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Flourishing or floundering? Prevalence and correlates of anxiety and depression among a population-based sample of adult cancer survivors 6 months after diagnosis

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ABSTRACT

Objective: To describe the prevalence of anxiety, depression and comorbid anxiety-depression among adult cancer survivors six months following diagnosis, and identify the individual, disease, health behaviour, psychological and social factors associated with psychological morbidity.

Methods: A population-based sample of adult cancer survivors was recruited from two state-based cancer registries in Australia. Data for 1323 survivors were obtained by self-report questionnaire and linkage with registry data. Anxiety and depression were assessed by the 14-item Hospital Anxiety and Depression Scale (HADS).

Results: The prevalence of psychological morbidity was 28% (95%CI: 23%-33%). Specifically, 24% (95% CI: 19%-29%) of survivors were identified as cases on anxiety (irrespective of depression), 14% (95% CI: 9%-19%) as cases on depression (irrespective of anxiety) and 10% (95% CI: 5%-15%) as cases on comorbid anxiety-depression. In addition to mental health history prior to cancer, modifiable health behaviours (physical activity, smoking status), psychological (helplessness-hopelessness, anxious preoccupation coping) and social (low positive social interaction) characteristics were stronger indicators of psychological morbidity than survivors' individual or disease characteristics.

Limitations: Psychological morbidity was assessed by self-report screening instrument rather than clinical interview. The extent to which psychological morbidity is age-related versus cancer-related cannot be determined without a gender- and age-matched control group.

Conclusion: Although lower than previously reported, psychological morbidity is prevalent six months after a cancer diagnosis and emphasises the need for

routine psychosocial assessment throughout the cancer trajectory to identify those at increased risk or in need of immediate intervention. Physical activity, smoking cessation and coping skills training interventions warrant further exploration.

INTRODUCTION

A cancer diagnosis is a life-changing experience that affects 1 in 5 men and 1 in 6 women before the age of 75 years (Ferlay et al, 2008). While cancer incidence is projected to almost double over the next two decades to 21.4 million new cases annually, the number of people living with a history of cancer (i.e. 'survivors') is expected to triple to 75 million worldwide by 2030 (Ferlay et al, 2008). This increasing global cancer burden has been described as a public health crisis (Boyle and Levin, 2008). Compared to the earlier phases of the cancer continuum, relatively little is known about the nature and extent of the impact of cancer on survivors, or how best to deliver care that optimises their health and wellbeing. With their need for care typically spanning many years, the growing population of cancer survivors has recently become the focus of researchers, clinicians and policy-makers (Hewitt et al, 2006; President's Cancer Panel, 2004).

The psychological effects of cancer range from common normal feelings of uncertainty about the future and fear of cancer recurrence (Hodgkinson et al, 2007; Deimling et al, 2006) to clinically significant anxiety and/or depression (Burgess et al, 2005) and post-traumatic stress disorder (Kangas et al, 2005). Psychological morbidity among those affected by cancer is an important clinical issue because of its association with poorer quality of life across multiple domains (Skartsein et al, 2000), more intense physical symptoms, increased functional impairment and poor treatment adherence (Fann et al, 2008). Further, some evidence suggests that there may be a relationship between psychological distress and cancer progression (Antoni et al, 2006); and reduced

overall survival (Groenvold et al, 2007), however this remains a contentious issue. Many approaches have been utilised to identify cancer survivors experiencing psychological morbidity and there is a range of effective pharmacological and psychological interventions to manage such morbidity (Jacobsen and Jim, 2008; Fann et al, 2008; Williams and Dale, 2006; Osborn et al, 2006; Stark and House, 2000).

Estimates of the prevalence of anxiety and depression among cancer survivors vary widely (Van't Spijker et al, 1997), largely as a result of different measurement techniques, different criteria to define anxiety and depression, and different study populations, making it difficult to compare between studies. It is generally agreed that anxiety and depression are highest at the time of diagnosis and decrease over time with levels of anxiety and depression typically returning to a level comparable to the general population around two years post-diagnosis (Mehnert et al, 2010; DiSipio et al, 2008). The transition from patient to survivor is often experienced as stressful as contact with the cancer care team decreases in frequency and the perceived safety of the hospital system is left behind (Jefford et al, 2008). At six months post-diagnosis, estimates of the prevalence of depression range from 22% to 28% (Korfage et al, 2006; Burgess et al, 2005; Kangas et al, 2005; De Leeuw et al, 2000; Gallagher et al, 2002; Goldberg et al, 1992) while one-third of survivors are estimated to experience anxiety (Korfage et al, 2006; Burgess et al, 2005; Kangas et al, 2005). However, psychological morbidity at this time has not been well documented in the wider population of recent cancer survivors, and to our

knowledge, there are no published studies reporting the prevalence of comorbid anxiety-depression six months after a cancer diagnosis.

