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# Cancer and mental health—a clinical and research unmet need

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**Background:** Poor mental health is the largest single source of disability in the UK, and co-morbid health problems, particularly with cancer, raise total health care costs significantly.
**Methods:** This study examined what research is being conducted into the intersection between cancer and mental health. Research papers captured by the intersection of sub-field filters—'mental disorder' and 'cancer'—were studied from the Web of Science over a 10-year period (2002–2011).
**Results:** There were 1463 papers dealing with the dual presence of cancer and mental disorder. They amounted to 0.26% of cancer research and 0.51% of mental health research over the 10-year period, indicating that their intersection receives little research attention. Eighty per cent of papers were concerned with the effects of cancer on mental health rather than the reverse; a few (5%) looked at the post-traumatic stress suffered by carers of cancer patients. Of cancer types, breast dominated (21%), followed by prostate (5%), lung (3%), oral (2%) and colorectal (2%) cancer. The area of mental health most studied in cancer was unipolar depression.
**Conclusions:** The paucity of research that exists at the intersection of cancer and mental health requires attention from policymakers and funders in order to address an important trans-disciplinary gap in health care research.
**Key words:** cancer, mental health, policy, research

## introduction

The diagnosis and treatment of cancer have a significant impact on mental health, and are associated with a physical, emotional and financial burden both on individuals and on society as a whole. Both these major non-communicable diseases have close interdependencies. Nevertheless, their clinical and research communities have traditionally not worked together much. This view has recently been reinforced by a report from the King's Fund and Centre for Mental Health [1].

Mental health problems are the largest single source of disability in the UK, and co-morbid health problems raise total health care costs significantly [2]. The King's Fund report found that for patients with co-morbid mental health problems and physical illness, health care costs were raised by at least 45% per person, and amounted to an annual total of between £8 and £13 billion in England in recent years.

Most research into cancer and mental health has focused on the effects of cancer on patients' mental health, specifically depression and anxiety, with evidence suggesting that co-morbidity of depression with cancer has a negative impact on physical morbidity and mortality [3]. In patients with pre-existing mental health problems, the question arises whether there is an increased or decreased incidence of cancer, and if the overall outcome is affected by their mental state. On the other hand, these patients often present with more advanced disease because they are less likely to attend routine screening clinics. Given the impact that both these areas of morbidity can have on individuals and on society, one might expect there to be substantial research effort to investigate their interaction.

The study presented in this article provides the first high-resolution, objective study of where current areas of overlap and weakness are in the mental health cancer R&D domains; thus providing a major intelligence source for policymakers wishing to bridge this important trans-disciplinary boundary. The intention was to determine the scale of such research and to identify areas of strength and weakness with a view to identify where policies could be developed that would fill research *lacunae* in this complex interdisciplinary area.

## methods

Research papers from the Web of Science (WoS) over a 10-year period (2002–2011) identified by two sub-field filters capturing mental disorder and cancer papers were studied. Each of these filters contained a list of specialist journals, e.g. *Cancer*, *British Journal of Psychiatry*, all of whose papers were retained, and of title words, e.g. carcinoma, leukaemia, Alzheimer's, depression. The lists of title words included drugs used exclusively for cancer or mental disorders, and genes that had been shown to pre-dispose to cancer or mental disorders. The filters were calibrated with

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reference to the outputs of eponymous departments in order to determine their precision (specificity) and recall (sensitivity); these were all above 0.9.

On a preliminary inspection, it was clear that many of the 5284 papers in the intersection of the two filters were not relevant. For example, some had 'suicide gene' or 'neurological malignant syndrome' in their titles, or were concerned with small laboratory animals (mice and rats), or were too molecular. We wished to limit the set of papers to those where cancer patients suffered also from mental disorders, or where people with mental disorders were more likely to be diagnosed with cancer, or to have difficulties with treatment or a worse prognosis as a result. Although many papers were concerned with alcohol and its carcinogenic effects, these were discarded unless its addictive properties were highlighted. The titles of the papers were checked individually (by SB) and almost three quarters of them were set aside as not relevant to our study.

