

## **Cancer and Severe Mental Illness: Bi-Directional Problems and Potential Solutions**

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## **Abstract**

**Objective:** Given the reported increased rates of physical morbidity and higher mortality rates amongst people with severe mental illness (SMI) (schizophrenia and severe mood disorders), with a life expectancy shorter of 15-20 years with respect to the general population, the aim of this paper was to call attention to the problem of cancer in SMI.

**Methods:** We conducted a narrative review of the most significant papers published in the areas of cancer screening, incidence, mortality and palliative care in SMI.

**Results:** Data from the literature confirm disparities in screening (e.g. mammography; pap-smear test; colorectal cancer screening) and prevention (e.g. clinical breast examination; smoking cessation). The incidence of cancer was found to be variable with a portion of the studies reporting a higher prevalence while others a similar or a lower prevalence of cancer compared to the general population. A lower percentage of patients with SMI received proper cancer treatment resulting in survival after cancer diagnosis significantly worse than people without SMI. Likewise, end-of-life care has been shown to be lacking with poorer levels of physical, psychological and spiritual care.

**Conclusions:** The problems of stigma and discrimination, poorer dignity, poorer health behavior, lack of integration in health-care services for people with SMI needs to be addressed and solved in cancer care. Psycho-oncology has a very specific and mandatory role in integrating the recommendation of the World Health Organization to improve the links between oncology and mental health settings for more specific psycho-oncology programs addressed for this vulnerable segment of the population.

**Keywords:** cancer, oncology, mental illness, schizophrenia, bipolar disorders, persistent depression, psycho-oncology

## Introduction

Worldwide, the prevalence of psychiatric disorder regards 1 out of 4 people with about 450 million having severe mental illness (SMI), of whom 300 million are living with depression, 21 million with schizophrenia and 46 million with bipolar disorders,[1] with similarities between North America [2] Europe [3] and other parts of the world, including Asian-Pacific areas [4]. In fact, a survey in Europe [3] involving 28 European Union countries plus Norway and Switzerland, also confirms that about 38% of residents of the EU, or around 165 million people, are affected by a mental illness at some point in any given year and that it is the challenge of the 21st century.

COVID-19 certainly has added to the detection and service delivery but the problems with the SMI and cancer care have been long standing. In fact, only about one-quarter of those with a mental illness in Europe received any treatment, and only about 10% had “nationally adequate” care and integrated medical, social, employment and psychological provision which is the key for recovery.[3]

Besides the several implications of SMI in terms of poor quality of life and level of functioning, problems at work, social integration and stigma, the last two decades have seen much of the research focused on physical health, not on the integration of SMI and cancer care.[5,6] One of the most important and recognized problems is that people with SMI, especially schizophrenia, bipolar disorders and severe depressive disorders, have both an increase rate of morbidity because of somatic disorders and higher mortality rates, aside from cancer [7,8,9]. The provisional conclusions of these studies is that there is sufficient evidence that people with SMI are less likely to receive standard levels of care for most diseases, such as diabetes and heart disease associated with lifestyle factors. They are less likely to be considered for screening such as for mammography or prostate surveillance; less likely to receive baseline testing of numerous important physical parameters such as obesity, high blood pressure; so that access to and quality of health care remains to be improved for individuals with SMI.[10] This is responsible for a shorter life expectancy of 15-20 years compared to the general population. This has brought clinical scientists to underline that the contravention of the international conventions for the right to health for the poorer physical healthcare and premature mortality is significantly worsened in people with SMI, and is a worldwide problem deserving attention and quick solutions.[11]

Whereas most studies have pointed attention to cardiovascular disease and related disorders, including hypertension, diabetes and metabolic syndrome, [12,13] cancer has been also considered an important topic to be taken into account in research and clinical practice [14,15,16].