Information about the characteristics of survivors most at risk of experiencing psychological morbidity is critical for identifying those that should be targeted for screening, evaluation and monitoring or intervention. There is an extensive literature on the individual (younger age, physical disability), disease and treatment (advanced disease, fatigue, pain), psychological (history of depression, adaptive coping styles), social (socially isolated, socially disadvantaged) and lifestyle factors (insufficiently active, substance abuse) associated with psychological morbidity at various stages of the cancer continuum (Banks et al, 2010; Fann et al, 2008; Massie, 2004; Stark and House, 2000; Van't Spijker et al, 1997). Although some studies have examined various subsets of these characteristics as predictors of poor adjustment after cancer (Lynch et al, 2008; Hammerlid et al, 1999), to date, no study has reported the relative contributions of a comprehensive range of individual, disease, psychological, social and lifestyle characteristics to the psychological morbidity experienced by cancer survivors in the late treatment to early survivorship phase of care.

There is an emerging body of high quality evidence describing the magnitude and nature of the psychological impact of cancer on survivors, particularly for breast and prostate cancer survivors. However, more comprehensive studies with representative samples of survivors with different cancer types, survival

probabilities, culturally and socially diverse backgrounds and geographic locations are needed in order to accurately assess the prevalence of the psychological effects of cancer among survivors and identify vulnerable subgroups. The landmark report *From Cancer Patient to Cancer Survivor: Lost in Transition* (Hewitt et al, 2006) recommended that large-scale population-based studies with the diversity of cancer survivors be undertaken as a priority in order to guide the development and delivery of effective survivorship care.

The aims of the current study were to:

1. Determine the prevalence of anxiety, depression and comorbid anxiety-depression at six months post-diagnosis overall and by cancer type.
2. Identify the factors (individual, disease, health behaviour, psychological, social) correlated with caseness for (a) anxiety, (b) depression and (c) comorbid anxiety-depression at six months post-diagnosis. It was hypothesised that psychological morbidity would be associated with (i) being aged less than 50 years, (ii) a history of mental health problems, (iii) insufficient physical activity (iv) consuming more than two standard drinks a day, and (vi) perceived poor social support.

METHOD

This paper is based on the *Cancer Survival Study*, a population-based longitudinal study tracking the psychosocial wellbeing and lifestyle behaviours of 1453 cancer survivors in Australia over the first five years since diagnosis. Time 1 (T1) data reported here were collected from participants at approximately six months post diagnosis.

Participants

Cancer survivors were prospectively recruited from new notifications to the two largest state-based cancer registries in Australia. Eligible participants were (1) diagnosed in the previous six months with their first primary cancer of one of the top eight incident cancer types in Australia (prostate, colorectal, female breast, lung, melanoma, Non-Hodgkin's lymphoma, leukaemia, head and neck); (2) aged between 18 and 80 years and living in the state of New South Wales (NSW) or Victoria (VIC) at the time of diagnosis; and (3) considered by their physician to be aware of their diagnosis as well as physically and mentally capable and proficient in English to complete a questionnaire.

Procedure

The registries attempted to contact by mail the physician of survivors identified as potentially eligible to participate. Physicians in NSW were required to provide active consent for the nominated survivor to be contacted about the study; those physicians who did not respond within four weeks received one reminder phone call. Passive physician consent was used in Victoria whereby physicians were required to notify the cancer registry within four weeks of any contraindications to the nominated survivor being contacted about the study. Potential participants with physician approval to be approached were contacted by mail by the registries to seek permission to pass their name and contact details to the research team. Non-responders received one mailed reminder package three weeks later and one reminder phone call after a further three weeks.

Using a modified Dillman (1978) approach, a study package was mailed to those survivors who agreed to be contacted about the study by the research team. Non-responders received one mailed reminder package three weeks later and one reminder phone call after a further three weeks. Consent to participate was indicated by return of a completed survey. The Human Research Ethics Committees of the University of Newcastle, Cancer Institute NSW and Cancer Council Victoria approved the study.

Measures

Data were collected through a combination of self-administered scannable questionnaire and linkage with the Cancer Registries.

