



## King's Research Portal

DOI:

[10.1136/bmjopen-2013-004295](https://doi.org/10.1136/bmjopen-2013-004295)

*Document Version*

Publisher's PDF, also known as Version of record

[Link to publication record in King's Research Portal](#)

*Citation for published version (APA):*

Chang, C.-K., Hayes, R., Broadbent, M., Hotopf, M., Davies, E., Møller, H., & Stewart, R. (2014). A cohort study on mental disorders, stage of cancer at diagnosis and subsequent survival. *BMJ Open*, 4(1), Article e004295. <https://doi.org/10.1136/bmjopen-2013-004295>

### **Citing this paper**

Please note that where the full-text provided on King's Research Portal is the Author Accepted Manuscript or Post-Print version this may differ from the final Published version. If citing, it is advised that you check and use the publisher's definitive version for pagination, volume/issue, and date of publication details. And where the final published version is provided on the Research Portal, if citing you are again advised to check the publisher's website for any subsequent corrections.

### **General rights**

Copyright and moral rights for the publications made accessible in the Research Portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognize and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the Research Portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the Research Portal

### **Take down policy**

If you believe that this document breaches copyright please contact [librarypure@kcl.ac.uk](mailto:librarypure@kcl.ac.uk) providing details, and we will remove access to the work immediately and investigate your claim.

# BMJ Open A cohort study on mental disorders, stage of cancer at diagnosis and subsequent survival

Chin-Kuo Chang,<sup>1</sup> Richard D Hayes,<sup>1</sup> Matthew T M Broadbent,<sup>2</sup> Matthew Hotopf,<sup>1</sup> Elizabeth Davies,<sup>3</sup> Henrik Møller,<sup>3</sup> Robert Stewart<sup>1</sup>

**To cite:** Chang C-K, Hayes RD, Broadbent MTM, *et al*. A cohort study on mental disorders, stage of cancer at diagnosis and subsequent survival. *BMJ Open* 2014;**4**:e004295. doi:10.1136/bmjopen-2013-004295

► Prepublication history for this paper is available online. To view these files please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2013-004295>).

Received 21 October 2013  
Revised 5 December 2013  
Accepted 9 December 2013

## ABSTRACT

**Objectives:** To assess the stage at cancer diagnosis and survival after cancer diagnosis among people served by secondary mental health services, compared with other local people.

**Setting:** Using the anonymised linkage between a regional monopoly secondary mental health service provider in southeast London of four London boroughs, Croydon, Lambeth, Lewisham and Southwark, and a population-based cancer register, a historical cohort study was constructed.

**Participants:** A total of 28 477 cancer cases aged 15+ years with stage of cancer recorded at diagnosis were identified. Among these, 2206 participants had been previously assessed or treated in secondary mental healthcare before their cancer diagnosis and 125 for severe mental illness (schizophrenia, schizoaffective or bipolar disorders).

**Primary and secondary outcome measures:** Stage when cancer was diagnosed and all-cause mortality after cancer diagnosis among cancer cases registered in the geographical area of southeast London.

**Results:** Comparisons between people with and without specific psychiatric diagnosis in the same residence area for risks of advanced stage of cancer at diagnosis and general survival after cancer diagnosed were analysed using logistic and Cox models. No associations were found between specific mental disorder diagnoses and beyond local spread of cancer at presentation. However, people with severe mental disorders, depression, dementia and substance use disorders had significantly worse survival after cancer diagnosis, independent of cancer stage at diagnosis and other potential confounders.

**Conclusions:** Previous findings of associations between mental disorders and cancer mortality are more likely to be accounted for by differences in survival after cancer diagnosis rather than by delayed diagnosis.

## INTRODUCTION

Numerous studies have indicated a higher risk of all-cause mortality and shorter life expectancy for people with severe mental

## Strengths and limitations of this study

- Longitudinal study design with a data linkage between two case register systems in London, UK.
- Mortality information was retrieved from the national registry of death certificates in the UK.
- The completeness rate of cancer stage was about 65%, which is within the range reported by other cancer registries in England and did not differ for most of the mental disorder groups of research interest compared with the remaining population.
- Lack of lifestyle factors (smoking, drinking, diet, obesity and physical activities) for confounding control in survival analysis.
- Small numbers of cancer cases with some specific mental disorders did not permit restricting the sample for sensitivity analyses. Also, size of the linked sample also did not allow further analyses of individual cancer diagnoses.

illness (SMI), including schizophrenia, bipolar disorder, schizoaffective disorder and, sometimes, depressive disorders.<sup>1–8</sup> The profile of causes of death among people with SMI is not substantially different from that in general population, although some specific patterns of death have been suggested, differing by sex, age group and mental disorder diagnosis.<sup>3 5–7 9–13</sup> In recent decades, cardiovascular disease, stroke, respiratory diseases, suicide and cancer have remained the leading causes.<sup>3 5–7 9–13</sup>

A recent population-based study revealed that men with psychiatric admissions before cancer registration had a significantly worse survival, especially for those with depressive disorders, neurotic and adjustment disorders, and alcohol-related or other substance use disorders.<sup>14</sup> Results from three population-based cohort studies showed significantly increased cancer mortality among people with schizophrenia for both genders,<sup>5 9 15</sup> but some other studies reported that it occurred in men<sup>7 13 16 17</sup> or women only.<sup>18</sup>



CrossMark

For numbered affiliations see end of article.