### **Prevention issues and screening for cancer in people with SMI**

Disparities in health services provided to people with SMI have been documented for preventive services in general. This is true also as far as prevention and screening for cancer. Regarding mammography for example, preliminary data on women with mental illness and/or substance abuse, regardless of severity, showed that there was a risk for underscreening [17]. Other research on patients with SMI indicate that women with mental illness are 32% less likely to undergo at least one screening mammography and among those who received at least one screening mammography, fewer women with mental illness received screening mammography on an annual basis. [18] These data are in line with a further study showing that women with a mental illness are at risk for not adhering to recommended routine breast cancer screening and may require more intensive efforts to achieve optimal rates of recommended breast cancer screening.[19] More recently, by examining different types of mental disorders (i.e., mood disorders, depression, severe mental illness (SMI), distress and anxiety conditions) Mitchell et al. [20], identified 24 studies reporting breast cancer screening practices in a large sample of 715,705 women with mental illness. Their pooled meta-analysis demonstrated significantly reduced rates of mammography screening in women with mental illness, especially mood disorders and schizophrenia.

Similar results were found as far as screening for cervical cancer with studies indicating that women with schizophrenia were less likely to have a Pap test (58.8% vs. 67.8%) compared to all other women.[21] A further review confirmed substantial evidence in the literature for disparities in breast and cervical cancer screening rates among women with SMI.[22]

For lung cancer, it has been shown that patients with SMI have less access to smoking cessation and cancer screening programs because of lack of clinician expertise tailoring communication about cancer care and tobacco cessation, and the fragmentation of mental health and cancer care.[23] Also treatment is poorer when lung cancer has been diagnosed. [24] Likewise,

a study in Hong Kong indicated a low cancer screening utilization for several conditions, including mammography; clinical breast examination; pap-smear test; prostate examination; and colorectal cancer screening [25].

A very large and recent metanalysis involving almost 5 million people (501, 559 patients with mental illness, and 4, 216 280 controls) from 47 publications and involving many possible mental illnesses (i.e. schizophrenia or schizoaffective or psychosis, depression or bipolar disorder or mania, eating disorder or anorexia nervosa or bulimia nervosa or binge eating disorder, obsessive-compulsive disorders, post-traumatic stress disorder, anxiety disorder or panic disorder) provided a global overview of the problem. Data included studies relative to screening for cancer with results showing that screening was significantly less frequent in people with any mental disease compared with the general population for breast cancer, cervical cancer, and prostate cancer, but not for colorectal cancer. [26]

### **Incidence of cancer and cancer mortality in people with SMI**

The problem of the incidence of cancer and cancer mortality among patients with SMI is still controversial, with some studies reporting a higher prevalence while others a similar or a lower prevalence . A series of reviews of data and meta-analyses which are available have tried to shed some light in this area. By analyzing the data from over 6,000 female patients with schizophrenia from 13 studies in comparison to age matched general populations from the relevant country from 1986 to 2008, Bushe et al. [27] reported widely discrepant results, ranging from 52% increase in risk to 40% decrease, with six of 13 studies showing an increased or marginally increased incidence of breast cancer. In a further meta-analysis of 12 cohort studies that included 125,760 women and in which conventional methods of meta-analysis had been used, schizophrenia in women was associated with an increased breast cancer incidence compared with the general population. [28] A further recent meta-analysis of studies [29] showed that compared with general populations, the prevalence rates of prostate and colorectal cancer in male patients with schizophrenia are lower, and lung cancer prevalence is higher in female patients, while no difference was found in a different meta-analysis for lung cancer [30]. There are also data indicating that the incidence of colon cancer was higher among people with schizophrenia in comparison with people with bipolar disorders or

the general population [31], while a different Northern European population-based study (time span 1990-2013 for 1 424 829 person-years of follow-up) showed a higher risk for female breast cancer, lung cancer, esophageal cancer and pancreatic cancer and a lower risk of prostate cancer, [32] as already reported in a previous study.[33]

It is possible that there might be protective factors or risk factors among patients with schizophrenia that relate to specific cancers. With respect to this, changes in endocrine hormones caused by antipsychotic medications, familial or genetic factors (e.g., tumor suppressor gene p53, enhanced natural killer cell activity, angiogenesis, or DNA repair mechanisms), reduced parity and hyperprolactinaemia may be factors contributing to determine such contradictory results. [34,35,36]

