

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form ([see an example](#)) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below. Some articles will have been accepted based in part or entirely on reviews undertaken for other BMJ Group journals. These will be reproduced where possible.

ARTICLE DETAILS

TITLE (PROVISIONAL)	A Cohort Study on Mental Disorders, Stage of Cancer at Diagnosis and Subsequent Survival
AUTHORS	Chang, Chin-Kuo; Hayes, Richard; Broadbent, Matthew; Hotopf, Matthew; Davies, Elizabeth; Moller, Henrik; Stewart, Robert

VERSION 1 - REVIEW

REVIEWER	Elsebeth Stenager Department of Psychiatry, Odense The Psychiatry in The Region of Southern Denmark and Institute of Regional Health Service, The University of Southern Denmark
REVIEW RETURNED	15-Nov-2013

GENERAL COMMENTS	<p>This study is about a very interesting topic, about mental disorders and cancer.</p> <p>The paper is well written and relevant data sources and statistics are used.</p> <p>I have a few comments to the study: Abstract : OK Introduction: OK Results: In the presentation of the study sample it seems unclear how the numbers of participants decline from 43746 to 28477. It is explained in the discussion, but I think it will be relevant to explain the study sample and the missing data in this section.</p> <p>In the explanation of the sample of cancer cases the authors refer to table 1, and a number of p-values are given in the text. The statistics used and the p-values should be given in the table 1. Table 2 and 3 are OK. The discussion is well written and includes relevant topics.</p>
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REVIEWER	David Lawrence Telethon Institute for Child Health Research, The University of Western Australia, Australia
REVIEW RETURNED	04-Dec-2013

GENERAL COMMENTS	<p>This study set out to examine cancer outcomes in people with mental disorders, and whether outcomes are related to stage of cancer at diagnosis. I think this study has been well conducted and well described in this paper, and it will make a useful contribution to the literature as very few previous studies have been able to look at stage of cancer at diagnosis. There is now a substantial literature demonstrating worse cancer outcomes for people with pre-existing mental disorders, but it remains unclear what are the primary drivers</p>
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	<p>of these outcomes. Although mental illness is associated with higher rates of exposure to known carcinogens, such as smoking, studies looking at outcomes from diagnosis show consistently poorer survival for people with mental disorders. One hypothesis is that people with mental disorders have more advanced cancer at time of diagnosis. This study was able to address this hypothesis by examining stage of cancer at diagnosis.</p> <p>This study has a number of limitations including relatively low statistical power due to the size of the cohort and duration of follow-up. With an average duration of follow-up of 5 years or less there are relatively few deaths in cancer patients with history of treatment for mental disorders. It may be valuable to revisit these data in the future when a larger number of cases has had time to accumulate or to consider collaborations with other databases to expand the geographic coverage of the data sets. Again, presumably because of power issues, cancer stage has been treated as a binary indicator into early or late stage. With more data over time it may be possible to examine stage of diagnosis in more detail. I think the limitations of the present study are appropriately acknowledged in the paper, and the conclusions seem appropriately drawn given the limitations of the study.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer Name: Elsebeth Stenager

Institution and Country Department of Psychiatry, Odense

The Psychiatry in The Region of Southern Denmark and Institute of Regional Health Service, The University of Southern Denmark

This study is about a very interesting topic, about mental disorders and cancer. The paper is well written and relevant data sources and statistics are used. I have a few comments to the study:

Abstract : OK

Introduction: OK

Results: In the presentation of the study sample it seems unclear how the numbers of participant decline from 43746 to 28477. It is explained in the discussion, but I think it will be relevant to explain the study sample and the missing data in this section.

Response: A sentence with the exact number of subjects with missing cancer stage at diagnosis was added in the first section of Results.

In the explanation of the sample of cancer cases the authors refer to table 1, and a number of p-values are given in the text. The statistics used and the p- values should be given in the table 1.

Response: Because of the huge numbers of either group, all the p-values were extremely low. But, we still added a column to present the details in Table 1.

Table 2 and 3 are OK.

The discussion is well written on include relevant topics.

Response: Thanks!

Reviewer Name: David Lawrence

Institution and Country Telethon Institute for Child Health Research, The University of Western Australia, Australia

This study set out to examine cancer outcomes in people with mental disorders, and whether outcomes are related to stage of cancer at diagnosis. I think this study has been well conducted and well described in this paper, and it will make a useful contribution to the literature as very few previous studies have been able to look at stage of cancer at diagnosis. There is now a substantial literature demonstrating worse cancer outcomes for people with pre-existing mental disorders, but it remains unclear what are the primary drivers of these outcomes. Although mental illness is associated with higher rates of exposure to known carcinogens, such as smoking, studies looking at outcomes from diagnosis show consistently poorer survival for people with mental disorders. One hypothesis is that people with mental disorders have more advanced cancer at time of diagnosis. This study was able to address this hypothesis by examining stage of cancer at diagnosis.

Response: Thanks for your appreciation and encouragement!

This study has a number of limitations including relatively low statistical power due to the size of the cohort and duration of follow-up. With an average duration of follow-up of 5 years or less there are relatively few deaths in cancer patients with history of treatment for mental disorders. It may be valuable to revisit these data in the future when a larger number of cases has had time to accumulate or to consider collaborations with other databases to expand the geographic coverage of the data sets. Again, presumably because of power issues, cancer stage has been treated as a binary indicator into early or late stage. With more data over time it may be possible to examine stage of diagnosis in more detail. I think the limitations of the present study are appropriately acknowledged in the paper, and the conclusions seem appropriately drawn given the limitations of the study.

Response: We are currently in the process of updating the linkage, which will yield a more than double-sized group of people with mental disorder comorbid with cancer and longer follow-up periods. We are also seeking funding to support our further analysis work on the linkage. In near future, there will be more studies coming up from our team to address related issues for mental disorder and cancer.