## Correspondence to

Dr Chin-Kuo Chang;  
[chin-kuo.chang@kcl.ac.uk](mailto:chin-kuo.chang@kcl.ac.uk)

However, other studies found no association with cancer mortality for SMI as a whole or schizophrenia specifically<sup>7 13 16 17</sup> and even a reduced risk was reported in one study.<sup>6</sup> Depression has also been found to be associated with an increase in cancer mortality.<sup>18</sup> Studies of the incidence of cancer in people with SMI have principally focused on schizophrenia with varying results, including reduced total cancer incidence,<sup>19–25</sup> no difference<sup>26–29</sup> or increased risk.<sup>30</sup> A meta-analysis pooling eight studies concluded no association between schizophrenia and incidence of cancer.<sup>27</sup> A history of depression or alcohol-related or substance use disorders has been associated with increased cancer,<sup>31</sup> but inconsistent findings have been found for bipolar disorder,<sup>32 33</sup> dementia<sup>15 18 34</sup> and null for schizoaffective disorder.<sup>29</sup> Evidence on the role of mental disease as a comorbidity factor in cancer is, therefore, still far from conclusive, but tends to indicate cancer incidence that is either reduced or not different, and cancer mortality that is increased.<sup>32 33</sup>

Thinking of how to solve the puzzle shown on conflicting research results and effects of mental disorders to cancer prognosis, there are two key research questions to be answered. First, to what extent might the reduced recognition of early cancer symptoms in people with mental disorders influence the stage of cancer at diagnosis?<sup>33 35–37</sup> And, second, what is the role of mental disorders on mortality after cancer diagnosis if the issue of later presentation of cancer could be ruled out? Then, an influence of mental disorders on cancer mortality in the absence of a clear effect on underlying risk could be explained by differences in treatment access, response and adherence, as previously raised by Kisely *et al.*<sup>15 38</sup> Utilising a data linkage between a large secondary mental healthcare case register in southeast London and the regional cancer registry, we sought to investigate associations between mental disorder and disease stage at cancer diagnosis and subsequent survival.

## MATERIALS AND METHODS

### The South London and Maudsley NHS Foundation Trust Biomedical Research Centre Case Register

The South London and Maudsley NHS Foundation Trust (SLAM) Biomedical Research Centre (BRC) Case Register was used to provide data on mental disorders for the current study. SLAM is the near-monopoly provider of comprehensive secondary mental health services for a geographic catchment consisting of four London boroughs (Southwark, Lambeth, Lewisham and Croydon) with approximately 1.23 million residents. Clients' records for all the services provided by SLAM were electronised in 2006. In 2008, the Clinical Record Interactive Search (CRIS) system was developed as a platform for investigators to search and access full but anonymised clinical data from the fully electronic health records system in SLAM for research purposes. All people receiving SLAM care for psychiatric assessments

and/or treatment were included in the database. The demographic characteristics and clinical profiles of the Case Register population have been fully described elsewhere.<sup>39</sup>

### Thames Cancer Registry

At the time of the study, Thames Cancer Registry (TCR) was the largest of eight population-based cancer registries in England, covering a population of 12 million residents in London, Kent, Surrey and Sussex. Registration was initiated by pathology reports and clinical records from hospitals and information on death certificates were received from the National Health Service (NHS) Central Register through the Office of National Statistics in 1999. When cancer is recorded as the main or contributing cause of death in Part 1 section, the certificate is routinely sent to the regional cancer registry. Further information on demographic, clinical details and treatments received within the first 6 months after cancer diagnosis was retrieved from hospitals or hospital databases by trained data collection officers. A central regional database was maintained with data added continuously and robust data quality controls. To avoid double counting, information about new tumours was cross-checked against existing registered cases. Cancer registration and cancer surveillance take place in English registries under provisions of Section 251 of the Health and Social Care Act and this permission is reviewed annually. The TCR was assessed to be more than 95% complete in 2001–2007, and considered as of sufficient quality for cancer outcome analyses.<sup>40 41</sup>

### Anonymised process of data linkage

Data from CRIS and TCR for residents in the SLAM geographic catchment were linked using an anonymisation process by the Health Research Support Service (HRSS) Pilot Programme which was operated by the Department of Health as part of the NHS Research Capability Programme in the UK. Memoranda of Understanding were signed between SLAM and TCR through HRSS, which in turn designed and created an infrastructure to provide a safe and confidential platform for health research. With HRSS as the 'trusted third party', the linkage was performed using a series of identifiers including the NHS number, and was then irreversibly deidentified, replacing the NHS number with an encrypted HRSS identification (HRSS id). The initial sample selected for analysis comprised individuals on the TCR dataset within SLAM coverage area. Thus, a retrospective cohort study of people under the care of secondary mental health services could be performed.