Regarding bipolar disorders, elderly people are reported to have a delay in receiving specific cancer treatment, although no studies have investigated treatment outcomes [37]. Also, a study carried out in Israel showed an enhanced cancer risk was found for bipolar disorder both in men (Standardized Incidence Ratio - SIR 1.59) and women, (SIR 1.75) [38] As stated by Howard et al. [39], when interpreting these results, it is useful to consider the effect of missing cancer diagnoses, shortened life expectancy, particular historical and health-service contexts, behavioural risk factors, and the possibility that genetic or drug effects can influence the results of the studies. It is mandatory for example, to control for age and sex in incidence studies since while SMI, including schizophrenia and bipolar disorders, are more common in young adults and are associated with a shortened life, most cancers are diagnosed in patients older than 60 years and the cancers affecting men and women differ. Also, patients with SMI have higher overall mortality rates, particularly from suicide and unnatural causes at younger ages.

With these caveats, mortality for cancer is demonstrated to be higher among people with SMI. For example, in a prospective study Chou et al. [40], showed that among 1,145 patients with schizophrenia and 5,294 controls, the incidence of breast cancer was lower (1.93% vs 2.97%), although the mortality rate among patients with schizophrenia was higher than that of the control group. Similar results were found among patients with schizophrenia and lung cancer, [41] who are reported not having received stage-appropriate treatment, resulting in poorer outcomes.[42]

With respect to prostate cancer, a study of 49,985 patients with locoregional high-grade (nonmetastatic) prostate cancer showed that having a SMI (bipolar disorder, schizophrenia, and other psychotic disorders) was associated with reduced odds of receiving surgery or radiation

concurrent with hormone therapy as initial treatments in the year after cancer diagnosis. Additionally, SMI was associated with higher hazard of 5-year cancer-specific death after accounting for competing risks of non-cancer death. [43] Again, in an Australian study, although the incidence of cancer was not higher than in the general population, psychiatric patients were more likely to have metastases at diagnosis and less likely to receive specialized interventions, with a greater case fatality.[44] Similar results were found in a study of 16,636 elderly women in which patients with comorbid anxiety and depression had an increased risk for diagnosis delay of  $\geq 90$  days from symptom recognition, and those with severe mental illness had an increased risk for initial treatment delay of  $\geq 60$  days from diagnosis [45]. More recently, in a large Danish study on 56,152 women with early-stage breast cancer diagnosed in 1995-2011, patients with schizophrenia or related disorders had a higher likelihood to not be provided proper cancer guideline treatment and to have a survival after breast cancer significantly worse than that of women without SMI.[46]

### **Palliative care in people with SMI**

The existence of disparities in health and health care between patients with schizophrenia and/or SMI and patients without a diagnosis of mental illness is extremely important, especially in end-of-life care. In concert with data underlining the problems of the stigma, poverty, lack of family support and social isolation, patient-level factors including cognitive impairment, psychiatric disabilities and chronicity [47], end-of-life care has been shown to be lacking for patients with schizophrenia and/or SMI [48].

In one of the first studies conducted in a palliative care setting, Chochinov et al. [49] found that compared to their matched cohort, Canadian patients with schizophrenia were less likely to see specialists other than psychiatrists, less likely to be prescribed analgesics, and less likely to receive palliative care. They also were much more likely to die in nursing homes where optimal physical, psychological and spiritual care is possibly less optimal than in palliative care units [50].

In a further Australian study [51], people with schizophrenia in the last year of life were less likely to be admitted to hospital and access community-based specialty palliative care, but more likely to attend emergency departments if male. Community-based specialist palliative care was associated with increased rates of hospital admissions. In general, what emerges is that stigma

affecting quality of care and access to care; issues related to consent and capacity for the patient's end-of-life care decisions and to appoint substitute decision makers; best practices for psychosocial interventions, pharmacology, family and health-care collaborations, goals of care, setting, and smoking; and barriers to care, including setting, communication, provider education, and access to care [52]. These data were more recently confirmed by other studies in Taiwan [53] and France [54]. In the latter, this was carried out on 2,481 patients with schizophrenia and 9,896 matched controls. The authors found that patients with schizophrenia were more likely to receive palliative care in the last 31 days of life and less likely to receive high-intensity end-of-life care (e.g. chemotherapy and surgery), were more likely to die younger and had a shorter duration between cancer diagnosis and death than controls.