Outcome measure

Anxiety and depression were measured by the commonly used 14-item Hospital Anxiety and Depression Scale (HADS). Items assess two subscales: anxiety (HADS-A) and depression (HADS-D). Each item is rated on a four point Likert scale and a score ranging from 0 to 21 calculated for each subscale, with a higher score indicating a higher level of anxiety or depression. A subscale score of 0-7 is considered normal (non-case), 8-11 considered borderline (doubtful case) and 12-21 considered clinically significant (probable case) (Zigmond and Snaith, 1983). Although there is debate about the optimal scoring method and cutpoint to use (Singer et al, 2009), a review of the validity of the individual HADS subscales found that the best trade-off between sensitivity and specificity was achieved using a subscale cutoff point of 8 or above for identifying 'cases' (Bjelland et al, 2002). To minimise the misclassification of survivors, we used

the established subscale cutoff point ≥ 8 to identify 'cases' on HADS-A and 'cases' on HADS-D. In addition, those who were cases on both HADS-A and HADS-D were classified as 'cases' on comorbid anxiety-depression. The HADS measures aspects of depression that are not confounded by the physical symptoms of cancer or its treatment such as fatigue, and was recommended as an instrument of choice for assessing cancer patients' psychological morbidity in recent reviews of patient reported outcome measures (Luckett et al, 2010; Ziegler et al, 2011).

Study factors

Individual: Age at diagnosis and sex were obtained directly from the cancer registry. Current marital status, highest level of education completed, health insurance coverage, current employment situation, geographical location, size of household, and presence of any physical comorbidities were obtained by standard self-report questionnaire items.

Disease: Primary cancer type and spread of disease at diagnosis were obtained directly from the cancer registry and survivors' cancer categorised as 'early/less progressed' (insitu or localised; grade 1 or 2; T1 or T2), 'late/more progressed' (invasion of adjacent organs, regional nodes or distant metastases; grade 3 or 4; not T1) or 'not applicable' (haematological cancers). Extent of disease at six months post-diagnosis, and cancer treatments received in the last month were obtained by standard self-report questionnaire items.

Health behaviours: Smoking behaviour was assessed by two questions and participants classified as 'current smoker' (has smoked at least 100 cigarettes

or the equivalent amount of tobacco in lifetime and currently smokes), 'former smoker' (has smoked at least 100 cigarettes or the equivalent amount of tobacco in lifetime but does not currently smoke) or 'never smoker' (never smoked more than 100 cigarettes or the equivalent amount of tobacco in lifetime) (AIHW, 1999). Alcohol consumption was assessed by two questions adapted from the Australian National Drug Strategy Household Survey (AIHW, 2002). Participants who consumed more than two standard drinks on any day were classified as being at increased lifetime risk of harm from alcohol related injury or disease (NHMRC, 2009). Physical activity was assessed by three items adapted from the Active Australia survey (AIHW, 2003) and participants classified as 'sufficiently active' (at least 150 minutes of activity over one week), 'insufficiently active' (participating in some physical activity but not enough in total time) or 'sedentary' (no physical activity) (DoHA, 1999).

Psychological: Mental health history was obtained by two self-report questionnaire items assessing treatment for a mental health illness (e.g. depression, anxiety, schizophrenia) before and since cancer diagnosis. Coping strategy was measured by the 21-item Mini Mental Adjustment to Cancer Scale (Mini-MAC). Items assess five cancer-specific coping strategies: helplessness-hopelessness, anxious preoccupation, fighting spirit, cognitive avoidance and fatalism. Items are rated on a 4-point scale and a score calculated for each subscale with a higher score indicating a stronger use of the coping strategy (Watson et al, 1994). Raw subscale scores were standardised from 0 to 100. As the distribution of scores was highly skewed, all coping subscales were dichotomised with survivors who scored in the top 16% of each distribution

classified as a 'case' on that specific coping strategy in accordance with the user manual (Watson et al, 1989).

Social: Social support was measured by the 20-item MOS Social Support Survey (MOS-SSS). Items assess four subscales of functional support: emotional/ informational, tangible, affectionate, and positive social interaction. Items are rated on a 5-point scale and a score calculated for each subscale with a higher score indicating a higher level of support (Sherbourne and Stewart, 1991). Raw subscale scores were standardised from 0 to 100. As all subscale scores were highly skewed, all social support subscales were dichotomised and survivors who scored in the bottom one-third of each distribution classified as 'low' on that particular type of social support (Sherbourne, personal communication, 19 May 2004).

Statistical Methods

In accordance with recommended procedures for the HADS, in those instances where no more than one item was missing on a subscale, the mean of the remaining subscale items was imputed. If more than one item on a subscale was missing, then the subscale score was not calculated. Data from survivors of Non-Hodgkin's Lymphoma or leukaemia were combined to form a 'haematological' cancer type due to small numbers. Scores were calculated for the HADS-A and HADS-D and descriptive statistics computed. The prevalence of each of the three outcomes (case on anxiety, case on depression, and case on comorbid anxiety-depression) was estimated with 95% confidence intervals for each cancer type. The association between the individual, disease, health

behaviour, psychological and social factors with each of the three outcomes was examined using chi-square analyses. Variables with a p value of 0.2 or less were included in a backward stepwise logistic regression model for each outcome. Variables were removed from the model if they had a p value of 0.05 or more on the likelihood ratio test. Odds ratio and 95% confidence intervals are reported for variables included in the final model.