### Covariates included

Mental disorder diagnoses were identified from two sources within CRIS: (1) a primary psychiatric diagnosis (Axis 1a) categorised by International Classification of Diseases (ICD)-10 code (a structured field, compulsory for completion by services, with a specific date in the

electronic clinical records system) and (2) a supplementary natural language processing application developed using General Architecture for Text Engineering (GATE) software which extracts text strings relating to a diagnosis statement in correspondence fields. The first diagnoses from either one or both sources were then categorised into the following groupings (ICD codes): dementia (F00–03), substance use disorders (F10–19), schizophrenia (F20), schizoaffective disorder (F25), bipolar disorder (F31), depressive disorders (F32–33), anxiety disorders (F40–42) and personality disorders (F60–61). SMI was defined as a diagnosis of schizophrenia (F20), schizoaffective disorder (F25) or bipolar disorder (F31). In the TCR data, tumour stage at presentation of cancer was routinely extracted from an individual's medical records and categorised as follows: 'local' (stage 1), 'extension beyond the organ of origin' (stage 2), 'regional lymph node involvement' (stage 3) and 'metastasis' (stage 4). Cases without sufficient information about disease stage were classified as 'not known'. Date of cancer diagnosis, date of birth, sex, type of cancer, primary care trust (geographic area) and ethnic group were also routinely collected in TCR and were used as covariates. In addition, the income domain of the index of multiple deprivations in 2007 was derived on the basis of the residential postcode.<sup>42</sup>

### Statistical analysis

All the cancer cases diagnosed in the period from 1999 to 2008 in residents of the catchment area of four London boroughs under SLAM service coverage were included in the current analyses. Through the linkage performed by HRSS, any cancer detected after a contact with SLAM was marked. If multiple tumours were registered in one person, only the first cancer onset was considered. Their primary psychiatric diagnosis given in SLAM services before the cancer was identified (if any) as the major exposure of interest in the current analyses. Stage of disease at cancer diagnosis was categorised into two groups: (1) early stage with no spread or only local extension beyond the organ of origin (localised stage) and (2) late stages with regional lymph node involvement or metastasis (advanced stage). This was treated as a binary dependent variable and was modelled against mental disorder diagnoses by logistic regressions. Cox regression models were then assembled to estimate the associations between mental disorder and survival after cancer diagnosis. The duration of follow-up was defined as the period from cancer diagnosis to the date of death (any cause) or the end of the follow-up period (12 June 2010), provided by TCR. Age at cancer diagnosis, gender, type of cancer, year of cancer diagnosis, primary care trust (geographic area), ethnic groups, deprivation score for income and stage at cancer diagnosis were treated as potential confounders, where appropriate. Area-level deprivation score for income was classified into quintiles, with the first quintile representing the most affluent areas and applied as the reference group

in modelling. Stata/IC V.12.1 software for Windows (Stata Corporation, 2011) was used for all the analyses.

## RESULTS

### The study sample

A total of 43 746 cancer cases were identified from TCR records. Among them, 15 166 participants (34.7%) had no information about their stage of cancer at diagnosis. No significant associations were found between psychiatric diagnosis and missing cancer stage data apart from a higher proportion of missing data in people with dementia (46.8%) compared with the remainder (35%). After the exclusion of people without confirmed cancer stage information and those younger than 15 years at cancer diagnosis (n=101), with missing date of birth (n=1) or date of cancer diagnosis (n=1), 28 477 cases (65.1%) remained and were included in our analyses. Among them, 55.3% were women. Up to the end of 2008, a total of 2206 of these cancer cases had received any SLAM service (ie, were present on the CRIS database), and 125 of these had received an SMI diagnosis prior to their cancer diagnosis.

### Factors associated with extent of disease at cancer diagnosis

Of the analysed sample of cancer cases, 64.2% (n=18 290) were diagnosed with localised stage of disease. Descriptive characteristics of the sample by stage at cancer diagnosis are presented in [table 1](#). Participants with advanced stage of cancer at diagnosis were older and more likely to be men (both p values <0.001), and there was significant variation by cancer type, year of diagnosis, primary care trust and ethnic group (all p values <0.001), although no clear linear trend for socioeconomic deprivation was evident (details not shown).

### Mental disorder and stage at cancer diagnosis

Associations between preceding mental disorders and stage at cancer diagnosis are summarised in [table 2](#). In summary, findings were null and there was no evidence of an association with any diagnostic group after adjustment for age, gender, type of cancer, year of cancer diagnosis, primary care trust, ethnicity and deprivation score for income.

### Mental disorder and survival after cancer diagnosis

Associations between mental disorders and survival after cancer diagnosis are summarised in [table 3](#). SMI as a whole (and schizophrenia and schizoaffective disorder individually), depression, dementia and substance use disorders were associated with worse survival after cancer diagnosis in fully adjusted models, with a relatively little attenuation following adjustment for stage at cancer diagnosis.

