter/2008 |
| | Substance use | | | | 1711* | 727 * | |
| Jeffery, 2012^d | Depression | Cancer survivors without condition | Follow-up | Total | * 8484 | NA | Annual/2009 |
| Li, 2015 ^{ad} | Mental health conditions | Individuals without a cancer history | Treatment | Total | Age 18–64: 73 Age 65: –39 | ı | Annual/2011 |
| | | | Follow-up | | Age 18–64: 224 Age 65: 28 | Age 18–64: –46* | |
| | | | Treatment | Out-of-pocket | Age 18–64: –13Age 65: –8 | Age 18–64: –23 * | |
| | | | Follow-up | | Age 18–64: 39 Age 65: 6 | ı | |

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| First author, year | Condition | Comparator | Phase of care | Service type | Unadjusted additional mean costs in \$ | Adjusted additional mean costs in \$ (95% confidence intervals) | Cost time frame/ reference year |
|----------------------------------|--------------------------|---|------------------|----------------------|--|---|------------------------------------|
| | | | Treatment | Mental health visit | Age 18–64: 74Age 65: –27 | I | |
| | | | Follow-up | | Age 18–64: 133 Age 65: 19 | | |
| | | | Treatment | Mental health drug | Age 18–64: –1 Age 65: –13 | Age 18–64: –52* | |
| | | | Follow-up | | Age 18–64: 91 Age 65: 8 | I | |
| Jayadevappa, 2012 ^{abc} | Depression | Cancer survivors without condition | Treatment | Total | 6,500 | I | Annual/2009 |
| | | | Follow-up year 1 | | 7,000 | | |
| | | | Follow-up year 2 | | 7,500 | | |
| | | | Terminal | | 10,000 | | |
| Pan, 2015 ^d | Depression | Cancer survivors without condition | NA | Total | 6310* | 2213 *C | Annual/2009 |
| | | | | Outpatient | *858 | I | |
| | | | | Prescription drugs | 2297* | 913 **C | |
| | | | | Inpatient | 2272* | 2,844 *C | |
| | | | | Emergency Department | 155* | 131 *C | |
| | | | | Other | 715* | 178 ** | |
| Subramanian, 2012 ^c | Mental health conditions | Cancer survivors without condition | Treatment | Total | 15,520 ^a | * * 11,009 | Semi-annual/2003 |
| | | | | Inpatient | NA | 6883 * | |
| | | | | Prescription drugs | | 715* | |
| | | | | Ambulatory services | | 1198* | |
| | | | | Long-term care | | 2214* | |

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| First author, year | Condition | Comparator | Phase of care | Service type | Unadjusted additional mean costs in \$ | Adjusted additional mean costs in \$ (95% confidence intervals) | Cost time frame/ reference year |
|--------------------|--------------------------|---|-------------------------------|---------------------|--|---|------------------------------------|
| | | Individuals without a cancer history | | Total | | , 4299 * | |
| | | | | Inpatient | | 4235* | |
| | | | | Prescription drugs | | I | |
| | | | | Ambulatory services | | -937 * | |
| | | | | Long-term care | | 1325 * | |
| Jayadevappa, 2016 | Substance use combined | Cancer survivors without condition | All phases combined Total | Total | Age 66–74: 29,395 Age 75: 21,915 | | Total costs over study period |
| | | Individuals without a cancer history | | | Age 66–74: 19,742 Age 75: 671 | | |
| Zhang, 2010^{ad} | Mental health conditions | Cancer survivors without condition | Treatment Follow-up Inpatient | Inpatient | 822 –1,274 | NA | Annual/2006 |

^{*} Statistically significant at p-value<0.05; – Not statistically significant; NA indicates values that are not available or missing.

 $^{^{\}it a}$ Statistical significance not tested in unadjusted analysis.

 $[^]b{\rm Approximate}$ values derived from Figure 2 of Jayadevappa et al. [26].

 $^{^{\}circ}_{c}$ 5% Confidence intervals or variance of the estimates are not reported in the study.

d We computed the estimates from these studies as difference between mean for the target group and the comparison group. Thus, 95% confidence intervals around these estimates were not available.