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Anxiety and depression symptoms in adult males in Atlantic Canada with or without a lifetime history of prostate cancer

Gabriela Ilie[1] | Robert Rutledge[2] | Ellen Sweeney[3]

[1]Department of Community Health and Epidemiology, Dalhousie University, Halifax, Nova Scotia, Canada

[2]Department of Radiation Oncology, Dalhousie University, Halifax, Nova Scotia, Canada

[3]Atlantic PATH, Faculty of Medicine, Dalhousie University, Halifax, Nova Scotia, Canada

Correspondence
Gabriela Ilie, Department of Community Health and Epidemiology, Dalhousie University, 5790 University Avenue, 4th Floor, Room 401, Halifax, Nova Scotia, B3H 1V7, Canada.
Email: gabriela.ilie@dal.ca

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Abstract

Objective: Prostate cancer (PCa) is the most prevalent form of cancer among men and has one of the most favorable survival rates among all cancers. Here we examine the association between depression and anxiety symptoms in a population-based sample of men.

Methods: A cross-sectional analysis was conducted on a subsample of 6 585 male participants aged 49-69 from 2009 to 2015 survey cycle of the Atlantic PATH. Mild, moderate or severe depression or anxiety indicators were primary outcomes and were assessed using the Generalized Anxiety Disorder (GAD-7) scale and the Patient Health Questionnaire (PHQ-9). The presence of a lifetime history of PCa, other forms of cancer (except PCa) or absence of either was the main predictor variable.

Results: An estimated 3.9% of men self-identified as having had a history of PCa diagnosis, 11.3% of men identified as having had a history of other forms of cancer and 84.9% reported never having had a diagnosis of cancer in their lifetime, respectively. Survivors of PCa had 2.45 or 2.05 statistically significantly higher odds of screening positive for current anxiety or depressive symptoms, respectively, compared with those who identified as without a lifetime history of any form of cancer in controlled analyses (including survivorship time).

Conclusions: Increased rates of anxiety and depression among men with a history of PCa highlight the need for mental health screening among PCa survivors. The findings highlight the importance of a multidisciplinary effort to prioritize and deliver comprehensive mental health support to PCa survivors.

KEYWORDS

anxiety, cancer, depression, mental health, oncology, prostate cancer, quality of life, survivorship

1 | BACKGROUND

Prostate cancer (PCa) is the most commonly diagnosed cancer among men in Canada.[1] On average, 99% of men with localizedPCasurvive for at least five years post-diagnosis, and nearly 98% will survive for at least 10 years, more than the average for more aggressive forms of cancer, such as lung and pancreatic cancer.[2] With a growing aging Canadian population and an increase in PCa detection among asymptomatic men the incidence rates of PCa are predicted to remain high in the decades to come.[3,4] As such, the management of PCa survivorship issues is becoming increasingly critical. Although mental health is a critical component of PCa survivorship, it is largely understudied.[5,6]

Anxiety and depression are the most common psychological conditions affecting cancer patients and survivors.[5,6] Previous studies have identified that the prevalence of anxiety and depression are

higher among PCa survivors than that among survivors of other forms of cancer, but typically these studies have focused on rates of mental health during diagnosis or treatment rather than long term survivorship.[7] In a recent review, Fervaha et al. in 2019, identified that one in six men affected by PCa will experience depression, and that suicidal ideation and death by suicide were higher compared with PCa survivors without depression.[5] Anxiety and depression considerably affect survivors' overall quality of life, adherence to ongoing treatment and therapies, and have been shown to negatively influence disease progression and negatively affectthe oncological outcomes.[5,8] Several relevant contributing factors for mental health have been identified including functional (erectile, urinary and/or bowel dysfunction), psychological (anxiety, stress, depressive symptoms, learned helplessness, lack of cognitive reframing strategies), and social issues (being single, lack of social support or choosing social isolation).[9-12] These findings have also been corroborated in a recent survey of PCa survivors in Nova Scotia, New Brunswick, and Prince Edward Island, Canada.[12] In this study, we examine the association of anxiety and depression symptoms among men residing in Atlantic Canada with a history of PCa or other cancers in controlled and uncontrolled analyses.