**Table 1** Descriptive statistics of patients with cancer in southeast London by stage at cancer presentation from 1999 to 2008

Variables	Number (%) / mean $\pm$ SD			p Value $\ddagger$
	All cases (N=43 454)*	Participants with stage at cancer diagnosis (N=28 477)		
		Localised stage (N=18 290)	Advanced stage (N=10 187)	
Age at cancer diagnosis (years)	63.31 $\pm$ 17.96	60.38 $\pm$ 19.15	66.80 $\pm$ 14.29	<0.01 $\ddagger$
Gender				<0.01 $\ddagger$
Female	23 242 (53.49)	10 257 (56.08)	5490 (53.89)	
Male	20 212 (46.51)	8033 (43.92)	4697 (46.11)	
Type of cancer				<0.01 $\ddagger$
Lung	5286 (12.16)	1724 (9.43)	2068 (20.30)	
Bladder	1170 (2.69)	636 (3.48)	111 (1.09)	
Breast	5943 (13.68)	2592 (14.17)	1833 (17.99)	
Skin	2189 (5.04)	1548 (8.46)	93 (0.91)	
Prostate	4975 (11.45)	2657 (14.53)	634 (6.22)	
Corpus uteri	804 (1.85)	485 (2.65)	121 (1.19)	
Colorectal	3979 (9.16)	1441 (7.88)	1531 (15.03)	
Others	19 108 (43.97)	7207 (39.40)	3796 (37.26)	
Ethnicity				<0.01 $\ddagger$
White	26 055 (59.96)	10 766 (58.86)	6797 (66.72)	
Black	5080 (11.69)	2293 (12.54)	1293 (12.69)	
East Asian	541 (1.24)	222 (1.21)	135 (1.33)	
South Asian	804 (1.85)	258 (1.41)	173 (1.70)	
Others/unknown/mixed	10 974 (25.25)	4751 (25.98)	1789 (17.56)	
Deprivation score (income)				<0.01 $\ddagger$
1st quintile	2465 (5.67)	709 (3.88)	417 (4.09)	
2nd quintile	3308 (7.61)	1098 (6.00)	629 (6.17)	
3rd quintile	6520 (15.00)	2844 (15.55)	1355 (13.30)	
4th quintile	14 114 (32.48)	6130 (33.52)	3308 (32.47)	
5th quintile	17 047 (39.23)	7509 (41.06)	4478 (43.96)	

\*Participants with demographic information.

 $\ddagger$ Independent t tests for continuous variables and  $\chi^2$  tests for categorical variables. $\ddagger$ Statistical significance.

## DISCUSSION

### Main findings

This linkage between a population-based cancer register and a near-monopoly secondary mental health service provider with a geographic catchment of approximately 1.23 million residents provided a sufficiently large sample for this investigation. The key findings were that people who had been diagnosed with specific mental disorders in the secondary mental health service were not more likely to have cancer with advanced stage at diagnosis, but that many of the mental disorder groups had worse subsequent survival. This latter finding was significant for SMI as a whole, and for schizophrenia and schizoaffective disorder individually, as well as for those with diagnoses of depression, dementia and substance use disorders prior to the cancer diagnosis. The stage of cancer at diagnosis in people with mental disorders did not explain their worse subsequent survival.

### Advantages and limitations

The study described benefited from the large size of the two data sources. The linkage allowed the longitudinal observation of a substantial number of cases with mental

disorder diagnoses who had subsequently developed cancer, and comparison group of the remaining people with cancer diagnoses from the same geographic catchment area. Ascertainment of vital status and deaths was achieved by linkage to death certificates provided electronically from the Office for National Statistics. Limitations include a fairly large proportion with missing data on cancer stage (34.7%). This completeness level is within the range reported by other English registries and represents the data available to the registration process. These levels have been improving with the receipt of electronic pathology data from hospitals. Importantly, the proportions with missing stage data did not differ for most of the mental disorder groups of primary interest compared with the remaining population (the only exception being dementia), and principal findings are therefore unlikely to have been biased by availability of stage information. The other issue was the lack of lifestyle factors for smoking, drinking, diet, obesity and physical activities in our dataset, which made further confounding control inapplicable. Another limitation was that some of the required data on mental disorders were drawn from years when there was less than

**Table 2** Associations between previous diagnosis received in secondary mental healthcare and stage at cancer diagnosis (N=28 477)