Looking at the qualitative issues related to patients with SMI, clinicians have indicated several problems to be addressed. A first regard problems with information processing and communication including those determined by cognitive impairment and lack of insight secondary to SMI. A second issue has to do with the problem of identify carers in the home environment because of previous family disruption or living in sharehouses, alone or being homeless). Also it has to be underlines the lack of experience, ill-informed assumptions about SMI, with lack of adequate educational resources and services, staff unprepared/lacking in specific training and lack of policies or guidelines, or fear and ignorance of staff among health carers. Last, there are common preoccupations related to the assumption that the patient will be unmanageable, the lack of identifiable institutional or community care staff to provide adequate care or sufficient resources.[55] A recent review [56] stressed the need for an increased awareness of potential healthcare disparities in this population, creative approaches in multidisciplinary care, and provision of adequate palliative services and resources can enhance end-of-life care in schizophrenia.

### **Possible mechanisms involved in the problem**

One of the most significant debates regarding poor health care in people with SMI is related to the problem of stigma leading to the problem of discrimination and reduced expression of human rights.[57,58,59] Available research in psychiatric settings indicates that stigma consists of both the auto perception of one-self as stigmatized and different form others (self-stigma, as the internalization of a negative stereotype that the person applies to oneself) [60] and the stigma



imposed by society (social stigma, as the series of stereotyped beliefs, prejudiced attitudes, and discriminatory attitudes). Elsewhere [61] we have considered the dimension of stigma as the expression of the other side of dignity, where also it is possible to distinguish a self-related sense of personal value and dignity (intrinsic dignity) and a reciprocal and interpersonal experience of dignity related to what others provide us in terms of value and dignity (extrinsic dignity). Being seen as an equal human being, with the potential to experience self-worth, meaning and purpose are key factors to maintaining dignity, despite suffering the consequences of mental illness and having to fight for one's rights.[62,63] Therefore, throughout the continuum of cancer care, the stigma of mental illness and poor dignity are factors influencing the management of the disease.

In the context of cancer, Irwin et al. [64] have suggested an interesting model that interrelated patient-based, provider-based, and systems-based factors, influenced by mental health stigma, may impact cancer prevention, diagnosis, treatment, and end of life care. More specifically the authors consider that disparities in cancer care for patients with schizophrenia (but it can be extended to others with SMI) is derived by interrelated patient-level, provider-level, and systems-level factors. From one side, patient's inappropriate affect, positive or negative psychotic symptoms, cognitive symptoms (e.g., impaired attention and executive function), disorganized behaviour, dysfunctional coping (e.g. pathological denial), and poor health behaviour (e.g. smoking, substance use and/or abuse, poor adherence) intervene to create part of the problem. It is demonstrated that the tendency to avoid the health care system, to minimize physical symptoms and not understand because of poor insight their physical condition, to not cooperate with caregivers, cause a delay in diagnosis and presentation at cancer centers with late-stage cancer.[65,66] Also functional impairment of people with SMI is one of the most significant predictor of lower screening rate [67]. On the other side, the difficulty of health-care providers (e.g. GPs, oncologists, nurses) in relating to these symptoms and poor functioning, that are unfamiliar and incomprehensible to the team, fear of violent behavior or suicide risk, prejudice on untreatability of the psychiatric condition can determine a second part of the problem. Finally, the fragmentation of health care services, the difficulty in creating a whole-person centered approach, the tendency of psychiatry and somatic medicine to work in a separate or non-integrated way are a third cause of the problem. All the three aspects are subsumed under the concept of stigma. This in turn negatively influences cancer care- from prevention and screening, to early diagnosis, treatment

and symptom management, as well as end-of-life care, with an impact in reducing both quality of life and survival. Therefore, it is important to improve the area of education and training, including communication skills and assessment and management of emotions and psychiatric symptoms when dealing with people with SMI in order to increase the quality of their cancer care, as well as of physical health in general [68].