RESULTS

Sample

A total of 3877 potential participants were assessed for study eligibility. Of the 3315 deemed eligible, 1691 consented to contact by the researchers and a total of 1360 returned a T1 questionnaire (overall 41% response rate at T1; VIC=49% and NSW=33%). Thirty seven participants returned their T1 questionnaire more than 9 months after diagnosis and were excluded. The 1323 survivors included in these analyses were surveyed at a median of 6 months after diagnosis (SD=1 month, range=4-9 months) and their median age was 63 years (SD=11 years, range=18-80). Table 1 shows that more than half (59%) were male, about half were diagnosed with early stage disease (52%), the most common diagnosis was prostate cancer (26%) and 72% had not received any active treatment in the last month. The sample reflected the national profile (AIHW and AACR, 2008) for the top eight incident cancers diagnosed in 2005 in terms of gender and age, however survivors of colorectal cancer were under-represented and haematological and head and neck cancers were over-represented.

Table 1: Selected characteristics of study sample compared to national cancer incidence data

| | Study sample ^a | | National ^b | |
|--|---------------------------|------|-----------------------|------|
| | N | (%) | N | (%) |
| Gender | 1323 | | 58,665 | |
| Male | 781 | (59) | 34,223 | (58) |
| Female | 542 | (41) | 24,442 | (42) |
| Age at diagnosis (years) | 1323 | | 58,665 | |
| 18-39 | 57 | (4) | 2826 | (5) |
| 40-49 | 138 | (10) | 6032 | (10) |
| 50-59 | 317 | (24) | 13,049 | (22) |
| 60-69 | 482 | (36) | 18,451 | (31) |
| 70 or more | 329 | (25) | 18,307 | (31) |
| Primary cancer | 1323 | | 58,665 | |
| Prostate | 343 | (26) | 13,886 | (24) |
| Breast (female) | 208 | (16) | 10,896 | (19) |
| Melanoma | 204 | (15) | 9197 | (16) |
| Haematological ^c | 183 | (14) | 4 935 | (8) |
| Colorectal | 157 | (12) | 10,108 | (17) |
| Lung | 133 | (10) | 7312 | (12) |
| Head and neck | 95 | (7) | 2331 | (4) |
| Stage of disease at diagnosis | 1323 | | | |
| Early/less progressed | 691 | (52) | | |
| Late/more progressed | 254 | (19) | | |
| Not applicable | 183 | (14) | | |
| Unknown | 195 | (15) | | |
| Treatment in last month | 1297 | | | |
| Active (surgery, chemo, radio) +/- passive treatment | 358 | (28) | | |
| Passive only (hormone, immunotherapy) | 151 | (12) | | |
| None | 788 | (61) | | |
| Treatment types in last month^d | 1297 | | | |
| Surgery | 58 | (5) | | |
| Chemotherapy | 198 | (16) | | |
| Radiotherapy | 131 | (10) | | |
| Hormone | 179 | (14) | | |
| Immunotherapy | 29 | (2) | | |

^a number of observations varies across characteristics due to missing data.

^b 2005 data restricted to 8 most incident cancer and those aged 20-79 years; data not available for all characteristics.

^c includes non-Hodgkin's Lymphoma and leukaemia.

^d multiple responses allowed.

Prevalence of anxiety and/or depression by cancer type

Overall, cancer survivors reported low levels of anxiety (median score=4, range=0-20) and depression (median score=2, range=0-19). A total of 369 (28%; 95% CI: 23%-33%) cancer survivors reported clinical/borderline level anxiety and/or depression at six months post-diagnosis. As shown in Table 2, 24% of survivors were identified as cases on anxiety (irrespective of depression) and 14% (95% CI: 9%-19%) as cases on depression (irrespective of anxiety). A total of 10% (95% CI: 5%-15%) were identified as cases on comorbid anxiety-depression.

There was significant variation across cancer types in the percentage of survivors that reported psychological morbidity. Lung cancer survivors were more affected than survivors of other cancer types with 40% (95% CI: 27%-53%) identified as cases on anxiety, 28% (95% CI: 14%-44%) as cases on depression and 24% (95% CI: 9%-39%) as cases on comorbid anxiety-depression. Compared to other cancer types, survivors of prostate cancer and melanoma reported the least psychological morbidity.

