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The Interaction Between Melanoma and Psychiatric Disorder

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1. Introduction

This chapter explores the interaction between melanoma and psychiatric disorder, updating our work with another decade of population-based data. Although psychiatric and physical disorders, such as melanoma, frequently co-exist, the relationship between the two may be complex. Psychiatric complaints may be secondary to physical illness, may cause or exacerbate physical symptoms, or the two may merely occur by chance in the same individual. When psychiatric disorder is secondary to cancer, it can be due to cancer-related factors, cancer-treatment-related factors, psychiatric history factors and social factors.[1] Melanoma is no exception to this. This chapter examines some of these possible interactions.

2. Neuropsychiatric complications of interventions used to treat melanoma

One obvious association between melanoma and psychiatric disorders is that many of the medications used to treat melanoma have psychiatric complications. A significant proportion of patients diagnosed with any form of cancer experience psychiatric morbidity in association with diagnosis and treatment. Factors that influence or increase the risk of psychiatric co-morbidity can be categorised as cancer-related factors, cancer-treatment-related factors, psychiatric history factors and social factors.[1] When we say that an intervention is a cause of an adverse health outcome we mean that it is a contributory cause of that outcome in the sense that use of that intervention is one of a complex set of conditions that jointly produced it.[2] In order to infer that the intervention is a contributory cause we need evidence that: (1) medicine use and the health outcome co - vary; and (2) evidence that other explanations of the relationship are implausible, leaving medicine use as the most plausible explanation of the adverse health outcome.[2] However, it can often be difficult to attribute a particular psychiatric state to a specific cancer treatment/intervention.
It is recognised that a range of cancer treatments can contribute to the development of psychiatric disorders in cancer patients. Disease modifying agents such as corticosteroids, chemotherapeutic agents (vincristine, vinblastine, asparaginase, intrathecal methotrexate, interferon, interleukin, amphotericin) and whole-brain radiation have all been associated with the development of depression, delirium or dementia. In addition, treatment of pain with high-dose opioids can be associated with acute confusional states (delirium), particularly in the elderly and terminally ill.[1]
There has been increasing concern about the psychiatric side effects of treatment with interferon (IFN), a therapy commonly used in the treatment of melanoma. Effects can occur

shortly after beginning IFN therapy or later as a consequence of sustained treatment.[3] Neurologic and neuropsychiatric complications include headaches, visual changes, paresthesias, hyperkinesia, decreased attention and concentration, and impairments in visual scanning, verbal memory, executive function, and motor control. Psychiatric complications include depression, anxiety, mania, and suicidal ideation. More rarely, IFN may induce mixed affective states in patients with melanoma with both depressive and manic symptoms. Patients are at particular risk of developing hypomania or mania when IFN doses are changed or when IFN-induced depression is treated with antidepressants without concomitant mood stabilisers. The risk of mood fluctuation continues after treatment with IFN stops. Greenburg et al reported that 40% of interferon-treated melanoma patients reported depressed mood and 8% reported severe depression with functional impairment or suicidal ideation.[4] Adverse events following IFN treatment also include attempted and completed suicides.[3]

Neuropsychiatric effects of IFN resulting in depression and/or anxiety may be mistaken by clinicians as representing the flu-like syndrome of IFN treatment, or as a reaction to the trauma of the cancer diagnosis. It is important that clinicians are able to recognise the treatment related psychiatric side effects of IFN and other interventions used to treat melanoma.

3. The incidence and mortality of melanoma in people with psychiatric disorder

This chapter focuses on another interaction, the incidence and mortality of melanoma in people with psychiatric disorder. Studies of overall cancer incidence and mortality in psychiatric patients have had mixed results. Some authors have reported lower than expected cancer incidence or mortality in psychiatric patients, whilst others have found no association.[5-7] Still others have found an increased risk of incidence or mortality.[8, 9] Some of this discrepancy may be explained by differences between psychiatric diagnoses. Schizophrenia has particularly been associated with a reduced incidence of cancer, including melanoma.[10-15] The possible reasons for this are discussed in section 3.4. The use of different methodologies and cancer outcomes may also account for some of the conflicting results. For instance, some studies are restricted to patients in hospital.[16] The reporting of cohort age at study conclusion may be an additional critical confounder. Populations where patients are not followed up to an age when cancer incidence and mortality is maximal may underestimate cancer mortality and incidence, making SMRs complex to interpret. Finally, cancer mortality may not be an ideal marker of the risk of cancer as it is affected by both the susceptibility to developing the disorder, and subsequent survival rates.[17]

Our population-based studies from Western Australia and Nova Scotia addressed some of these issues by evaluating both the incidence and mortality associated with melanoma at the same time in the same population using a standard methodology.[18] The studies used the administrative databases of each jurisdiction, which have several advantages over community surveys or data derived from individual clinical settings[19], in that they provide accessible longitudinal data for an entire jurisdiction at relatively little cost. In both, rates were calculated using the inception cohort method.[20] The start of follow-up was taken as the date of each patient's first contact with mental health services. Patients were censored at the time of occurrence of the event under study, death, or the end of follow-up. The cohort was

limited to people whose first contact with a clinician occurred in the study period, excluding people whose first contact occurred prior to the start of follow-up. This avoids the possibility of survivorship bias, which could otherwise occur if cancer risk changes with time since first contact with a clinician. After reviewing our previous work from Western Australia and Nova Scotia, we present another decade of Australian data to further explore these relationships through to 2007.

3.1 The psychiatric disorders of interest

The psychiatric disorders that form the focus of this chapter include all the mental and behavioural conditions covered in Chapter 5 of ICD9 (290 through 319 inclusive), or ICD10 chapter F. These capture organic psychiatric disorders such as dementia, alcohol and substance use disorders, psychosis, non-psychotic diagnoses including depression, anxiety, and somatoform conditions, and personality and adjustment disorders. Some of the studies also capture ICD external cause codes X60 – X84 (Intentional Self Harm) and non-Chapter 5 codes that cover health service use for mental health issues in the absence of a formal psychiatric diagnosis.

3.2 The Western Australia study 1982-1998

Within the WA Health Services Research Linked Database, we identified all psychiatric patients in Western Australia who had a diagnosis of cancer. The dataset contains information from several different core data sets. These were the Hospital Morbidity Data System (HMDS), the register of births, the register of deaths, Mental Health Information System, and the Cancer Registry. The Mental Health Information System (MHIS) is a register of patients who have had contact with state run community-based or outpatient mental health services in WA or who have been psychiatric inpatients of any public or private hospital in the state since 1966. Although the MHIS has been operating since 1966, the WA Cancer Register only commenced in 1982. Thus the linked cancer registrations covered the period 1982 to 1998. Diagnoses were coded according to ICD-8 until 1978 and according to ICD-9 from 1979 onwards. The last occurring psychiatric diagnosis across the episodes was then assigned as the principal diagnosis according to a hierarchy of diagnoses. If an earlier diagnosis was higher in the hierarchy than the last recorded diagnosis, then the earlier diagnosis was taken as the principal diagnosis. The hierarchy was as follows:

i. ICD-9 290, 293±296: dementia, organic psychotic conditions, schizophrenia and affective psychosis.
ii. ICD-9 291±292, 297±305, 313±315: alcohol and drug psychoses, paranoid states, other nonorganic psychoses, neurotic disorders, personality disorders, sexual deviations, alcohol and drug dependence, and childhood disorders.
iii. ICD-9 306±312, 317±319: adjustment reaction, reaction to stress, depressive disorders nec[1], conduct disorders nec, special syndromes nec and mental retardation.
iv. Other than chapter 5 (mental disorders) diagnoses.

Preference was given to diagnoses made in inpatient treatment units over diagnoses made in acute inpatient units or longer-term psychiatric residential units. Diagnoses made prior to 1979 were mapped from ICD-8 to ICD-9 using the nearest equivalent code. The purpose of these procedures was to allow more specific psychiatric diagnoses to take precedence over less specific diagnoses, and to favour an underlying condition rather than a non-specific

[1] Not elsewhere classified

symptom or event. Cancers were classified according to the ICD-9 classification of diseases at the three-digit level. This classification followed the same system used for classifying cancers by the WA Cancer Register.