Variables	Cancer stage at diagnosis		Unadjusted OR for advanced cancer stage (95% CI)	Age- and gender-adjusted OR for advanced cancer stage (95% CI)	Fully adjusted OR for advanced cancer stage* (95% CI)
	Localised stage (N=18 290)	Advanced stage (N=10 187)			
SMI†					
No	18 208 (64.22)	10 144 (35.78)	Ref	Ref	Ref
Yes	82 (65.60)	43 (34.40)	0.94 (0.65 to 1.36)	1.01 (0.70 to 1.47)	0.94 (0.64 to 1.39)
Schizophrenia					
No	18 233 (64.24)	10 151 (35.76)	Ref	Ref	Ref
Yes	57 (61.29)	36 (38.71)	1.13 (0.75 to 1.72)	1.23 (0.81 to 1.88)	1.10 (0.71 to 1.71)
Bipolar disorder					
No	18 266 (64.21)	10 180 (35.79)	Ref	Ref	Ref
Yes	24 (77.42)	7 (22.58)	0.52 (0.22 to 1.22)	0.55 (0.24 to 1.30)	0.60 (0.25 to 1.42)
Schizoaffective disorder					
No	18 286 (64.22)	10 186 (35.78)	Ref	Ref	Ref
Yes	4 (80.0)	1 (20.0)	0.45 (0.05 to 4.02)	0.47 (0.05 to 4.38)	0.47 (0.04 to 4.95)
Depression					
No	18 184 (64.22)	10 129 (35.78)	Ref	Ref	Ref
Yes	106 (64.63)	58 (36.37)	0.98 (0.71 to 1.35)	0.91 (0.66 to 1.26)	0.90 (0.64 to 1.27)
Dementia					
No	18 229 (64.26)	10 137 (35.74)	Ref	Ref	Ref
Yes	61 (54.95)	50 (45.05)	1.47 (1.01 to 2.14)‡	1.00 (0.68 to 1.46)	1.23 (0.82 to 1.85)
Substance use disorders					
No	18 260 (64.23)	10 171 (35.77)	Ref	Ref	Ref
Yes	30 (65.22)	16 (34.78)	0.96 (0.52 to 1.76)	1.01 (0.55 to 1.87)	0.99 (0.52 to 1.89)
Anxiety disorders					
No	18 263 (64.22)	10 173 (35.78)	Ref	Ref	Ref
Yes	27 (65.85)	14 (34.14)	0.93 (0.49 to 1.78)	0.98 (0.51 to 1.89)	1.15 (0.58 to 2.28)
Personality disorders					
No	18 282 (64.24)	10 179 (35.76)	Ref	Ref	Ref
Yes	8 (50.00)	8 (50.00)	1.80 (0.67 to 4.79)	2.15 (0.80 to 5.76)	1.78 (0.65 to 4.88)

\*Adjust for age, gender, type of cancer, year of cancer diagnosis, primary care trust, ethnicity and deprivation score for income.

†SMI: schizophrenia, bipolar disorder or schizoaffective disorder.

‡Statistical significance.

SMI, severe mental illness.

full information, since electronic records became comprehensive across all SLAM services during 2006; however, the numbers of cases did not permit restricting the sample any further for sensitivity analyses. The size of the linked sample also did not permit analyses of individual cancer diagnoses. Besides, the significant finding of schizoaffective disorder for survival after cancer diagnosis in table 3 was based on five cases only.

### Comparisons with related studies

In the relatively scarce literature about potentially delayed cancer diagnoses among people with mental disorders, the most recent published study reported a significantly higher proportion of metastasis at cancer presentation for psychiatric patients compared with general population (7.1% vs 6.1%) in Western Australia, especially for the cancer of breast and lung.<sup>15</sup> A US study, linking Surveillance, Epidemiology and End Results data to Medicare, found that people without mental disorder were slightly more likely to have an

earlier detection of colon cancer than people who had any mental disorder (53.3% vs 49.7%), although it was partially contributed by higher proportion with unknown stage when colon cancer was diagnosed (6.2% vs 14.6%). The frequency of diagnosis at autopsy for colon cancer among people without mental disorder was also significantly lower than cases (1.1% vs 4.4%).<sup>35</sup> However, these two studies did not adjust for potential confounders in their analyses, especially for type of cancer.<sup>15 35</sup> Another study focusing on breast cancer with confounders adjusted found that a history of major depression was associated with a delayed diagnosis of breast cancer representing an almost 10-fold increased risk, but the opposite direction of association was found for phobia.<sup>43</sup> Although we should have sufficient statistical power to identify the differences, our null findings for people undergoing assessment and treatment in secondary mental health services made the issue about delayed diagnosis of cancer among people with mental illness still inconclusive. Although potential explanation

**Table 3** Crude and adjusted relative risks for the effect of pre-existing mental disorders on general mortality among patients with cancer in southeast London by Cox models (N=43 449)