The papers were further analysed and each paper marked as follows:

- By the fractional count (e.g. a paper with one address in France and two in the UK would be counted as 0.33 and 0.67, respectively for the two countries on a fractional count basis, but as one each on an integer count basis.) of each country represented in the address field;
- By whether the paper concerned 1 of 16 tumour sites (e.g. breast, lung, prostate, etc.), based on a series of sub-filters developed (by RS); these consisted of journal name strings and title words. Some papers covered more than one site; others did not specify a site;
- By whether the paper concerned 1 of 11 research types (e.g. chemotherapy, surgery, palliative care, etc.), again based on sub-filters developed by RS, and with possible overlaps;
- By whether the paper concerned 1 of 17 mental disorders (e.g. Alzheimer's disease, depression, schizophrenia), similarly defined by sub-filters developed by GS;
- By whether the paper was about the effects of cancer on patients' mental health (coded O > M) or about patients' mental health having an effect on the diagnosis, treatment or prognosis of cancer (coded M > O), based on individual inspection by SB.

For papers published in the last 3 years, 2009–2011, funding data were available from the WoS (fields FU and FX). The funders were classified by country and sector and given codes from a thesaurus [4] and since extended.

## results

During the 10 years of the study period, there were 1463 papers dealing with the dual presence of cancer and mental health problems according to the criteria described above. They amounted to 0.26% of all cancer research over the 10-year period and 0.51% of all mental health research, demonstrating that the intersection between mental disorders and cancer research receives relatively very little attention despite mounting evidence of high costs and increased mortality.

However, the subject is increasing in output faster than either of the two component sub-fields, see Figure 1. Of the world total, the USA published the most, with just over 40% on an integer-count basis. The UK was second, with just over 9%, followed by Germany and Canada, see supplementary Table S1, available at *Annals of Oncology* online. Some countries, notably four in Scandinavia, Australia and the UK, carried out substantially better in terms of their percentage presence in the composite subject area compared with their presence in cancer research overall. However, the four east Asian countries and four large continental European ones (Germany, France, Italy and Spain) all carried out worse in the composite than in cancer research, see Figure 2. However, this may have been owing to the absence of the clinical journals from these countries from coverage in the WoS.

Most papers (80%) were concerned with the effects of cancer on mental health rather than the reverse; a few (5%) looked at the post-traumatic stress suffered by cancer patients' carers, especially by parents of young children. The cancer site of principal interest was the breast (21% of papers) followed by the prostate (5%), lung (3%), mouth and colon and rectum (2%) (supplementary Table 2, available at *Annals of Oncology* online). This emphasis on breast cancer was not simply a reflection of the importance given to research on this tumour site in the United States and other western European countries [5], since the pattern was similar in four East Asian countries (Japan, Taiwan, South Korea and China), even though the incidence of breast cancer there is relatively less.

The mental disorder that was most studied was unipolar depression (43%); far behind were post-traumatic stress disorder (PTSD) (5%), dementia (3.6%), suicide/self-harm (3.5%) and schizophrenia (2.6%) (supplementary Table 3, available at *Annals of Oncology* online). Supplementary Table 4, available at *Annals of Oncology* online shows the research type, which may be taken as the causative element studied in how cancer causes poor mental health, or perhaps vice versa. The research types of primary concern to clinicians and scientists were palliative care and quality of life (QoL), each accounting for more than half the total, and in combination for nearly 45%. One of them (epidemiology) was more concerned with the effects of mental ill-health on cancer, but overall, the vast majority of papers (1206 of 1463, 82%) were concerned with poor mental health resulting from cancer.

During the period 2009–2011, there were only 58 UK papers, and funding was dominated by the leading cancer charity, Cancer Research, UK, with 19 acknowledgements to this source, of which two were implicit from the addresses (the Beatson Research Institute in Glasgow), and all but two were concerned with the mental disorders arising from cancer, rather than vice versa. No other funder had more than nine papers (the National Institute of Health Research, the research wing of the UK National Health Service), and the Medical Research Council supported only two papers.

## discussion

The interdisciplinary nexus between cancer and mental health forms a very small percentage of all research carried out in these two major areas of non-communicable disease, although this appears to be slowly increasing. The UK's research output in this area of importance is low compared with the USA. The preponderance of research carried out is on the impact of cancer on mental health rather than the reverse, with the focus being on the effects of cancer on, especially, depression and anxiety. The predominant tumour types where patient mental health was studied were breast cancer followed by prostate, lung, oral and colorectal cancer. The area of mental health most investigated was unipolar depression in breast cancer patients with these patients experiencing poorer mental health predominantly while receiving palliative care.