Overall there were 672 melanoma patients, of whom 285 were male (Table 1). Males were significantly less likely to be diagnosed as having a melanoma while females had the same rate as that of the general population. There was little variation between psychiatric diagnoses although conclusions were limited by the small number of cases for some of the categories (Table 1). In no case was incidence higher than that of the general population (Table 1).

Proportional hazards regression analysis was used to examine the difference in case fatality between psychiatric patients with cancer and other cancer patients in the general population. After adjusting for demographic factors, there was a 103% higher case fatality following a diagnosis of melanoma in male psychiatric patients than in the general population (95% CI: 46% - 282%) and an 89% higher case fatality rate in females (95% CI: 43%-274%). This represented the highest case fatality rate ratios for any cancer site.

Psychiatric diagnosis	Male			Female		
	N	RR	95% CI		RR	95% CI
Dementia	12	0.67	(0.19 -2.45)	9	0.47	(0.02 – 14.5)
Alcohol/drug disorders	35	0.41	(0.18 -0.94)	12	0.46	(0.13 - 1.59)
Schizophrenia	22	0.76	(0.42 - 1.38)	20	0.93	(0.50 - 1.71)
Affective psychosis	19	0.70	(0.33 - 1.49)	43	1.06	(0.73 - 1.54)
Other psychoses	6	0.62	(0.15 -2.54)	12	0.49	(0.14 – 1.71)
Neurotic disorders	67	0.99	(0.76 - 1.30)	129	1.10	(0.91 - 1.33)
Personality disorders	20	1.29	(0.85 - 1.95)	15	1.26	(0.76 – 2.10)
Stress/Adjustment reaction	8	0.46	(0.09 - 2.37)	24	0.78	(0.45 - 1.38)
Depressive disorder	8	0.61	(0.19 - 1.93)	21	0.99	(0.57 - 1.70)
Other mental disorder	31	0.79	(0.48 - 1.30)	26	0.72	(0.38 - 1.34)
Attempted self-harm	14	0.68	(0.29 - 1.61)	26	1.14	(0.76 – 1.70)
Non-specific diagnosis	43	1.11	(0.84 - 1.46)	50	0.85	(0.60 - 1.21)
Total	285	0.75	(0.64 - 0.89)	387	0.92	(0.82 – 1.04)

Table 1. Cancer Site - Malignant Melanoma, by Principal Psychiatric Diagnosis. WA 1982 – 1998.

3.3 The Nova Scotian study

The West Australian administrative data do not include treatment for mental health disorders in private settings. Accordingly, studies from Australia, where both private health insurance and hospitals play a sizable role in providing medically necessary care, may not apply to jurisdictions such as Canada with universal health care provision. We therefore compared cancer incidence, first admission and mortality rates for people with psychiatric disorder in relation to the general population of one Canadian province, Nova Scotia. In addition, the Australian data were restricted to people in contact with specialist mental health services and did not include primary care where the majority of people with mental health problems are treated. Lastly Canadian data allowed for the study of patterns of melanoma in a less sunny environment.

Under the Canada Health Act, all Canadian residents are entitled to inpatient or outpatient care that is free at the point of delivery.[21] Patients receive treatment at publicly -funded facilities or are seen by private psychiatrists or general practitioners in the community who bill the Provincial health plan. However, the Provincial health plan does not cover visits to private psychologists or other mental health professionals in private practice. Importantly, there are no private psychiatric beds.[21]

We evaluated the association between mortality and psychiatric disorder for all patients of specialist services and primary care across Nova Scotia, using the province's linked administrative databases. The one-million residents have similar morbidity and mortality rates to the rest of Canada, although more live in rural areas than in other provinces. Halifax is the major metropolitan centre.

We evaluated the association between cancer mortality and psychiatric disorder for all patients of specialist services and primary care across Nova Scotia. We used the following Provincial administrative databases, held at the Population Health Research Unit (PHRU) of Dalhousie University, to identify anyone in contact with health services for psychiatric problems:[22]

- The Medical Services Insurance (MSI) database of all fee-for-service claims by physicians including patient demographics, date of service and diagnosis from the Clinical Modification of the 9th Revision of the International Classification of Diseases (ICD-9-CM). This includes family physicians and psychiatrists.
- The Canadian Institute for Health Information (CIHI) Discharge Abstract Database (DAD), which includes admissions, separation dates, diagnoses and procedures.
- Mental Health Outpatient Information System data (MHOIS), which records service contacts, demographics and diagnoses in the public sector. This includes contacts with all mental health clinicians, not just physicians.

This method was consistent with the definition used by the Public Health Agency of Canada (PHAC) for the surveillance of treated psychiatric disorder.[19, 23] As in Western Australia, we used an inception cohort. We included patients whose first psychiatric contact with primary or specialist services occurred between January 1, 1995 and December 31, 2001, and linked data using the provincial health card number as a unique identifier. Health card numbers are present in over 99% of records irrespective of database, and encrypted to ensure confidentiality.

We included everyone with ICD 9 codes of 290 through 319 inclusive, or their ICD-10 (chapter F) or DSM-IV equivalents. We also included non-specific mental disorders outside Chapter 5 of ICD-9 (formal mental disorders), such as injury of undetermined intention or psychosocial factors influencing health status, to ensure comparability with previous Australian work.[17] We did not include non-chapter 5 diagnoses of primary care patients, as they would not necessarily be psychiatric. We included contacts with primary or specialist services. We used a hierarchy of inpatient versus outpatient, and specialist versus primary care, reflecting both the increasing percentage of patients with severe mental illness and data reliability. It also allowed comparison with Australian data

We then transferred this data file to Cancer Care Nova Scotia who linked it to the Nova Scotia Cancer Registry (NSCR) to identify cancer incidence rates for the cohort. The NSCR has population-based incidence data that dates from 1964.[28] All malignant and in-situ tumours are reportable by law within the province. Other sources of data include Pathology Reports (1982 onwards) and death certificate information for all provincial deaths (from

1989 onwards). Registry operations meet the consensus on cancer registration standards outlined by both the Canadian Cancer Registry (CCR) and the North American Association of Central Cancer Registries (NAACCR).[18] The NSCR works collaboratively with Statistics Canada to ensure that Nova Scotia data is part of the national Canadian Cancer Registry. We classified cancers according to the ICD-9 classification of diseases at the three-digit level. This classification followed the same system used for classifying cancers by the NSCR. The cancer sites selected for analysis were the most frequent cancers in males and females.

We grouped disorders into dementia and other organic conditions (290-294), schizophrenia (295), other non-affective psychoses (297, 298.0, 298.1), alcohol/drug disorders (303-305), mood disorders (affective psychoses/depression-296, 298.2-298.9, 300.4, 311), neuroses (300 except 300.4), personality disorders (301), adjustment reactions (308-309), and other mental disorders (all remaining Chapter 5 diagnoses and those outside Chapter 5). Rates were again calculated using the inception cohort method.[20] The start of follow-up was taken as the date of each patient's first contact with a mental health clinician. Patients were censored at the time of occurrence of the event under study, death, or 31st December 2001. The cohort was limited to people whose first contact with a mental health clinician occurred in the study period, excluding people whose first contact occurred prior to the start of follow-up. We derived mortality rates from the Statistics Canada Vital Statistics Database. Person-years at risk were calculated separately for each outcome.

We calculated age- and sex-adjusted mortality, first admission and incidence rates for carcinoma by direct standardisation, using the average population distributions in Nova Scotia from 1995-2001 inclusive as the standard weights. We then calculated rate ratios (RRs) relative to the rate in the general NS population, using 95% confidence intervals to test for significance. Variance of the standardised rate ratios was calculated using expansion in Taylor series, using a logarithmic transformation of the ratio.[24] We assessed whether the rate ratios for mortality, first admission and incidence in psychiatric patients were significantly different from the general population of Nova Scotia as indicated by 95% confidence intervals that included a value of 1.0. We also assessed whether there were differences between mortality, first admission and incidence rate ratios. Unlike the Australian study, we were not able to investigate predictors of cancer incidence using Cox regression of NSRC records because of the nature of the data sharing agreement and therefore were unable to compare adjusted hazard ratios for incidence, first admission and mortality.

Table 2 presents the unadjusted rate ratios. Incidence rate ratios (RRs) were lower than might be expected given the mortality and first admission RRs, and no higher than that of the general population. By contrast the mortality rate was higher especially for men.