Variables	HR (95% CI)		
	Age- and gender-adjusted	Model 1*	Model 2†
SMI‡			
No	Ref	Ref	Ref
Yes	1.53 (1.27 to 1.85)§	1.71 (1.44 to 2.06)§	1.74 (1.44 to 2.10)§
Schizophrenia			
No	Ref	Ref	Ref
Yes	1.71 (1.38 to 2.11)§	1.91 (1.55 to 2.37)§	1.90 (1.54 to 2.36)§
Bipolar disorder			
No	Ref	Ref	Ref
Yes	1.01 (0.66 to 1.55)	1.13 (0.74 to 1.73)	1.20 (0.78 to 1.85)
Schizo affective disorder			
No	Ref	Ref	Ref
Yes	3.22 (1.45 to 7.17)§	2.69 (1.21 to 5.98)§	2.33 (1.05 to 5.20)§
Depression			
No	Ref	Ref	Ref
Yes	1.22 (1.04 to 1.44)§	1.27 (1.07 to 1.49)§	1.30 (1.11 to 1.54)§
Dementia			
No	Ref	Ref	Ref
Yes	1.36 (1.17 to 1.58)§	1.65 (1.42 to 1.92)§	1.66 (1.43 to 1.94)§
Substance use disorders			
No	Ref	Ref	Ref
Yes	1.24 (0.89 to 1.72)	1.41 (1.02 to 1.96)§	1.42 (1.02 to 1.97)§
Anxiety disorders			
No	Ref	Ref	Ref
Yes	0.74 (0.50 to 1.10)	0.86 (0.58 to 1.30)	0.73 (0.49 to 1.10)
Personality disorders			
No	Ref	Ref	Ref
Yes	1.65 (0.94 to 2.91)	1.58 (0.90 to 2.79)	1.50 (0.85 to 2.64)

\*Model 1: adjusted for age, gender, type of cancer, year of cancer diagnosis, primary care trust, ethnicity and deprivation score for income.

†Model 2: adjusted for age, gender, type of cancer, year of cancer diagnosis, primary care trust, ethnicity, deprivation score for income and stage at cancer diagnosis.

‡SMI: schizophrenia, bipolar disorder or schizo affective disorder.

§Statistical significance.

SMI, severe mental illness.

about specific psychological characteristics of dispositional insensitivity to threat (if the relation really exists) was found to be associated with delayed help seeking for symptoms of rectal cancer,<sup>36</sup> further in-depth investigations on the effect of mental disorders to physical healthcare utilisations are needed.

On the issue of survival for people with mental disorders after cancer diagnosis, a previous study of a population-based male Swedish cohort with psychiatric admissions before cancer diagnosis by registration found significantly worse survival, especially for those who had had depressive disorders, neurotic and adjustment disorders, and alcohol-related or other substance use disorders.<sup>14</sup> With a similar study design, Kisely *et al*<sup>38</sup> identified a significantly elevated risk of cancer mortality for people with psychiatric disorder in Canada. Advanced analyses exploring the reasons for elevated all-cause mortality following cancer diagnosis were also reported for people with known mental disorders in Western Australia, finding a reduced likelihood of surgery after diagnosis of colorectal, breast and cervical

cancers in people with mental disorders and less radiotherapy or chemotherapy receipt.<sup>15</sup> The US linkage between Surveillance, Epidemiology and End Results data and Medicare found that receipt of colon cancer treatment (any treatment at all stages or chemotherapy at stage 3 only) was significantly lower for people with pre-existing any mental disorder, mood disorder, psychiatric disorder and dementia.<sup>35</sup> Our study provided additional support to the finding that, although the stage of diagnosis for cancer of people with mental illness was not more advanced, these people were still at higher risk of death compared with their counterparts without mental illness. The underlying reasons might differ by medical care system in countries. Further details about the treatment trajectories after cancer diagnosis for people with mental disorder are needed for advanced studies.

#### Implications and direction for future studies

The wider question about cancer risk and outcome in people with mental disorders has received considerable

attention over the years, although studies have principally investigated overall cancer-related mortality or cancer incidence. While findings about cancer screening uptake rates among people with SMI were inconsistent across and within countries,<sup>44</sup> one possible reason for reasonably consistent raised cancer-related mortality in people with mental disorders but inconsistent evidence for raised cancer incidence is that the mortality is explained by delays in presentation rather than increased risk. However, we found no evidence that prior mental disorder was associated with more advanced stage of cancer at diagnosis, a measure of delay in presentation, which might be because that, in the UK, since 2003, general practitioners have been incentivised under the guide of Quality and Outcomes Framework<sup>45</sup> to offer regular physical health reviews to people with long-term mental health problems, including preventative cancer screening appropriate to age and gender since 2006.

Instead, consistent with other findings,<sup>14 15 35 38</sup> we found an association with worse survival after cancer diagnosis that was not explained by stage at presentation. This suggests that effects of mental disorder on cancer mortality primarily exert themselves after the diagnosis. Causal pathways might include reduced access to medical treatment and care, differing decisions about or tolerance of intensive regimes, and the influence of other health problems or drug effects on survival. Also, there might be differences between cancers on the impact to survival for early diagnosis, but there were insufficient data to analyse such differences among types of cancer. Clearly, the components of such disadvantage require further evaluation. A greater understanding is needed on the levels of utilisation of healthcare services and potential barriers to this among people with mental illness, including the extent to which this is present across individual cancer diagnoses and to which it is accounted for by the specific symptoms of the mental disorders themselves, by accompanying social disadvantage, or potentially by stigma. Also worthy of further evaluation is the potential impact that mental healthcare could have on improving physical health and other indirect influences of mental disorders on adverse health outcomes.