Table 2: Prevalence of anxiety and/or depression at 6 months post-diagnosis by cancer type

| | Total ^a n (%) | Prostate n (%) | Breast n (%) | Melanoma n (%) | Blood ^b n (%) | Colorectal n (%) | Lung n (%) | Head and neck n (%) |
|---|-----------------------------|-------------------|-----------------|-------------------|-----------------------------|---------------------|---------------|------------------------|
| Anxiety (irrespective of depression) | | | | | | | | |
| Case | 310 (24) | 48 (14) | 63 (30) | 44 (22) | 48 (27) | 32 (20) | 53 (40) | 22 (24) |
| Non-case | 1004 (76) | 294 (86) | 144 (70) | 157 (78) | 133 (73) | 125 (80) | 80 (60) | 71 (76) |
| $\chi^2=44.29$; df=6; p<0.001 | | | | | | | | |
| Depression (irrespective of anxiety) | | | | | | | | |
| Case | 189 (14) | 34 (10) | 32 (15) | 14 (7) | 30 (17) | 23 (15) | 38 (29) | 18 (19) |
| Non-case | 1126 (86) | 308 (90) | 175 (85) | 188 (93) | 151 (83) | 134 (85) | 95 (71) | 75 (81) |
| $\chi^2=39.13$; df=6; p<0.001 | | | | | | | | |
| Co-morbid anxiety-depression | | | | | | | | |
| Case | 130 (10) | 22 (6) | 26 (13) | 7 (3) | 20 (11) | 14 (9) | 32 (24) | 9 (10) |
| Non-case | 1184 (90) | 320 (94) | 181 (87) | 194 (97) | 161 (89) | 143 (91) | 101(76) | 84 (90) |
| $\chi^2=45.89$; df=6; p<0.001 | | | | | | | | |

^a number of observations varies across outcomes due to missing data

^b includes non-Hodgkin's Lymphoma and leukaemia

Factors associated with anxiety and/or depression

Individual characteristics: As shown in Table 3, the odds of caseness for anxiety increased with decreasing age, and were higher among survivors who lived alone (OR=1.8) compared to those who lived with another adult.

Table 3: Factors significantly correlated with caseness for anxiety

| | Adjusted OR (95%CI) | p |
|---|---------------------|--------|
| Individual | | |
| Age at diagnosis (years) | | 0.023 |
| 49 and younger | 2.7 (1.4-5.3) | |
| 50-59 | 2.0 (1.1-3.6) | |
| 60-69 | 1.8 (1.1-3.2) | |
| 70 and older | 1.00 | |
| Number of adults live with | | 0.04 |
| Nil – live alone | 1.8 (1.1-2.9) | |
| More than 1 | 1.5 (0.94-2.3) | |
| 1 | 1.00 | |
| Disease and treatment | | |
| Cancer type | | 0.027 |
| Breast | 1.4 (0.76-2.5) | |
| Colorectal | 1.6 (0.85-3.2) | |
| Haematological | 1.1 (0.59-2.1) | |
| Head & neck | 0.75 (0.33-1.7) | |
| Lung | 2.3 (1.2-4.5) | |
| Melanoma | 2.1 (1.1-3.9) | |
| Prostate | 1.00 | |
| Psychological | | |
| Mental health treatment before cancer diagnosis | | <0.001 |
| Yes | 2.8 (1.7-4.5) | |
| No | 1.00 | |

| | | |
|--|----------------|--------|
| Mental health treatment since cancer diagnosis | | 0.002 |
| Yes | 2.2 (1.1-4.3) | |
| No | 1.00 | |
| Helpless-hopeless coping | | <0.001 |
| Case | 2.7 (1.8-4.0) | |
| No case | 1.00 | |
| Anxious preoccupation | | <0.001 |
| Case | 8.4 (5.6-12.6) | |
| No case | 1.00 | |
| Cognitive avoidance | | 0.007 |
| Case | 1.7 (1.1-2.4) | |
| No case | 1.00 | |
| Social | | |
| Positive social interaction | | 0.021 |
| Low | 1.6 (1.1-2.3) | |
| Some | 1.00 | |

OR = odds ratio; CI = confidence interval; p-value on the Wald chi-square analysis of effects test

Disease characteristics: Cancer type, chemotherapy and hormone treatment were the only disease characteristics associated with psychological morbidity. Compared to survivors of prostate cancer, those diagnosed with lung cancer (OR=2.3) or melanoma (OR=2.1) had twice the odds of caseness for anxiety (Table 3). Those who received chemotherapy in the last month had almost twice the odds (OR=1.9) of caseness for depression compared to those who didn't receive this treatment, while survivors who received hormone treatment had lower odds (OR=0.46) of caseness for depression compared to those who didn't receive this treatment (Table 4).