Gender	**Mortality rate**			**Cancer Incidence**		
	N	RR	95% CI	N	RR	95% CI
Males	17	2.18	(1.34-3.44)	151	1.05	(0.92-1.21)
Females	3	1.37	(0.64-2.92)	99	0.91	(0.73-1.07)
Total	20	2.00	(1.20 – 3.30)	250	0.98	(0.85-1.14)

Table 2. Comparing Cancer Incidence and Cancer Mortality rates: Nova Scotia, 1995 – 2001.

Melanoma was only one of a few cancers to show this pattern, the others being prostate, bladder and colorectal cancers. This pattern was especially noticeable in males (Figure 1).

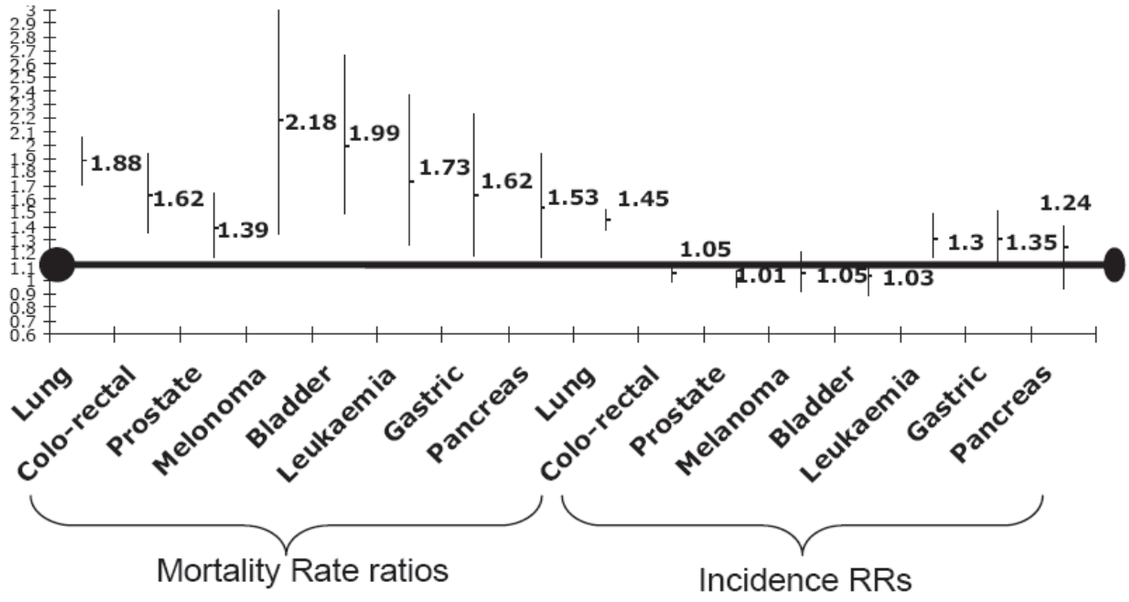

Fig. 1. Comparing cancer mortality & incidence in male Nova Scotian psychiatric patients

3.4 Implications of both studies

There is a common assumption that problems in self-care might explain the increased mortality from cancer, including melanoma, for patients with psychiatric disorder. If that were the sole explanation, incidence would consistently reflect the increased mortality rate. However, our work in both Canada and Australia suggests that psychiatric patients are no more likely to develop melanoma than the general population but still have increased mortality for the same condition. There may be a number of explanations for this increased case fatality rate. One might be that psychiatric patients present later, and with more advanced disease, than the general population. Another possibility is reduced access to general medical care. If doctors are less inclined to treat skin cancer in people with psychiatric disorder than in others, people with psychiatric disorder and skin cancer might be less likely to be admitted to hospital and therefore be selectively missed by researchers. This inequity would be of concern, and would confirm work from Ontario showing that other marginalised populations, such as those of low income, are less likely to receive specialist procedures such as adjuvant or palliative radiotherapy.[25]

Decreased screening for early lesions could also explain the increased mortality so that psychiatric patients only present when symptoms or signs become more obvious in later stages of the disease. In places without universal health care, ability to pay for care may be a factor. Even with universal health care, psychiatric patients may have problems in registering with a family physician, missed appointments, or difficulties in communication or scheduling appointments. Finally, psychiatric patients may have a worse prognosis even after adjusting for staging at presentation. Survival from cancer is associated with levels of depression, emotional expression and support. Some work suggests that individuals with depression prior to the diagnosis of the cancer have a worse survival rate than those with depression following diagnosis.[26] In the case of melanoma, several psychosocial variables measured at baseline are independently prognostic of survival. [26] The greatest protective effect was conferred by a belief that treatment would lead to cure or long-term survival and by marital status. [26] For those patients who were positive about the outcome of their

treatment (i.e., who thought treatment would cure them or prolong their life long term), the risk of dying was reduced by 65%. Similarly, for patients who were married, the risk of dying was reduced by 50%. Two aspects of psychological adjustment were also protective. Patients who reported that their melanoma did not greatly affect their day-to-day life survived significantly longer than those who felt it was having a big impact on their lives, and those who exhibited greater levels of anger about their situation survived longer. Finally, quality of life scores were also significantly predictive of outcome. Further support for the importance of psychiatric factors in survival from melanoma comes from findings that structured group psychotherapy may help extend survival.

3.5 The special case of schizophrenia

In the case of schizophrenia, there is a suggestion that the incidence of skin cancer including melanoma is especially lower than the rest of the population. A Danish record linkage study investigated the incidence of cancer in a cohort of 9156 first admitted schizophrenic patients.[13] Reduced cancer incidence was particularly marked for genital cancers, and skin cancers, including malignant melanoma. The standardised incidence ratio for malignant melanoma was 0.14, although the study was limited by small numbers (1 case of melanoma). Goldacre and colleagues reported a similar finding in a cohort analysis of linked hospital and death records comparing cancer rates in people with schizophrenia with a reference cohort in the south of England[27]. They reported an adjusted rate ratio for melanoma of 0.2 (95% CI 0.02-0.74). A recent meta-analysis of cancer incidence rates in patients with schizophrenia combined 16 data collections from 15 studies. The pooled standardised incidence rate ratio of melanoma in patients with schizophrenia was significantly reduced (SIR 0.71 CI 0.57-0.87). A similar finding was reported for prostate cancer.[28]

Several biological hypotheses have been proposed to explain why people with schizophrenia might be protected against cancer in general, including a protective effect of excess dopamine, enhanced natural killer cell activity, an increase in the rate of apoptosis and modulation by antipsychotic drugs of the human cytochrome enzymes involved in mutagen activation and elimination[27].

There may be other reasons that are more specific to melanoma. One possibility is that people with schizophrenia may spend less time in the sun than the general population, and this may be compounded by issues such as weight gain (a common side effect of anti-psychotic medication) that may reduce both the desire and ability to engage in physical activity outdoors. Conversely if they do go out into the sun, people with schizophrenia might be less likely to take protective measures such as sunscreen or a hat. Against this explanation is that malignant melanoma is mainly related to childhood sun exposure,[29] and there is no evidence of reduced childhood sun exposure in individuals who subsequently develop schizophrenia.

In addition, sun exposure, perhaps through its role in vitamin D synthesis, may actually have a protective role in the development of schizophrenia. [30] McGrath has suggested that vitamin D deficiency in the neonate might be a risk factor for the subsequent development of schizophrenia. The same author also suggested that relative vitamin D deficiency might explain some of the epidemiological features of schizophrenia such as the excess of winter births, and the increased incidence of schizophrenia in dark-skinned migrants when they move to countries with more limited sunshine[31]. It is therefore possible that an inverse relationship between sun exposure and the development of schizophrenia could also partially explain why melanoma is seen less frequently in people with schizophrenia.

4. Our latest findings

We extended our work with another decade of data from Western Australia to further explore these relationships through to 2007. As before we used the linked administrative data from Western Australia from 1988 to 2007 employing the same databases. We also extended our study to the Australian State of Queensland, which has the highest rate of melanoma in Australia. On this occasion we investigated whether the pattern of psychiatric patients being no more likely to develop melanoma than the general population, but still having increased mortality for the same condition could be related to either:

1. delayed diagnosis or late presentation by comparing cancer staging at the time of diagnosis in psychiatric patients & the general population as determined by the presence of metastases; or
2. reduced access to specialised cancer therapy such as chemotherapy, radiotherapy and surgery once the diagnosis has been made.