#### Author affiliations

<sup>1</sup>King's College London (Institute of Psychiatry), London, UK

<sup>2</sup>South London and Maudsley NHS Foundation Trust, London, UK

<sup>3</sup>King's College London (Section of Cancer Epidemiology and Population Health), London, UK

**Contributors** All the authors were involved in (1) substantial contributions to conception and design, acquisition of the data or analysis and interpretation of the data; (2) drafting the article or revising it critically for important intellectual content and (3) final approval of the version to be published.

**Funding** This research was supported by the Biomedical Research Nucleus data management and informatics facility at South London and Maudsley NHS Foundation Trust, which is funded by the National Institute for Health Research (NIHR) Mental Health Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King's College London and a joint

infrastructure grant from Guy's and St Thomas' Charity and the Maudsley Charity. The Thames Cancer Registry, King's College London, receives funding from the Department of Health.

**Competing interests** C-KC, RDH, MTMB, MH and RS are partly funded by the NIHR Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King's College London.

**Patient consent** Obtained.

**Ethics approval** Ethical approval as an anonymised data resource for secondary analyses was received from Oxfordshire REC C in 2008 (reference number 08/H0606/71).

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Data sharing statement** We declare that we are willing to share our data for the purpose of collaborations to investigators in related academic fields.

**Open Access** This is an Open Access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 3.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/3.0/>

#### REFERENCES

1. Chang CK, Hayes RD, Broadbent M, *et al.* All-cause mortality among people with serious mental illness (SMI), substance use disorders, and depressive disorders in southeast London: a cohort study. *BMC Psychiatry* 2010;10:77.
2. Chang CK, Hayes RD, Perera G, *et al.* Life expectancy at birth for people with serious mental illness and other major disorders from a secondary mental health care case register in London. *PLoS ONE* 2011;6:e19590.
3. Laursen TM, Munk-Olsen T, Nordentoft M, *et al.* Increased mortality among patients admitted with major psychiatric disorders: a register-based study comparing mortality in unipolar depressive disorder, bipolar affective disorder, schizoaffective disorder, and schizophrenia. *J Clin Psychiatry* 2007;68:899–907.
4. Piatt EE, Munetz MR, Ritter C. An examination of premature mortality among decedents with serious mental illness and those in the general population. *Psychiatr Serv* 2010;61:663–8.
5. Brown S, Inskip H, Barraclough B. Causes of the excess mortality of schizophrenia. *Br J Psychiatry* 2000;177:212–17.
6. Dembling BP, Chen DT, Vachon L. Life expectancy and causes of death in a population treated for serious mental illness. *Psychiatr Serv* 1999;50:1036–42.
7. Kiviniemi M, Suvisaari J, Pirkola S, *et al.* Regional differences in five-year mortality after a first episode of schizophrenia in Finland. *Psychiatr Serv* 2010;61:272–9.
8. Saha S, Chant D, McGrath J. A systematic review of mortality in schizophrenia: is the differential mortality gap worsening over time? *Arch Gen Psychiatry* 2007;64:1123–31.
9. Brown S. Excess mortality of schizophrenia. A meta-analysis. *Br J Psychiatry* 1997;171:502–8.
10. Hoang U, Stewart R, Goldacre MJ. Mortality after hospital discharge for people with schizophrenia or bipolar disorder: retrospective study of linked English hospital episode statistics, 1999–2006. *BMJ* 2011;343:d5422.
11. Viron MJ, Stern TA. The impact of serious mental illness on health and healthcare. *Psychosomatics* 2010;51:458–65.
12. Weiner M, Warren L, Fiedorowicz JG. Cardiovascular morbidity and mortality in bipolar disorder. *Ann Clin Psychiatry* 2011;23:40–7.
13. Brown S, Kim M, Mitchell C, *et al.* Twenty-five year mortality of a community cohort with schizophrenia. *Br J Psychiatry* 2010;196:116–21.
14. Batty GD, Whitley E, Gale CR, *et al.* Impact of mental health problems on case fatality in male cancer patients. *Br J Cancer* 2012;106:1842–5.
15. Kisely S, Crowe E, Lawrence D. Cancer-related mortality in people with mental illness. *JAMA Psychiatry* 2012;70:209–17.
16. Saku M, Tokudome S, Ikeda M, *et al.* Mortality in psychiatric patients, with a specific focus on cancer mortality associated with schizophrenia. *Int J Epidemiol* 1995;24:366–72.
17. Osborn DP, Levy G, Nazareth I, *et al.* Relative risk of cardiovascular and cancer mortality in people with severe mental illness from the United Kingdom's General Practice Research Database. *Arch Gen Psychiatry* 2007;64:242–9.