Table 4: Factors significantly correlated with caseness for depression

| | Adjusted OR (95%CI) | p |
|---|---------------------|--------|
| Disease and treatment | | |
| Chemotherapy last month | | 0.01 |
| Yes | 1.9 (1.2-3.1) | |
| No/don't know | 1.00 | |
| Hormone treatment last month | | 0.037 |
| Yes | 0.46 (0.22-0.95) | |
| No/don't know | 1.00 | |
| Health behaviours | | |
| Physical activity | | <0.001 |
| Sedentary | 3.5 (2.0-6.2) | |
| Insufficiently active | 1.8 (1.1-3.1) | |
| Sufficiently active | 1.00 | |
| Smoking status | | 0.044 |
| Current | 2.4 (1.2-4.8) | |
| Former | 1.0 (0.68-1.6) | |
| Never | 1.00 | |
| Alcohol consumption | | 0.002 |
| Increased risk of harm | 0.45 (0.27-0.74) | |
| No increased risk of harm | 1.00 | |
| Psychological | | |
| Mental health treatment before cancer diagnosis | | 0.005 |
| Yes | 2.00 (1.2-3.3) | |
| No | 1.00 | |
| Helpless-hopeless coping | | <0.001 |
| Case | 2.7 (1.7-4.3) | |
| No case | 1.00 | |
| Anxious preoccupation | | <0.001 |
| Case | 4.6 (2.9-7.3) | |
| No case | 1.00 | |

| | | |
|-----------------------------|------------------|--------|
| Fighting spirit | | 0.005 |
| Case | 0.40 (0.21-0.75) | |
| No case | 1.00 | |
| Social | | |
| Positive social interaction | | <0.001 |
| Low | 2.4 (1.6-3.7) | |
| Some | 1.00 | |

OR = odds ratio; CI = confidence interval; p-value on the Wald chi-square analysis of effects test

Health behaviours: Physical activity, smoking status and alcohol consumption were associated with psychological morbidity (Tables 4 and 5). Compared to survivors who were sufficiently active, those who were sedentary or insufficiently active had two to four times the odds of caseness for depression (OR=3.5, 1.8) and comorbid anxiety-depression (OR=4.0, 2.4). Compared to survivors who had never smoked, current smokers had twice the odds of being a case on depression (OR=2.47) and comorbid anxiety-depression (OR=2.2). Survivors who consumed alcohol at a level that placed them at increased risk of harm had lower odds (OR=0.45) of caseness for depression than those whose drank alcohol at safe levels.

Table 5: Factors significantly correlated with caseness for comorbid anxiety-depression

| | Adjusted OR (95%CI) | p |
|---|---------------------|--------|
| Health behaviours | | |
| Physical activity | | <0.001 |
| Sedentary | 4.0 (2.1-7.7) | |
| Insufficiently active | 2.4 (1.3-4.4) | |
| Sufficiently active | 1.00 | |
| Smoking status | | 0.046 |
| Current | 2.2 (1.0-4.5) | |
| Former | 0.87 (0.53-1.4) | |
| Never | 1.00 | |
| Psychological | | |
| Mental health treatment before cancer diagnosis | | 0.008 |
| Yes | 2.1 (1.2-3.6) | |
| No | 1.00 | |
| Helpless-hopeless coping | | <0.001 |
| Case | 3.5 (2.1-5.8) | |
| No case | 1.00 | |
| Anxious preoccupation | | <0.001 |
| Case | 6.4 (3.9-10.6) | |
| No case | 1.00 | |
| Social | | |
| Positive social interaction | | <0.001 |
| Low | 2.5 (1.6-4.1) | |
| Some | 1.00 | |

OR = odds ratio; CI = confidence interval; p-value on the Wald chi-square analysis of effects test

Psychological: A history of mental health treatment and coping strategy were significantly associated with all three outcomes (Tables 3-5). Compared to those without a history of mental health problems, survivors who had been treated for mental health problems before their cancer diagnosis had at least twice the odds of caseness for anxiety (OR=2.8), depression (OR=2.0) and comorbid anxiety-depression (OR=2.1) while those treated for mental health problems since their cancer diagnosis had higher odds of being a case on anxiety (OR=2.2). Survivors who engaged in the maladaptive coping strategies helplessness-hopelessness or anxious preoccupation had two to eight times the odds of being a case on anxiety (OR=2.7, 8.4), depression (OR=2.7, 4.6) and comorbid anxiety-depression (OR=3.5, 6.4) compared to survivors who did not use these strategies. In addition, survivors who used cognitive avoidance coping (OR=1.7) had greater odds of being a case on anxiety while those who used fighting spirit had lower odds (OR=0.40) of being a case on depression.