If the former were true, it would indicate that specific action is required to ensure that clinicians and patients themselves consider the diagnosis of cancer in response to new symptoms, and that psychiatric patients are encouraged by their GP to attend, and are able to access appropriate routine cancer screening services. If the second were true it would indicate inequity of access to surgery, and adjuvant or palliative radio- and chemotherapy.

To investigate the first question, we calculated the proportion of patients with metastases at diagnosis, as melanoma staging is not collected in the cancer registry in WA. This was undertaken by extracting the behaviour code, which forms the end digit of the morphology code, a code that must be provided should a neoplasm ICD10 code be recorded (C00 – C96, D00 – D48). Behaviour code /6 refers to a malignant neoplasm that is stated or presumed to be secondary so a morphology code of M8720/6 refers to melanoma that is stated or presumed to be secondary. Also ICD10 code C80 is a malignant neoplasm of unknown primary origin; these have also been extracted to represent secondary cancers at diagnosis. In Queensland, the cancer registry does collect data on melanoma staging based on Clark's level, thickness and ulceration but it is impossible to determine when the cancer metastasised. Data on the time of metastasis were therefore extracted from hospital admissions using ICD10 codes C77 – C79, which are the particular ICD10 codes for a secondary cancer site. We also measured the proportion of patients developing metastases at 90 days and one year after presentation.

To investigate the second question, we collected basic information on cancer treatment, including chemotherapy (yes/no), radiotherapy (yes/no) and surgery (yes/no). For surgery we also collected information on time to surgery from diagnosis. For palliative care we assessed the proportion of cases that had at least one course of palliative radiotherapy (PRT) in the last 2 years of life. This measure has been used elsewhere as a proxy for access to radiotherapy services.[32] For surgery we collected information on time to surgery from diagnosis. We used the method of Valery, Coory et al in their studies of cancer services in Indigenous Queenslanders to compare access to chemotherapy, radiotherapy and surgery.[23]

4.1 Aims

The aims were to investigate the following:

1. To compare the incidence and mortality of melanoma in psychiatric patients and the general population of Western Australia and Queensland from 1988 to 2007 (2002 to 2007 in the case of Queensland) and to determine whether there are significant

differences between types of psychiatric illness (e.g. schizophrenia, affective disorder) in incidence, and mortality rates.
2. To determine whether psychiatric patients present at a more advanced stage of melanoma at diagnosis than the general population as determined by the presence of metastases and whether there is a difference in cancer stage at presentation between male and female psychiatric patients.
3. To determine whether psychiatric patients have a poorer prognosis after controlling for cancer stage at presentation and whether there is a difference in prognosis between males and females.
4. To determine whether psychiatric patients diagnosed with cancer access surgical services equally in comparison with the general population diagnosed with cancer, and whether there is a difference in access by gender.
5. To determine whether psychiatric patients diagnosed with cancer access adjuvant or palliative chemotherapies & radiotherapies equally in comparison with the general population , and whether there is a difference by gender

4.2 The hypotheses

The hypotheses were that:
1. Psychiatric patients would be more likely to present with more advanced cancer, as determined by the presence of metastases.
2. Psychiatric patients would also be less likely to receive the appropriate specialist surgical procedures, adjuvant or palliative chemotherapies & radiotherapies than the general population, even after adjusting for socio-demographic and clinical features (including the presence of metastases).
3. These effects would be more marked for patients with severe mental illnesses in terms of either diagnoses (e.g. schizophrenia) or of having ever required admission to a psychiatric unit, and more marked in men than women.

4.3 Study design

This was a population-based record-linkage analysis from the two Australian states (Western Australia and Queensland), using a historical cohort to calculate rate ratios. In the case of the Western Australian data we also calculated rate ratios using the inception cohort method. We could not do the same for the Queensland data as these did not extend far enough to identify an inception cohort. It is important to do both. Inception cohort studies that study incident psychiatric cases over a period of time are less subject to survivorship bias given that the majority of excess deaths due to physical causes occur in the first seven years after psychiatric diagnosis.[17] However as they are based on incident cases, there may be fewer subjects than a study based on prevalence, and so a greater chance of insufficient statistical power. This is particularly relevant for less common outcomes such as mortality in individual psychiatric diagnoses that are less common such as schizophrenia. Using an inception cohort also allowed comparison with our previous studies from Western Australia and Canada. Historical cohorts are based on prevalent psychiatric cases and so yield larger numbers. They are therefore more appropriate for rarer outcomes. In this case, use of an historical cohort allowed the addition of Queensland data, so further increasing statistical power. On the other hand, historical cohorts may underestimate overall mortality risk because of survivorship bias.

4.4 Data sources

The project used linked datasets provided by the data linkage centres of Queensland and Western Australia. Both form part of Australia's Population Health Research Network (PHRN) (Figure 2). PHRN is a national network of Australia's extensive health data that provides linkage across data sets in all States and Territories for population health research (Figure 2). Subject anonymity was preserved by a rigorous privacy protocol, as it was not possible to obtain informed consent given we were using large population datasets. In each case, the relevant data custodian provided demographic data, but no other information, to data linkage centres within the Health Department of each jurisdiction. Within the linkage centre, probabilistic and deterministic matching were used to link within and between the datasets based on identifying information (ID), including name, date of birth, aliases, sex, and Indigenous status. Each person was assigned a unique project ID that was returned to the data custodians. The data custodian attached the relevant clinical or service information to the unique project ID, but no identifying information. These anonymised data extracts were then released to the researchers.

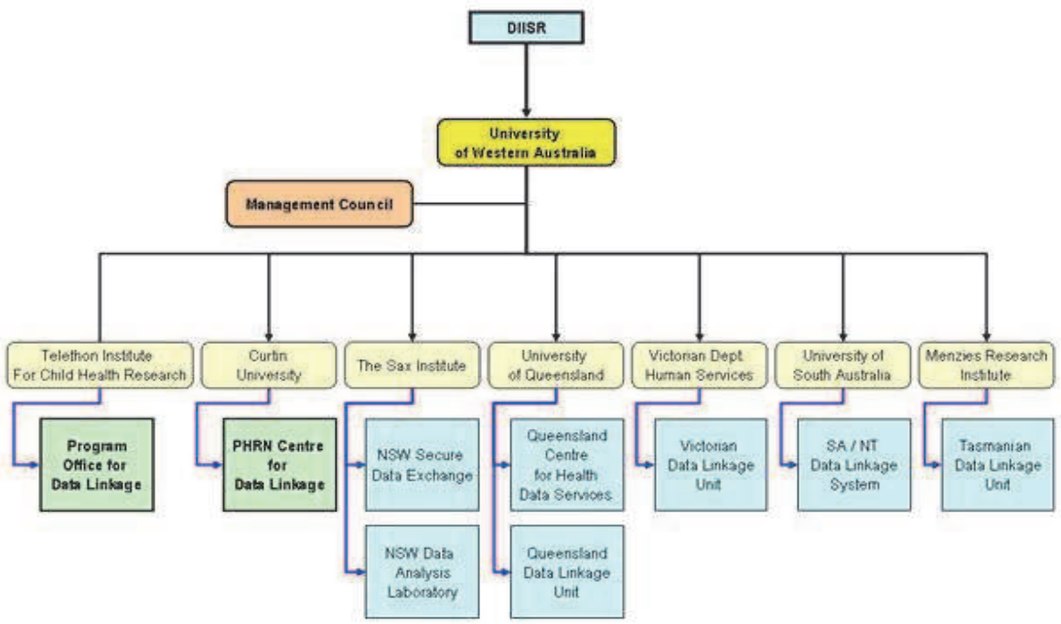

Fig. 2. Australia's Population Health Research Network.

4.4.1 Western Australia

We identified users of mental health services in WA with cancer registrations and death records, using the WA Health Services Research Linked Database. In this database, individual patient records have been linked by means of probabilistic matching, using the Automatch software package,[33] as there are no unique identification numbers in use on the core data sets. Name, residential address, date of birth and sex are the principal fields used in the probabilistic matching.[20] The probabilistic matching technique is based on estimating

the probability that any two records represent the same person (or event), while allowing for the possibility of errors or changes in the identifying information used for matching.[20] The dataset contains information from several different core data sets. As before, we used the following: Hospital Morbidity Data System (HMDS), the register of births, the register of deaths, Mental Health Information System, and the Cancer Registry (Figure 3). The Mental Health Information System is a register of patients who have had contact with state run community-based or outpatient mental health services in WA or who have been psychiatric inpatients of any public or private hospital in the state.