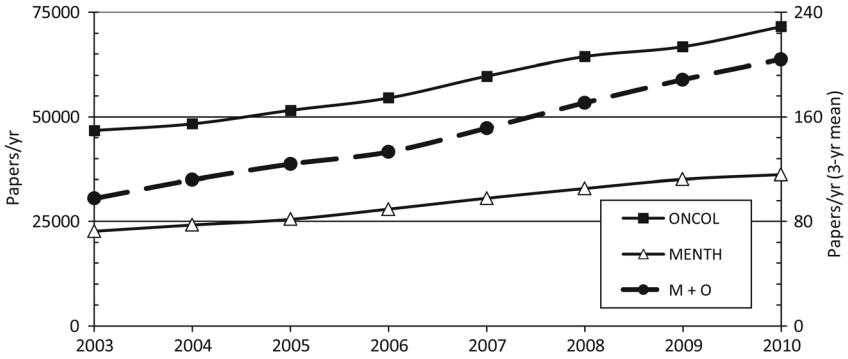


**Figure 1.** World outputs of papers in cancer research (ONCOL), mental disorders research (MENTH) and their intersection, filtered manually (M + O); 3-year running means.

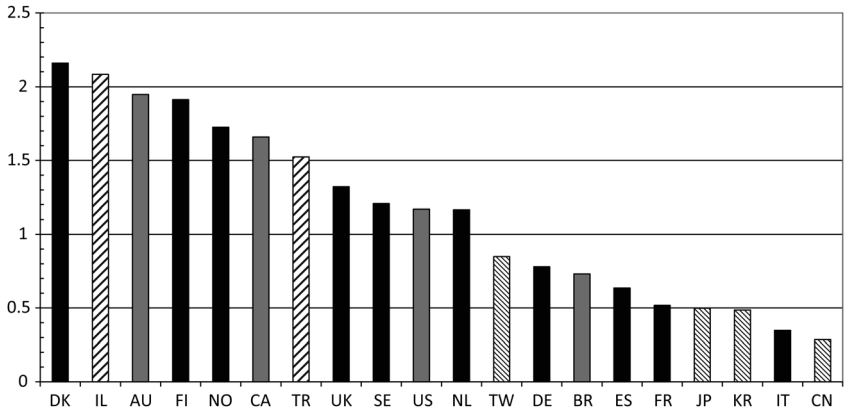


**Figure 2.** Ratio between percentage presence of 20 countries in the combination of cancer research and mental disorders and in cancer research alone, 2002–2011, in the Web of Science. Country codes are in supplementary Table 1, available at *Annals of Oncology* online. European countries: black bars; Middle East countries: wide diagonal stripes at 45°; East Asian countries: narrow diagonal stripes at 315°; others: grey bars.

The importance of addressing the overall paucity of research into cancer and mental health is highlighted by evidence suggesting that the co-morbidity of depression with cancer has a negative impact on morbidity and mortality, with depression being an independent predictor of poor survival in patients with advanced cancer [3]. Depression also impacts on QoL, cancer treatment non-adherence, the duration of hospital stay and the costs of health care. The co-existence of cancer and depression is associated with a significantly increased risk of death, although the effect of depression differs by cancer site [6].

This study has shown that the dominant area of research has been in breast cancer and depression. Breast cancer patients with depression have a significantly higher risk of mortality [7]. Independent variables in breast cancer patients such as social status and low social support were independent risk factors for depressive symptoms [8]. Socioeconomically deprived women with a history of somatic and psychiatric disease may represent a group that warrants special attention, who might benefit from screening for mental illness and appropriate interventions as required since psychological problems in cancer patients often go undiagnosed unless they are specifically sought.

Assessment and treatment of depression could improve the QoL for cancer patients suffering with unrecognised depression and reduce their risk of suicide. The strongest risk factors for suicide in all cancers appear to be male sex [9–17] and older age, with incidence of suicide being reported to be from 2 to 11 times the rate in the general population [10].

A smaller number of papers on the interaction between gastrointestinal cancers (oesophageal, stomach and colorectal) and mental health was noted. Pre-existing psychiatric disorders in patients act as an independent risk factor for delayed diagnosis in abdominal cancers, and they are also associated with a decreased likelihood of receiving surgical therapy [11]. If these patients do undergo surgery, they may have an increased risk of complications, including pneumonia and compromised nutrition post-operatively [12]. Integration of treatment by surgeons and psychiatrists might potentially reduce the incidence of morbidity in these patients. There is clearly a lack of research in some site-specific cancers where there is also obvious psychiatric morbidity, e.g. head and neck or oral cancers after surgical excision and reconstruction.