Social: Positive social interaction was the only type of social support associated with psychological morbidity. Survivors who perceived that they had low levels of positive social interaction had about twice the odds of being a case on anxiety (OR=1.6), depression (OR=2.4) and comorbid anxiety-depression (OR=2.5) compared to survivors who perceived they had at least some positive social interaction.

DISCUSSION

It is undisputed that a diagnosis of and treatment for cancer is a stressful life event and therefore it is to be expected that some survivors will report

psychological distress. In this population-based study, only 28% of cancer survivors at six months post-diagnosis reported clinical/borderline levels of anxiety and/or depression. A total of 24% of survivors were identified as cases on anxiety (irrespective of depression) and 14% as cases on depression (irrespective of anxiety). Overall, 10% were identified as cases for comorbid anxiety-depression. That is, about two-thirds (69%) of depressed survivors experienced anxiety at the same time, which is consistent with findings from a large heterogeneous sample of cancer patients receiving treatment at one clinic (Brintzenhofe-Szoc et al, 2009). Although comorbid anxiety-depression accounted for a relatively low proportion of survivors, these individuals are likely to be suffering greatly and should be actively identified, and vigorously targeted for intervention.

The level of anxiety and depression identified in this study is lower than that reported by other studies of survivors at a similar timeframe post-diagnosis (Goldberg et al, 1992; De Leeuw et al, 2000; Gallagher et al, 2002; Kangas et al, 2005). While this can be explained in part by the use of different measurement techniques or outcome measures, previous studies have tended to use convenience samples of survivors of a single cancer type recruited from one clinic and are therefore prone to selection bias. One of the major strengths of this study is the use of the two largest state-based cancer registries in Australia as the sampling frame to recruit a population-based sample of survivors in the early stages of survivorship. As the study sample is generally representative of its source population, we are confident that our findings are generalisable.

Unlike previous studies which have included only one or two cancer types (mainly breast), our large-scale study included a diversity of survivors which enabled us to directly compare psychological morbidity across seven common cancer types which together account for 70% of all new cancer diagnoses in Australia (AIHW and AACR, 2008). Univariate analyses indicated that the prevalence of all three outcomes varied significantly across cancer type with the percentage of survivors who reported anxiety, depression and comorbid anxiety-depression highest among lung cancer survivors. However, multivariable analyses found that such variation across cancer type existed only for anxiety, and is likely to reflect the challenges associated with poor prognosis and deteriorating health that those diagnosed with lung cancer face.

A history of mental health treatment before cancer, greater use of anxious preoccupation and helplessness-hopelessness coping strategies, and perceived low levels of positive social interaction were strongly associated with caseness for anxiety, depression and comorbid anxiety-depression. In addition to these, indicators of social isolation (live alone, younger, mental health problems) and cancer type (lung, melanoma) were uniquely and strongly associated with anxiety. Health behaviours (lack of physical activity and current smoker) were strongly associated with both depression and comorbid anxiety-depression.

The current study found that when considered together, health behaviours, psychological characteristics and social factors were more strongly associated (demonstrated by high odds ratios and highly significant p-values) with

psychological morbidity than survivors' individual and disease characteristics. While causality cannot be inferred from cross-sectional data, these findings are notable because health behaviours, coping strategies and social support are potentially modifiable and therefore have considerable promise for intervention efforts. For example, interventions targeting physical activity have been shown to reduce not only anxiety and depression, but also risk of cancer recurrence, other chronic illnesses and fatigue (Park and Gaffey, 2007; WCRF and AICR, 2007). Importantly, it has also been determined that it is generally safe and feasible for individuals affected by cancer to engage in physical activity during treatment and survivorship (Doyle et al, 2006). Reviews of the evidence have recommended that coping skills training that maximises the use of adaptive coping (Osborn et al, 2006) and social skills training that emphasises reciprocal support (Hogan et al, 2002) should be integrated within interventions to impact upon psychological distress.

Contrary to our hypothesis, drinking alcohol at levels considered to be at increased risk of harm was associated with lower odds of depression. A possible explanation for this unexpected finding is that cancer survivors may use alcohol as a strategy to block or blunt feelings of sadness. Alternatively, having faced their own mortality and survived, survivors may simply be living each day to the fullest. It is also possible that this is a spurious finding resulting from methodological limitations. Although adapted from an existing questionnaire, the items assessing alcohol consumption were generally poorly completed with many responses missing. Further, although we conformed to current guidelines to classify survivors' drinking levels, the criteria are crude and

may have resulted in misclassification of drinking levels. Given the social stigma associated with excessive alcohol consumption, it is plausible that heavy drinkers under-reported their alcohol intake or avoided answering these questions (DelBoca and Darkes, 2003). We recommend that future studies further explore the association between alcohol consumption and psychological morbidity among recent cancer survivors.