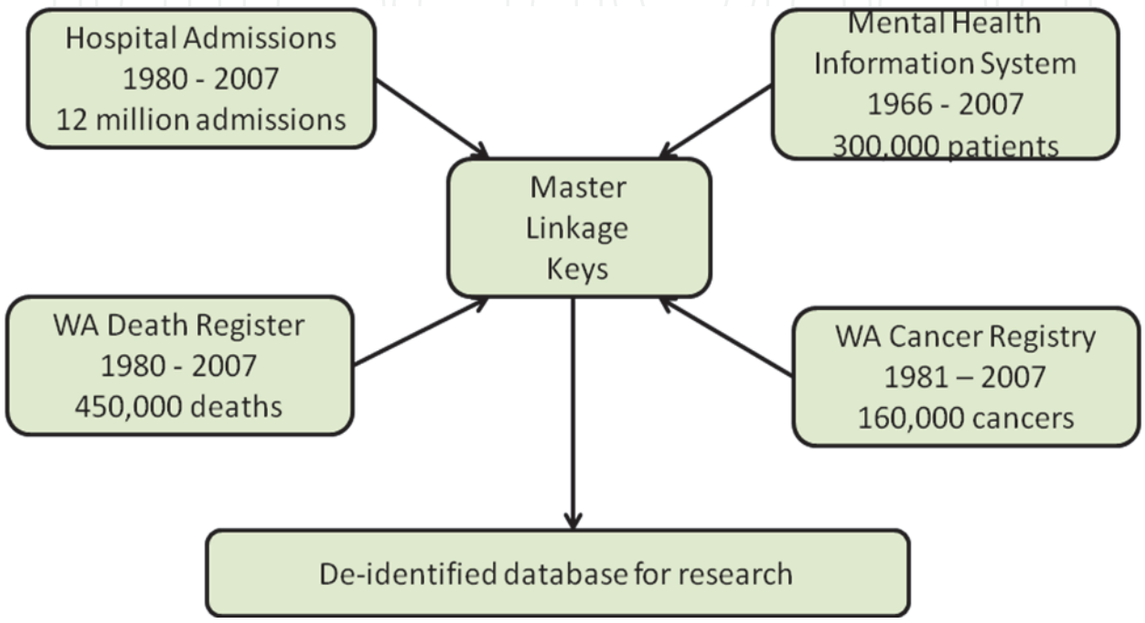

Fig. 3. Schema of the WA Health Services Research Linked Database

Within the WA Health Services Research Linked Database, we identified all psychiatric patients in Western Australia who had a diagnosis of cancer. We used the same case definition for psychiatric disorder that has been validated by the Public Health Agency of Canada (PHAC) for use in administrative databases.[23] This is any contact with a health service with an ICD-9 diagnosis of 290-319 or ICD10 equivalent. As stated previously, we used both the historical and inception cohort method. For the latter, we restricted the study cohort to those patients whose first contact with mental health services occurred between 1988 and December 2007. The start of follow-up was the date of each patient's first contact with mental health services.

Patients were censored at the occurrence of the event under study, death, or 31st December 2007. We compared the outcomes of this cohort to the general population through the calculation of age-, sex-standardised rates, which were then adjusted for confounders using multivariate analyses (see section 4.6 on statistical methods). Outcomes were mortality, metastases and access to surgery or radiotherapy. Data linkage of all administrative data, including epidemiological databases, was carried out by the Data Linkage Branch at the WA Department of Health which houses the Western Australian Health Linked Database.

4.4.2 Queensland

We used a similar methodology in Queensland. We extracted data from the following datasets: the Queensland Hospital Admitted Patients' Data Collection (QHAPDC), the Client Event Services Application (CESA – now called CIMHA, community integrated mental health application), Queensland Cancer Registry (including death data), BreastScreen QLD and the Australian Bureau of Statistics Estimated Resident Population (Table 3). As in Western Australia, we identified all psychiatric patients in Queensland with the diagnosis of cancer using the Public Health Agency of Canada (PHAC) case definition of psychiatric disorder. In this case, the Link King software package was used to link individual patient records probabilistically and deterministically.

Data source	Data obtained
Queensland Hospital Admitted Patients' Data Collection	In-patients receiving treatment in a designated psychiatric unit in a public hospital or public psychiatric hospital in QLD; all cancer admissions in public & private hospitals and all co morbidity data in the twelve months prior to the cancer diagnosis (Charlson Deyo)
Client Event Services Application (CESA)	Clients receiving treatment in a public-sector community mental health service
Queensland Cancer Registry	All QLD cancer registrations, with details of diagnosis including date, ICD-10 site code, morphology code. Data on people who die of cancer or cancer patients who die of other diseases linked to mortality files of the Registrar of Births, Deaths & Marriages & linked to hospital & pathology data.
BreastScreen QLD	All voluntary screening records for patients subsequently diagnosed with breast cancer
Australian Bureau of Statistics	Estimated resident population for all of Queensland

Table 3. Queensland data sources

4.5 Data quality

The WA Health Services Research Linked Database is unique in Australia and one of only a small number of comprehensive record linkage systems in the world.[20] These include the Oxford Record Linkage Study, the Scottish Record Linkage System, the Rochester Epidemiology Project, the Manitoba Population Health Information System, the Nova Scotian linkable database system and the Scandinavian case registers. Probabilistic matching of records is based on estimating the probability that any two records represent the same person (or event), while allowing for the possibility of errors or changes in the identifying information used for matching. The WA Data Linkage System uses a chain of links method to map the linkage of records. Each individual source record from each of the component data sets is assigned a unique record number. Separate individuals are then identified by assigning a number to identify the chain, called the root number. This root number is the record number of the first record in the chain for each person. A master linkage file records pointers specifying the root number for each individual source record in the system, enabling chains of records for each individual to be created.

The master linkage file is date stamped and records the history of all updates to the system, so the state of the linkage can be reconstructed as it existed on any previous date.[20] The construction of the WA Linked Database and its ongoing maintenance are performed by an extramural unit of the Centre for Health Services Research located within the Health Information Centre. Access to identifying information is restricted to the staff of the extra-mural unit. Once the data have been linked, a second de-identified copy of the WA Linked Database is created. The de-identified version does not contain names, addresses (except for postcode), dates of birth (except for month and year of birth), individual hospital identifiers or individual doctor identifiers. Most research is conducted from this second de-identified copy of the database. The system allows for the protection of the confidentiality of individual patients and the information contained in the administrative health records, while still allowing population-based health services research to be performed.

The WA Health Services Research Linked Database currently contains in excess of 12 million records, and occupies over 12 Gb of storage space. By far the largest component of the database is the Hospital Morbidity Data System (HMDS) which contains over 7 million records. The register of births contains around 400,000 entries, while the register of deaths contains approximately 450,000 entries. The MHIS contains details for just over 300,000 patients of mental health services (Figure 3). As the WA Data Linkage System brings together separate records for each person, it is possible to examine the consistency of recording fixed personal characteristics such as sex, aboriginality, and date of birth. For each of these characteristics, the entire set of records for each patient have been examined to check that the field was recorded the same in all core data records regardless of their source. Overall, sex was consistently recorded across all records for 98.5% of the study population, aboriginality was consistently recorded for 97.3% of the study population and date of birth was consistently recorded (to an exact date) for 83.3% of the study population

Data linkage in Queensland has not progressed as far as that in Western Australia since the state has only recently begun developing linkage infrastructure whereas WA began this process in 1995. There are a large number of databases available but currently linkages exist only within the Queensland Hospital Admitted Patient Data Collection (QHAPDC) for years 2003/04-2008/09 and between QHAPDC and the Registrar General's (RG) Mortality data. RG mortality data is available from 1996 onward and contains approximately 360,000 records. RG birth data (over 64,000 records in 2010) is also available but the exact dates that are available for research are yet to be determined and this collection hasn't yet been linked with other databases. QHAPDC data collection began in January 1993 and on average there are about 1.8 million episodes of care added to the QHAPDC database each year. Episodes of care for admitted mental health patients are also captured within this database and a mental health module was added in July 1996. Non-admitted mental health patients that are seen by community mental health facilities are included in the Consumer Integrated Mental Health Application (CIMHA) database which, over a five year period (2006 – 2010), contained over 280,000 consumer (patient) records.