18. Lawrence D, Holman CD, Jablensky AV, *et al*. Excess cancer mortality in Western Australian psychiatric patients due to higher case fatality rates. *Acta Psychiatr Scand* 2000;101:382–8.
19. Pinquart M, Duberstein PR. Depression and cancer mortality: a meta-analysis. *Psychol Med* 2010;40:1797–810.
20. Barak Y, Achiron A, Mandel M, *et al*. Reduced cancer incidence among patients with schizophrenia. *Cancer* 2005;104:2817–21.
21. Barak Y, Levy T, Achiron A, *et al*. Breast cancer in women suffering from serious mental illness. *Schizophr Res* 2008;102:249–53.
22. Chou FH, Tsai KY, Su CY, *et al*. The incidence and relative risk factors for developing cancer among patients with schizophrenia: a nine-year follow-up study. *Schizophr Res* 2011;129:97–103.
23. Cohen M, Dembling B, Schorling J. The association between schizophrenia and cancer: a population-based mortality study. *Schizophr Res* 2002;57:139–46.
24. Grinshpoon A, Barchana M, Ponizovsky A, *et al*. Cancer in schizophrenia: is the risk higher or lower? *Schizophr Res* 2005;73:333–41.
25. Mortensen PB. The occurrence of cancer in first admitted schizophrenic patients. *Schizophr Res* 1994;12:185–94.
26. Goldacre MJ, Kurina LM, Wotton CJ, *et al*. Schizophrenia and cancer: an epidemiological study. *Br J Psychiatry* 2005;187:334–8.
27. Catts VS, Catts SV, O'Toole BI, *et al*. Cancer incidence in patients with schizophrenia and their first-degree relatives—a meta-analysis. *Acta Psychiatr Scand* 2008;117:323–36.
28. Levav I, Lipshitz I, Novikov I, *et al*. Cancer risk among parents and siblings of patients with schizophrenia. *Br J Psychiatry* 2007;190:156–61.
29. Levav I, Kohn R, Barchana M, *et al*. The risk for cancer among patients with schizoaffective disorders. *J Affect Disord* 2009;114:316–20.
30. Lichtermann D, Ekelund J, Pukkala E, *et al*. Incidence of cancer among persons with schizophrenia and their relatives. *Arch Gen Psychiatry* 2001;58:573–8.
31. Gross AL, Gallo JJ, Eaton WW. Depression and cancer risk: 24 years of follow-up of the Baltimore Epidemiologic Catchment Area sample. *Cancer Causes Control* 2010;21:191–9.
32. Bushe CJ, Hodgson R. Schizophrenia and cancer: in 2010 do we understand the connection? *Can J Psychiatry* 2010;55:761–7.
33. Hodgson R, Wildgust HJ, Bushe CJ. Cancer and schizophrenia: is there a paradox? *J Psychopharmacol* 2010;24(4 Suppl):51–60.
34. Attner B, Lithman T, Noreen D, *et al*. Low cancer rates among patients with dementia in a population-based register study in Sweden. *Dement Geriatr Cogn Disord* 2010;30:39–42.
35. Baillargeon J, Kuo YF, Lin YL, *et al*. Effect of mental disorders on diagnosis, treatment, and survival of older adults with colon cancer. *J Am Geriatr Soc* 2011;59:1268–73.
36. Ristvedt SL, Trinkaus KM. Psychological factors related to delay in consultation for cancer symptoms. *Psychooncology* 2005; 14:339–50.
37. Robertson R, Campbell NC, Smith S, *et al*. Factors influencing time from presentation to treatment of colorectal and breast cancer in urban and rural areas. *Br J Cancer* 2004;90:1479–85.
38. Kisely S, Sadek J, MacKenzie A, *et al*. Excess cancer mortality in psychiatric patients. *Can J Psychiatry* 2008;53:753–61.
39. Stewart R, Soremekun M, Perera G, *et al*. The South London and Maudsley NHS Foundation Trust Biomedical Research Centre (SLAM BRC) case register: development and descriptive data. *BMC Psychiatry* 2009;9:51.
40. Moller H, Richards S, Hanchett N, *et al*. Completeness of case ascertainment and survival time error in English cancer registries: impact on 1-year survival estimates. *Br J Cancer* 2011;105:170–6.
41. Robinson D, Sankila R, Hakulinen T, *et al*. Interpreting international comparisons of cancer survival: the effects of incomplete registration and the presence of death certificate only cases on survival estimates. *Eur J Cancer* 2007;43:909–13.
42. Department for Communities and Local Government, UK. The English Indices of Deprivation 2007, 2008.
43. Desai MM, Bruce ML, Kasl SV. The effects of major depression and phobia on stage at diagnosis of breast cancer. *Int J Psychiatry Med* 1999;29:29–45.
44. Howard LM, Barley EA, Davies E, *et al*. Cancer diagnosis in people with severe mental illness: practical and ethical issues. *Lancet Oncol* 2010;11:797–804.
45. General Practitioners Committee, British Medical Association. Quality and Outcomes Framework (QOF), Guidance—Updated August 2004, 2004:59. [http://www.dh.gov.uk/prod\\_consum\\_dh/groups/dh\\_digitalassets/@dh/@en/documents/digitalasset/dh\\_4088693.pdf](http://webarchive.nationalarchives.gov.uk/20130107105354/http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_4088693.pdf) (accessed 18 Oct, 2013).