Strengths and limitations

To our knowledge, this is the first study to examine the prevalence of psychological morbidity among a large-scale population-based sample of diverse cancer survivors who at six months post-diagnosis are in the very early stages of cancer survivorship. For logistical reasons related to patient recruitment via the cancer registries, the study sample was restricted to the eight most incident cancer types. None the less, the sample included survivors of understudied cancers (colorectal, head and neck, haematological, lung). The use of rapid case ascertainment procedures and registry policies prohibiting individuals being approached for more than one study meant the sampling frame from which the sample was recruited was incomplete. For example, young men (less than 55 years) diagnosed with prostate cancer and those diagnosed with early stage colorectal cancer were unable to be approached by one registry for this study due to other studies targeting these patients. This contributed to differences between NSW and VIC participants in terms of gender, cancer type, stage of disease and treatments. Ideally, the sample recruited from each state would have been stratified by cancer type proportionate to its incidence in that state.

The T1 response rate of 41% (1360/3315 eligible individuals) may raise concerns about response bias. Due to privacy, confidentiality, and adverse event concerns, the cancer registries used a multistep recruitment process to identify potential participants on behalf of the research team; this process provided many opportunities for non-response and non-consent by clinicians and survivors prior to any contact from the researchers (Clinton-McHarg et al, 2011). The reported response rate almost certainly underestimates the true response rate because it assumes that all survivors of unknown eligibility (i.e. 764 survivors for whom the physician was uncontactable or refused, and 426 survivors who were uncontactable or non-responders) were eligible and therefore included in the denominator. While it exceeds the adjusted recruitment rate (34%) achieved by another study which used an equivalent method to recruit a similarly diverse sample of recent adult survivors via cancer registries (Smith et al, 2007b), it is lower than other register-based studies which have recruited samples of recent survivors of a homogeneous cancer type (Beesley et al, 2008; DiSipio et al, 2008; Smith et al, 2007a). On the basis that the sample is generally representative of the cancer population, we propose that the impact of the response rate on the accuracy of the prevalence estimates reported is likely to be minimal.

Although Australia has one of the most multicultural populations worldwide (ABS, 2010), survivors who were not proficient in English were excluded due to prohibitive costs involved in translation of the questionnaire into other languages. This may have resulted in an underestimate of the prevalence of

anxiety and depression given that language barriers limit access to health care services and information (Butow et al, 2010; Fiscella et al, 2002). The range of static and modifiable individual, disease, health behaviour, psychological and social correlates examined in this study is considerably wider than that of previous studies. Although cross-sectional in nature, it enabled us to identify the relationships between variables that should be further explored in longitudinal analysis. The large-scale sample meant that it was not feasible to assess psychological morbidity by clinical interview, however, the HADS has good sensitivity and specificity in detecting cases of anxiety and depression compared to clinical interview. Using the recommended HADS subscale cutoff score of ≥ 8 maximised the possibility of identifying all of the survivors with 'caseness' for anxiety and/or depression. However, it is possible that by using this lower threshold, some survivors may have been misclassified as 'cases', resulting in a small over-estimate of psychological morbidity. Nevertheless, the rates of psychological morbidity found in this study are lower than that previously reported. In balancing the questionnaire breadth and length, it was not possible to measure other potential correlates such as personality traits. While the lack of a gender and age-matched non-cancer control group makes it difficult to determine if the psychological morbidity reported by survivors is age-related or cancer-related, the presence of other self-reported comorbid diseases (eg. arthritis, hypertension) was assessed and found on multivariable analysis to not be associated with the outcomes examined. Furthermore, given that the rates of anxiety (24%) and depression (14%) were approximately double the rate of 12-month anxiety disorder (14%) and 12-month affective disorder (6%)

found in the general population of Australia (ABS, 2007), it is likely that much of the psychological morbidity reported by survivors in this study is cancer-related.

Conclusions

About one quarter of cancer survivors in this study reported caseness for anxiety and/or depression at six months post-diagnosis, emphasising the importance of repeated assessment of psychological well-being during end of treatment and routine post-treatment follow-up care, and provision of appropriate interventions. In addition to mental health history, modifiable health behaviours (particularly physical activity and smoking behaviour), psychological characteristics (helplessness-hopelessness coping, and anxious preoccupation coping) and social characteristics (low positive social interaction) were found to be stronger indicators of psychological morbidity than survivors' individual and disease characteristics. Knowledge of the characteristics of survivors at increased risk of psychological morbidity may guide health care professionals in which survivors to target for monitoring and early intervention. These findings suggest that focusing on healthy lifestyle behaviours, coping skills training and social skills training warrant further exploration and will likely require a multidisciplinary approach including psychosocial, medical, allied health, and community services.

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