There is also less information on the quality of the Queensland data as these datasets have only recently been used for research. Some published information is available on the quality of variables such as Indigenous status, which can be defined either through place of residence or through the recording of Indigenous status in datasets such as the Queensland Hospital Admitted Patient Data Collection (QHAPDC). Indigenous status is correctly identified in about 89% of cases with variation by definition used.[34]

4.6 Statistical methods

We identified cancer type, cancer stage at diagnosis by cancer type, principle psychiatric diagnosis, and time from psychiatric contact with service until cancer incidence. We initially calculated the age- and sex-standardised mortality rate, cancer incidence and proportion with metastases at diagnosis for all cancers for anyone meeting the PHAC case definition of psychiatric disorder. We used the method of Lawrence et al. to group cases in terms of severity of psychiatric diagnosis.[20] We also calculated separate age- and sex-standardised ratios for cases who had ever had inpatient psychiatric treatment as opposed to those who had only had outpatient treatment, as a marker of psychiatric disease severity. Finally we calculated rates of surgery, and adjuvant or palliative radio- and chemotherapy in the same way.

The average population distribution in Western Australia over the period 1988-2007 was used as a standard weight. In all cases we used direct standardisation. Rates were calculated overall, and by principal psychiatric diagnosis. Relative risks for mortality, 1st admissions, incidence, and cancer stage for different cancer types were calculated in groups of patients in the study cohort relative to the rate in the WA population. Denominators were taken from estimated resident population counts. We compared relative risks by psychiatric diagnosis, cancer type, diagnostic case complexity and treatment setting (ever admitted as an in-patient versus outpatient or community care).

The relative importance of factors that were identified on univariate analysis as being associated with the particular outcome under study (e.g. presence of metastases, mortality) were further analysed using the Cox proportional hazards model. This methodology requires the identification of a terminal event that marks either survivors or non-survivors. Consequently, there are two basic requirements for a survival analysis design- time of origin into the study and the meaning of failure. In our study, the former was entry into the study, and the failure was defined as mortality. One advantage of survival analysis is that it allows an examination of data from all participants who entered the study over the sampling timeframe (until the end of the study) without imposing arbitrary cut-off dates on the data. Participants who were still alive at the end of the study were treated as censored observations (i.e. an observation for which the event does not occur). Cox's model allowed us to quantify the weight of or significance of variables that increased or decreased the risk of admission. Using the statistical technique of "backward elimination," we eliminated non-significant variables from each group of variables sequentially in order to retain the relative risk of each significant variable. For longitudinal items (e.g. mortality), we included the presence of metastases, as well as all other relevant socio-demographic & clinical variables. Survival analysis is more appropriate than logistic regression for studying time to event data (e.g. time to mortality following cancer diagnosis) while logistic regression is useful in developing an initial model.

4.7 Preliminary results

We present initial results from the Western Australian arm of the study, as Queensland data are as yet unavailable. Because the results are confined to Western Australia, we have given greater prominence to the inception, as opposed to historical cohort although we present the results of both. For all persons in WA between 1988 - 2007, malignant melanoma represented approximately 10% of all diagnosed cancers in people with a psychiatric disorder (n 618 / 6586).

4.7.1 Baseline characteristics

During this period there were 618 psychiatric patients in the inception cohort who had a diagnosis of malignant melanoma, 285 of whom were male (Table 4). There were 14,059 non psychiatric patients with melanoma. Both males and females were significantly less likely to be diagnosed as having a melanoma than the general population. There was little variation between psychiatric diagnoses although conclusions were limited by the small number of cases for some of the categories. The only disorders associated with increased incidence were Other Psychoses and Other Mental Disorders (both male and female) as well as Attempted Self Harm (females). Melanoma incidence in patients with schizophrenia was no higher than that of the general population, although the 95% confidence intervals were wide, reflecting the small number (24) of patients with schizophrenia who developed melanoma (Table 4). Some diagnoses were actually associated with increased melanoma risk: attempted self harm in females and other psychoses and other mental disorder in both males and females. There was no clear pattern with the other diagnoses, again possibly because of small numbers and wide confidence intervals.

Psychiatric diagnosis	Male			Female		
	N	RR	95% CI	N	RR	95% CI
Dementia	37	0.87	(0.63 - 1.19)	52	0.90	(0.80 - 1.02)
Alcohol/drug disorders	20	0.79	(0.51 - 1.21)	7	1.10	(0.78 - 1.54)
Schizophrenia	12	0.90	(0.68 - 1.19)	12	1.21	(0.86 - 1.71)
Affective psychosis	39	1.03	(0.79 - 1.35)	40	0.86	(0.63 - 1.19)
Other psychoses	28	1.33	(1.05 - 1.69)	18	2.12	(1.71 - 2.63)
Neurotic disorders	17	0.72	(0.43 - 1.19)	42	0.93	(0.66 - 1.29)
Personality disorders	6	1.47	(0.93 - 2.32)	5	1.30	(0.91 - 1.86)
Stress/Adjustment reaction	37	0.83	(0.55 - 1.25)	48	0.86	(0.56 - 1.32)
Depressive disorder	40	0.89	(0.63 - 1.25)	62	1.12	(0.90 - 1.39)
Other mental disorder	28	1.35	(1.01 - 1.80)	13	1.44	(1.12 - 1.86)
Attempted self-harm	5	1.38	(0.95 - 2.02)	5	2.24	(1.62 - 3.11)
Non-specific diagnosis	16	1.05	(0.73 - 1.51)	29	1.14	(0.91 - 1.43)
Total	285	0.72	(0.61 - 0.86)	333	0.84	(0.73 - 0.96)

Table 4. Cancer Site - Malignant Melanoma, by principal psychiatric diagnosis. WA, 1988 – 2007 (inception cohort).

In both psychiatric patients and the general population, melanoma incidence rate increased with age. The rate was higher in males than in females, except in psychiatric patients between the ages of 35-55 years. The peak incidence for both the general population and psychiatric patients was between 75 – 85 years of age (Figure 4).

In the case of the historical cohort, there were 1,166 psychiatric patients who had a diagnosis of malignant melanoma, 526 of whom were male (Table 5). On average, incidence rates using the historical cohort method were slightly lower than those calculated using the inception cohort approach. As in the inception cohort, males and females were significantly less likely to be diagnosed as having a melanoma. There was little variation between psychiatric diagnoses although conclusions were again limited by the small number of cases for some of the categories. As before, rates increased with age and the rate was higher in males than in females, except between the ages of 35-55 years (data not shown).

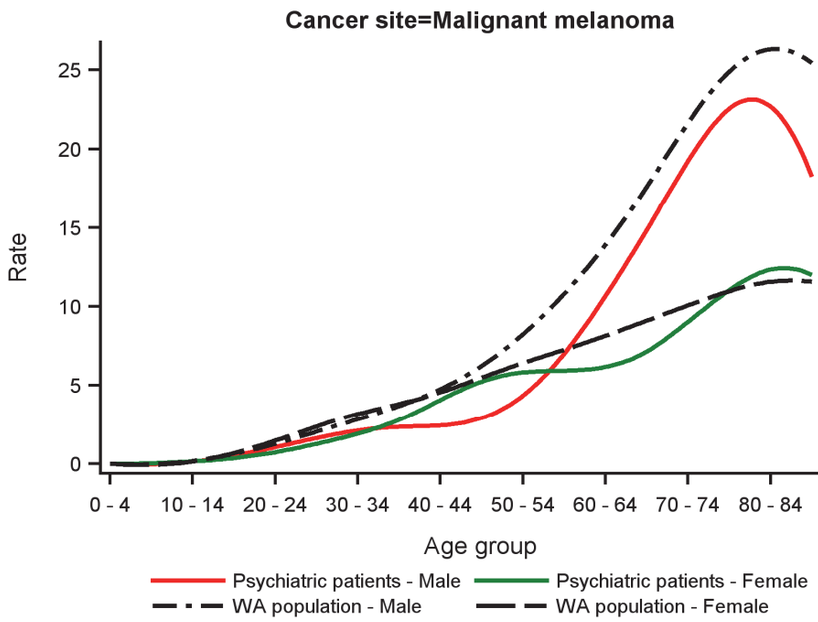

Fig. 4. Age-specific melanoma incidence rates, psychiatric patients versus WA population (inception cohort).