### **Clinical Implications**

There are several considerations to be mentioned in the analysis we have done about the problem of cancer care among people with SMI.

One of the most important findings emerging from the psycho-oncology literature concerning people with SMI is that there are now significant data indicating major disparities in screening and treatment for cancer for this vulnerable population compared with that of the general population. A second issue is that people with SMI are less likely to receive optimal treatment after diagnosis with poorer cancer-specific prognosis and lower survival time.

These data are in line with what has been shown in the literature regarding poorer physical health in patients with SMI and the need, as indicated by Tosh et al. [69], that physical health can be the target of intervention in both psychiatry and medicine in general, in order to favor the access to health services which, in turn, facilitates longer-term benefits, such as reduced mortality or morbidity. On the other hand, the WHO Comprehensive Mental Health Action Plan, endorsed by the World Health Assembly in 2013, has repeatedly outlined the need that Member States and organizations [e.g., 70,71], develop and implement effective policies, strategies and plans to improve the health, both physical and mental, of people living with SMI. The WHO itself indicates in fact actions that can be taken such as: creating protocols for physical and mental health needs of patients in the areas of prevention, identification, assessment and treatment; improving access to general health services through the integration of physical and mental health services; working to overcome the stigma associated mental illness and discrimination.

With specific reference to cancer, in order to decrease the early mortality of patients with SMI, especially schizophrenia, Chou et al. [72] have proposed a series of steps to be rapidly taken by the health care systems, namely:

- (i) enhance early detection and early treatment, such as increasing the cancer screening rate for patients with schizophrenia;
- (ii) provide effective, timely treatment and rehabilitation;
- (iii) improve patients' psychiatric symptoms and cognitive impairment;
- (iv) promote healthy behaviour in the general population and emphasize healthy lifestyles in vulnerable populations;
- (v) act on reducing the stigma of schizophrenia.

Regarding palliative care several recommendations have been stressed by Woods et al. [73] who underlined that palliative care needs of people with SMI are similar to the general population (e.g. pain and symptom control, maintenance of function, enhancement of quality of life, support for relationships, and the possibility of dying well); that palliative care must be centered on these needs of the individual person with SMI basing a therapeutic relationship created by respect, dignity, hope, and non-abandonment, integrating principles of hospice palliative care in end-of-life care for people with SMI; that there is a profound need to revise or develop policies and guidelines to address the needs of this population by integrating the systems of care (mental health care, palliative care, family medicine, social services) for better intervention for people with SMI and their families.

## **Conclusions**

Psycho-oncology has a very specific and mandatory role in this area and its commitment to better understanding health inequalities in cancer care for people with SMI and in planning and developing effective interventions. The time has come to bridge the gap between stigma and mental illness, and improve the links between oncology and mental health for more specific psycho-oncology programs addressed to this vulnerable segment of the population. Some interesting experiences have been reported in the area with data demonstrating that specific tailored screening and management intervention are possible for patients with severe mental disorders, such as schizophrenia, if organized in an integrated multidisciplinary way. [74,75] With respect to this, it is important to stress the fact that the introduction of psycho-oncologists in teams and the establishment of psycho-oncology departments / units should consider not only a link with

specialties in oncology (e.g. medical oncology, hematology, radiation oncology, surgery, palliative care), or biological sciences (e.g. epidemiology, immunology, biology, pathology, genetics), but a more structured liaison with mental health department.[76]

With this as background, the aim of this paper is to draw attention to the problem of cancer amongst people with SMI, both in terms of screening, incidence and mortality as well as palliative care. The time has come for psycho-oncology to take into consideration these issues and to launch a campaign, through a special issue of the Journal, to analyze in detail the various and complex aspects regarding this area of urgent clinical need.

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