A significant number of papers looked at the effect of cancer diagnosis and treatment on patients and their families [13]. The psychological 'sequelae' for parents of children with cancer ranged from anxiety and depression to post-traumatic stress symptoms and PTSD [14], often lasting for long periods after treatment was completed [15]. Many caregivers of advanced cancer patients meet criteria, or are being treated, for psychiatric

problems, and there are high levels of burden and distress in these people [16]. Researchers and clinicians need to be aware that cancer affects the whole family, and there is a need for the development of social policy and the mobilisation of resources to support the provision of care for cancer patients and their families.

Intriguingly, there appear to be protective genetic effects against cancer in some patient groups, for example those with schizophrenia [17] or Alzheimer's disease [18]. In patients with schizophrenia, some studies have suggested that they have a significantly lower cancer incidence, consistent with a protective effect, despite higher cancer risk exposure, e.g. from smoking [17]. However, if these patients do go on to develop cancer, they subsequently have a higher mortality rate than patients without schizophrenia [19]. Although the incidence of both cancer and dementia increases with age, there is very little known about the effect of dementia on cancer and vice versa [20]. Furthermore, schizophrenia and dementia patients are both more likely to present with more advanced disease that is no longer amenable to first-line therapy.

Cancer survivors appear to have a lower risk of Alzheimer's disease than those without cancer, and patients with Alzheimer's disease have a lower risk of cancer. In patients who survive smoking-related cancers, the risk of Alzheimer's disease is the lowest, and this cannot simply be explained by survival bias. This pattern for cancer is similar to that seen in Parkinson's disease and suggests an inverse association between cancer and neuro-degeneration [18].

Several studies have addressed the effects that tricyclic antidepressants (TCAs) and selective serotonin reuptake inhibitors (SSRIs) may have on the incidence of cancer. Sternbach looked at 13 studies that predominantly examined TCAs and found a significant ($n = 3$) or trend increase ($n = 4$) in cancer incidence, with no increase observed in the remaining six studies [21]. SSRI use has not been found to increase cancer risk [22], and some studies have even suggested a protective effect with decreased incidence of lung cancer [23] and colon cancer [24, 25].

Finally, there appears to be an influence of depression on the uptake of invitations to be screened within population-based breast and cervical cancer screening programmes [26]. This may result in delayed presentation and poorer outcomes.

Many of the areas briefly sketched above require further investigation. The relationship between cancer and mental health merits close attention from policymakers and funding bodies. In high-income countries, cancer research funders in particular are in a significant position to lead joint initiatives with mental health funders to create joint action programs focusing on important mutual interests, such as survivorship and mental health. To date, no such programs have been created, and this study provides core intelligence to develop such programs.

The present study's strengths lie in its wide-ranging approach to examination of research on the relationship between cancer and mental health. It has not attempted to define and prioritise specific areas of research requiring immediate attention. Indeed, it has determined where a large amount of research is focussed (depression among women with breast cancer receiving palliative care who are concerned about their QoL), but this is not necessarily where the clinical need is the greatest. The next step must surely be to investigate the clinical situation so as to identify other potential problem areas that are in need of more research. However, it does provide an overview of the research currently being done in many countries thereby helping to inform future strategic thinking.

The question of what can be done to address the overall paucity of interdisciplinary research also needs to be addressed? There are probably many reasons for the lack of research in this area. Researchers may find it difficult to think in interdisciplinary terms, and some research disciplines may have little formal contact between clinicians or researchers. Added to this, there may perhaps be a dearth of hypotheses or good ideas for testing. The existing situation where as a result, potential funders may be ignorant of the extent of the health problems and its their impact on clinical care. Furthermore, this area of research may fall between funding stools. Given that there are no large mental health charities, should this area of research be funded by cancer charities?—which appears to be the situation in the UK. Alternatively, is there an opportunity for dual funding by cancer and mental health charities or should this responsibility fall largely on government, essentially on the National Institute of Health Research? Finally, it is worth noting that as an indicator of the seriousness of physical health problems in people with serious mental illness, quite startling figures on the years of life lost by people with a psychosis are beginning to emerge, in some studies almost 20 years compared with the age-matched general population [27]. This is a very serious cost to the health as well as the moral welfare of our society.

The relative lack of research at the intersection of cancer and mental health requires attention from researchers, policymakers and funders in order to address a large unmet need in health care. This study provides key intelligence for the research communities and funders in cancer and mental health to create new partnership opportunities to bridge the disciplinary divide and accelerate the prevention and treatment of mental health problems in cancer patients.

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## disclosure

The authors have declared no conflicts of interest.

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