With greater numbers (n=57), melanoma incidence in people with schizophrenia was significantly lower in both males (0.51 - 95% CI 0.29 - 0.92) and females (0.68 - 95% CI 0.46 - 0.99). Again with more subjects and narrower confidence intervals, melanoma incidence was also lower in dementia and affective psychoses in both sexes. They were lowest in males with alcohol and drug disorders. The only situation where incidence was higher than that of the general population was for females who attempted self harm (Table 5).

Psychiatric diagnosis	Male			Female		
	N	RR	95% CI	N	RR	95% CI
Dementia	59	0.69	0.51 - 0.93	67	0.79	0.71 - 0.88
Alcohol/drug disorders	36	0.49	0.29 - 0.82	16	0.78	0.52 - 1.18
Schizophrenia	33	0.51	0.29 – 0.92	24	0.68	0.46 – 0.99
Affective psychosis	67	0.71	0.51 – 0.99	88	0.68	0.50 – 0.93
Other psychoses	44	0.81	0.58 – 1.15	29	1.08	0.70 – 1.67
Neurotic disorders	48	0.76	0.54 – 1.06	83	0.78	0.58 – 1.04
Personality disorders	19	0.98	0.67 – 1.44	15	0.91	0.60 – 1.38
Stress/Adjustment reaction	53	0.61	0.39 – 0.98	84	0.69	0.46 – 1.03
Depressive disorder	68	0.68	0.48 – 0.95	135	0.90	0.74 – 1.09
Other mental disorder	44	1.06	0.77 – 1.48	24	1.16	0.86 – 1.55
Attempted self-harm	6	1.13	0.86 – 1.48	11	1.61	1.17 – 2.20
Non-specific diagnosis	49	0.86	0.64 – 1.16	64	1.02	0.79 – 1.30
Total	526	0.60	0.52 – 0.70	640	0.71	0.64 – 0.80

Table 5. Cancer Site - Malignant Malignant Melanoma, by principal psychiatric diagnosis. WA, 1988 – 2007 (historical cohort).

4.7.2 Presence of metastases at baseline or follow-up

50 inception cohort patients with primary melanoma had metastasised at time of original diagnosis as determined from the tumour behaviour code (8.1%) This was not significantly different from that of the general population (9.9% - p = 0.107).

Ninety days later, 3 patients had developed metastases. Again there was no difference between psychiatric patients and the general population (0.5% and 0.6% p=0.771). By one year, 7 patients had developed metastases. As before, there was no difference between psychiatric patients and the general population (1.2% and 1.6% respectively P=0.332).

For the historical cohort, 86 (7.4%) patients with an assigned primary melanoma had metastasised at time of original diagnosis as determined from the tumour behaviour code. This was slightly yet significantly different from the general population 9.9% p=0.002. Ninety days later, 7 patients had developed metastases. Again there was no difference between psychiatric patients and the general population (0.6% and 0.6% respectively p=0.720). By one year, 12 patients had developed metastases. As before, there was no difference between psychiatric patients and the general population (1.1% and 1.6% respectively p=0.157).

4.7.3 Receipt of chemotherapy or radiotherapy and time to surgery

We then investigated differences between psychiatric patients and the general population with regards access to surgery and receipt of chemotherapy and radiotherapy. 0.7% (n=4) of psychiatric patients received chemotherapy for their melanoma within 90 days of diagnosis compared with 1% of melanoma patients with no contact with MHS. This difference was not statistically significant (p=0.216, Table 6). A similar proportion of psychiatric patients and people from the general population received radiotherapy (p=0.196 Table 6).

Procedure	Cohort	
	Inception	No contact with MHS
Started chemotherapy within 90 days of cancer diagnosis	0.7%	1.0%
Received radiotherapy	1.4%	2.1%

Table 6. Receipt of chemotherapy and radiotherapy.

We found similar results for the historical cohort (data not shown).

Finally, we investigated time to surgical removal of tumour. In the inception cohort 126 psychiatric patients with malignant melanoma received surgical intervention within 90 days of cancer diagnosis. There was no significant difference between psychiatric patients and the general population in time to surgery (Figure 5) (p=0.473). Again, we found similar results for the historical cohort (data not shown).

4.7.4 Mortality in psychiatric patients with melanoma

Using the inception cohort approach, 149 psychiatric patients with malignant melanoma died during the follow-up period. Of these deaths, 58 were coded as primary cause of death being malignant melanoma (Table 7). Of the 2,840 deaths during the follow-up period among malignant melanoma patients who had not had any prior contact with mental health services, 1,558 deaths were classified as malignant melanoma being the primary cause (Table 7).

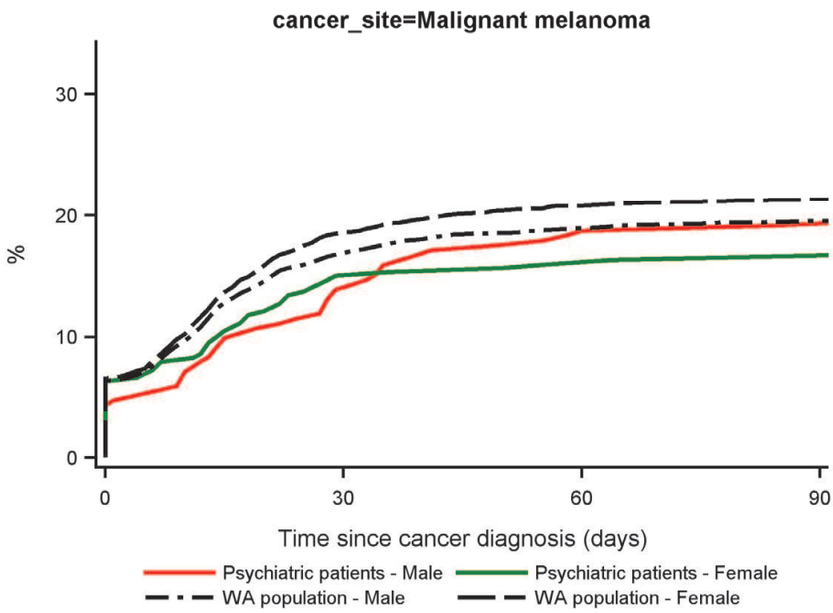

Fig. 5. % of patients who accessed surgery up to 90 days after diagnosis of their melanoma, WA, 1988 – 2007.

	Inception cohort		**Historical cohort**	
	Psychiatric case	Non Psychiatric case	Psychiatric case	Non Psychiatric case
All cause mortality	149	2840	263	2840
All cause hazard ratio	1.81 (1.53 – 2.14)		1.67 (1.47 – 1.90)	
Cancer specific mortality	58	1558	118	1558
Cancer specific hazard ratio	1.34 (1.03 – 1.74)		1.32 (1.10 – 1.60)	
Total patients with melanoma	618	14059	1166	14059

Table 7. Mortality in Psychiatric Patients with Melanoma WA, 1988 – 2007.

We compared the mortality rates between melanoma patients with and without a history of contact with mental health services using proportional hazards regression. This model allowed us to adjust for differences in the age and sex make-up of the two different cohorts. After adjusting for age, sex and socio-economic status (based on area of residence), psychiatric patients had a higher risk of all cause- and melanoma-specific mortality (Table 7). The difference between these two rates indicates that melanoma patients with a history of contact with mental health services were more likely to die as a direct result of melanoma, and also more likely to die from other causes. After malignant melanoma itself, the most common cause of death among melanoma patients with a history of contact with mental health services was coronary heart disease. In common with our findings on cancer incidence, all-cause and cancer specific mortally were lower in the historical than in the inception cohort. However both were significantly greater than those of the general population.

