

Increased cancer-specific mortality in individuals developing mental disorders after cancer diagnosis: biomedical factors versus psychosocial support

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The role of mental health is gaining greater prominence in outcomes research; and increasingly, recent studies are investigating cancer-related outcomes (1,2), including cancer screening, stage at diagnosis, receipt of treatment, and survival, in the presence of comorbid mental conditions. Prior studies have documented excess cancer mortality in people with mental illness (3,4). However, most such studies have addressed pre-existing mental illness and how individuals with depression or other psychiatric conditions fare once they develop cancer. Less is known about the impact of mental disorders on cancer outcomes when mental disorders develop after cancer diagnosis.

In a recent article by Zhu *et al.* (5), the authors present findings from a study analyzing cancer-specific mortality in nearly 250,000 cancer patients identified from the cancer registry in Sweden, diagnosed with cancer during the years 2004–2009 and followed through 2010. They later used Swedish Patient Registry to identify patients who were diagnosed with mood, anxiety, or substance abuse disorders, based on the 10th Swedish revision of International Classification of Disease. To further classify patients with new-onset of mental disorders following cancer diagnosis, the authors relied on the first date of diagnosis of mental disorders relative to the date of cancer diagnosis.

The findings indicate that patients with first onset of mental disorders after cancer diagnosis are at increased risk for cancer-specific mortality. These differences persisted after adjusting for potential confounders, including patient demographics, educational attainment, cancer stage at diagnosis, number of close relatives, as well as for waiting-time for surgery.

This is a novel study that generates a number of hypotheses regarding the underlying mechanisms for the increased cancer-specific mortality in patients with first onset of mental disorders after cancer diagnosis. The authors propose different pathways, including treatment decisions that may be affected by the presence of mental illness and psychopharmacological treatment, which may mediate the association between mental conditions and cancer survival.

Additional analyses are needed to address the limitations of the study by Zhu *et al.* First, in terms of varying cancer treatment patterns relative to first-onset of mental disorders after cancer diagnosis, it appears that the only factor taken into account was waiting-time to surgery. The models do not adjust for stage-appropriate adjuvant or neo-adjuvant chemotherapy, radiation, or hormonal therapy. As a result, it is not possible to conclude whether these patients received standard treatment, and experienced worse survival

outcomes despite undergoing standard treatment. Second, while these patients were diagnosed with mood-, anxiety-, or substance abuse-related disorders, the study does not indicate whether they were treated for these conditions; and if so, what the treatment was, and whether it was adequate. Third, although the authors attempted to control for psychosocial support, they could only account for the number of close relatives. While this may be an important measure, it is deficient in its ability to assess the extent to which this variable may actually translate into an adequate measure of psychosocial support.

Mental illness may be associated with poor adherence to recommended treatment, which, in the case of cancer treatment, may be regimental, complex, and burdensome. These potential barriers are likely compounded by depression or other symptoms of psychiatric conditions. In addition, patients with mental illness may have difficulty recognizing, communicating, and/or self-managing treatment-related complications, which may also contribute to poor outcomes. Taken together patients with mental illness may not be able to derive optimal value from treatments aimed at improving survival.

The authors' explanation on potential psychopharmacological pathways deserves to be explored further. First, however, it is important to analyze, with high granularity, the association between first onset of mental disorders and poor cancer outcomes in patients with and without treatment for mental illness and/or cancer. Certainly, a growing body of literature associates mental conditions with stress-related biomarkers (6), perhaps compounding the inflammatory milieu seen with cancer. In fact, the association between stress and psychosocial factors with cancer incidence, survival, and mortality has been demonstrated previously (7). As importantly, however, the drug-drug interactions between antidepressants, anxiolytics, and other substances with cancer treatment modalities may moderate the association between cancer treatment and outcomes. These associations are understudied, and seldom accounted for in clinical practice or in research; as a result, little is known about whether and the extent to which outcomes are affected by these treatment modalities and related complications.

Cancer patients with mental illness, whether mental conditions were pre-existing or developed after cancer diagnosis, constitute a vulnerable subgroup of patients who may experience considerable barriers to timely and adequate care, as well as high rates of complications and poor outcomes. Detailed studies are warranted to elucidate

and target the biological and psychosocial factors associated with cancer and/or comorbidity-related outcomes in this patient population, as well as the provider- and system-level barriers to care. While we wait for scientific advances in the field, however, it is critically important for primary care, oncology care, and psychiatric care to be coordinated to help achieve optimal outcomes.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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