5. Discussion

There is literature on the adverse affect of depression on survival from melanoma. There is also literature on the incidence of melanoma in people with schizophrenia, and whether this is lower than that of the general population.[35, 36] Lastly, there is limited literature comparing incidence and mortality in patients of specialist psychiatric services.[17] To our knowledge, these studies conducted in WA and QLD are the first to investigate melanoma incidence and mortality rates in people with psychiatric disorder that include outpatient data, where the vast majority of people receive treatment. Our findings therefore give a fuller picture of the relationship between psychiatric disorder and melanoma. Another strength is the use of both inception and historical cohort data, exploiting the advantages of each. Historical cohorts may have greater statistical power because of increased numbers, but may underestimate mortality risk because of survivorship bias. Our findings of lower incidence and mortality rates in the historical as opposed to inception cohort would be consistent with this pattern. Inception cohorts may be more sensitive to the increased mortality risk faced by patients but be underpowered to detect rarer outcomes. Again, this was suggested by our study where analysis of subgroups, such as schizophrenia only yielded significant results in our historical cohort.

Our latest findings confirm our previous work on melanoma from Western Australia and Canada. With a further 10 years of data we found a continued pattern of an incidence that was lower, or no higher, than that of the general population alongside a mortality that was higher. This pattern is not unique to melanoma and has been identified for other cancers such as lung, colorectal, breast and prostate cancers even after adjusting for factors such as smoking.[28] Studying melanoma has particular advantages as this site may be less affected by potential medication or lifestyle confounders such as diet or alcohol and substance use. Studies of cancers, such as colorectal and lung, can only control for known lifestyle confounders and, even then, it is not possible to adjust for all of these.[28] By contrast, malignant melanoma is mainly related to childhood sun exposure,[29] and there is no evidence of reduced childhood sun exposure in individuals who subsequently develop psychiatric disorder.[28] As such, this cancer may be less subject to confounding by concurrent factors of lifestyle.

As regards schizophrenia, our historical cohort findings are consistent with a large meta-analysis by Catts et al that reported significantly reduced standardised incidence ratios (SIRs) for malignant melanoma of 0.71 for patients with schizophrenia (CI 0.57–0.87; P = 0.002).[28] The absence of any significant reduction in our inception cohort may be partly explained by the low numbers (n=24). Our historical cohort results also suggest that this effect extends to other psychiatric diagnoses, which tends to militate against biological hypotheses of why people with schizophrenia might be protected against cancer in general. Biological explanations include a protective effect of excess dopamine, enhanced natural killer cell activity, increased apoptosis, or modulation by antipsychotic drugs of cytochrome enzymes involved in mutagen activation and elimination, as well as the hypothesis of relative vitamin D deficiency.[27]

If biological explanations may be less applicable to the pattern we observed for melanoma for people with all types of psychiatric disorder, other hypotheses merit consideration. One is that cancer is undiagnosed in people with psychiatric disorder. Reduced cancer incidence

rates in psychiatric disorder in general, and schizophrenia in particular, could be due to lower detection rates related to poorer self-care and substandard preventive health care.[28] However, it has been argued that while medical comorbidity in general is under-recognized, this does not seem to apply to cancer in general.[28] For instance, post-mortem data collected between 1966 and 1980 in Denmark, where the autopsy rates were in the order of 30–50% in both patients with schizophrenia and the general population, indicated that the post-mortem diagnosis of previously unrecognized cancer was rare. It is unclear whether these findings would apply to melanoma because unlike cancers such as lung or colorectal cancer, there may be few obvious early symptoms.[28]

Another explanation is that people with psychiatric disorder receive poorer care. Work from Ontario shows that other marginalised populations, such as those of low income, are less likely to receive specialist procedures such as adjuvant or palliative radiotherapy, even under universal health care.[32] We have also shown that psychiatric patients are less likely to receive appropriate specialised procedures for cardiovascular disease in both Australia and Canada.[17, 37] In the case of the former, one explanation might be that many of the procedures are carried out in the private health system for which people with many psychiatric disorders would be unable to find insurance. This would not apply to Canada, where the private health sector has no role in the provision of medically necessary procedures.

It is possible that physicians are reluctant to offer some procedures because of the ensuing psychological stress, concerns about capacity or compliance with postoperative care, or the presence of contra-indications such as smoking. In addition, psychiatric patients may be more at risk of developing complications following medical or surgical interventions[38] or to have poorer outcomes post-operatively.[39]

So what do our latest results suggest about the role of under-diagnosis, delayed diagnosis or inequity in treatment? Our project could not address the first explanation as this would require a detailed investigation of death register or post-mortem records to ascertain the presence of melanoma at death that had not been previously treated. Our study does not particularly shed light on the other two explanations. Psychiatric patients in the historical cohort were significantly more likely to have metastases at time of original diagnosis ($p=0.002$). Otherwise, psychiatric patients were no more likely to present with metastases, or develop them 90 days or 1 year afterwards, than the general population. Neither were they less likely to receive specialised procedures such as radio- or chemotherapy.

These findings would be consistent with work on cancer in general showing there is little evidence of delayed detection in people with psychiatric disorder such as schizophrenia.[28] However, as discussed in the following paragraph, this study may have been under-powered to detect any difference in the presence of metastases, or of treatment access.

5.1 Study limitations

We used routinely collected administrative data to maximise coverage across the state, keep within budget and maximise statistical power. However reliance on secondary data meant that we were unable to collect information on quality of life. The WA cancer register does not contain information on staging other than the presence or absence of metastases. Administrative data may also be subject to recording bias, especially for diagnosis. Most data concerning the validity of our case–definition of treated psychiatric disorder are for overall morbidity rather than specific diagnoses. We have therefore emphasised overall psychiatric morbidity, not sub-categories, to minimise possible bias. We were unable to study the effects of lifestyle such as use of sunscreen and sun exposure. However, this

would not explain our finding of an increased risk of mortality in the presence of an incidence that was no higher than that of the general population. We were unable to separately study the relationship between specific psychiatric disorder and melanoma because of small numbers. In a similar vein, this study may have been under-powered to detect any difference in the presence of metastases, or of treatment access. Our results so far have been confined to Western Australia. The addition of Queensland data covering a population that is more than double that of Western Australia may address study power. In addition, the Queensland Cancer Registry has the advantage over Western Australia of collecting staging data on melanoma. Lastly, we were only able to capture data on access to surgery as well as admissions for radio- or chemotherapy, and so cannot comment on access to other interventions for melanoma.

6. Conclusions

This chapter has illustrated some of the complex interactions between melanoma and psychiatric disorder. It extends our previous work with another decade of Australian data to further explore these relationships through to 2007. These findings provide further evidence of a melanoma incidence in psychiatric patients that was lower or no higher than that of the general population alongside a mortality that was higher. Furthermore, this pattern extends to a broad range of psychiatric disorders and not just schizophrenia, where the low incidence of melanoma was first described. Although we were unable to show any clear reason in terms of delays in presentation as shown by metastases, or of access to treatment, the availability of just West Australian data may have meant the study was underpowered. The addition of Queensland data may rectify this. More research is certainly needed on why psychiatric patients with melanoma are more likely to die of the condition, but no more likely to develop it in the first place. This has implications for both primary and secondary care, including access to appropriate treatment for psychiatric patients with melanoma, as well as of awareness of the psychiatric symptoms of treatments for melanoma.

7. Acknowledgements

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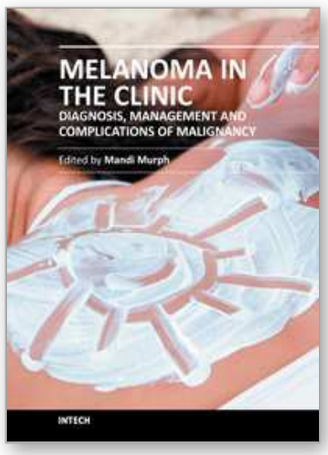

Melanoma in the Clinic - Diagnosis, Management and Complications of Malignancy

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This book provides an excellent overview of how melanoma is treated in the clinic. Since oncologists and clinicians across the globe contributed to this book, each area also explores the unique burdens that geographical areas experience from melanoma subtypes and how these are treated in different settings. It also includes several chapters that illustrate novel methods for diagnosing melanoma in the clinic using new technologies, which are likely to significantly improve outcomes. Several chapters cover surgical techniques and other present very rare or challenging clinical cases of melanoma and how these were treated. The book is geared towards informing clinicians and even patients how melanoma arises, what tools are available and which decisions need to be made by patients and their families in order to treat this devastating disease.

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