2 | METHODS

This analysis is based on a subsample of 6 585 men (ages 49-69-years old, M = 58.94 years old) surveyed between 2009 and 2015 as part of the Atlantic Partnership for Tomorrow's Health (Atlantic PATH) study which is a component of the larger Canadian Partnership for Tomorrow Project (CPTP), a pan-Canadian longitudinal cohort study examining the role of genetic, environmental, behavioral, and lifestyle factors in the development of cancer and chronic disease.[13] Although the age range of the total sample of men was 35 to 69 (n = 9,445), we narrowed our selection to include participants within the age range (49-69-years old) of men who reported a lifetime history of PCa diagnosis. The men in this study were residents of one of the four Atlantic Canada provinces (Nova Scotia, New Brunswick, Prince Edward Island, and Newfoundland and Labrador). All procedures performed in this study were in accordance with the ethical standards of the institutional ethics committee (Dalhousie University + 2018-4462) and with the 1964 Helsinki declaration and its later amendments or comparable ethicalstandards. All participants provided written informed consent. Details on recruitment and data collection have been previously described.[14,15] In brief, participants completed a set of paper and pencil standardized surveys on sociodemographic characteristics, health history, and lifestyle factors, as well as provided physical measures and biological samples.

2.1 | Measures

2.1.1 | History of PCa diagnosis

Participants were asked to identify if they have ever been diagnosed with cancer, their age at diagnosis and type of cancer. Type of cancer included bladder, brain, breast, colon, esophagus, kidney, larynx, leukemia, liver, lung and bronchus, non-Hodgkin's lymphoma, pancreas, prostate, rectum, skin, stomach, thyroid, trachea, and other. The absence of a lifetime history of cancer was coded 0, the presence of a lifetime history of PCa diagnosis was coded 1, the presence of a lifetime history of other types of cancer was coded 2.

Anxiety. Participants were asked to complete the generalized anxiety disorder scale (GAD-7), a self-reported seven-item scale that is used to calculate an anxiety score based on symptoms experienced over a 2-week period.[16,17] GAD-7 is a well-established measure that has proven to be highly reliable. The GAD-7 is based on the Primary Care Evaluation of Mental Disorders (PRIME-MD) diagnostic instrument and uses a four-point Likert Scale ranging from zero (“not at all”), one (“several days”), two (“more than half the days”), to three (“nearly every day”). Scores on GAD-7 range between 0 to 21, with scores under 5 indicating good mental health, 5-9 indicating mild anxiety symptoms, 10-14 indicating moderate anxiety symptoms, 15-21 indicating severe anxiety symptoms.[17] To insure adequate cases, scores on GAD-7 were binary coded to depict the absence or presence of anxiety symptoms (scores below 5 were coded 0, and those ≥5, representing mild, moderate or severe symptoms were coded 1). The dichotomization of the presence or absence of mental health symptoms of mild or greater severity is common in the literature.[16,18]

2.1.2 | Depression

The Patient Health Questionnaire (PHQ-9) is a self-reported nine-item scale and was used to calculate a depression severity score based on symptoms over a two-week period.[19] The PHQ-9 is based on the Primary Care Evaluation of Mental Disorders (PRIME-MD) diagnostic instrument and utilizes nine DSM-IV criteria that were measured using a four-point Likert Scale ranging from zero (“not at all”), one (“several days”), two (“more than half the days”), to three (“nearly every day”).[19-21] Scores on PHQ-9 range between 0 to 27, with scores under 5 indicating good mental health, 5-9 indicating mild depression symptoms, 10-14 indicating moderate depression symptoms, 15-19 indicating moderately severe depression symptoms, and 20 to 27 indicating severe depression symptoms. To ensure adequate cases, scores on PHQ-9 were binary coded to depict the absence or presence of anxiety symptoms (scores below 5 were coded 0, and those ≥5 were coded 1).

2.1.3 | Covariates

Six covariates were also modeled, including age (coded 1 for 39-49, 2 for 50-69 years old) and relationship status, coded as 1 for married or living with a partner, or 2 for divorced, widowed, separated, or single, never married. Current province of residence was coded as 1 for Nova Scotia, 2 for New Brunswick, 3 for Prince Edward Island, 4 for Newfoundland and Labrador). Education level was coded as 1 for high-school or less, 2 for community college, trade or non-university certificate, 3 for undergraduate degree, and 4 for graduate degree. Household income was coded as 1 for under $50 000, 2 for

TABLE 1 Binary logistic regression analyses predicting anxiety or depression symptoms by history of prostate cancer diagnosis and covariates among adult men residing in Atlantic Canada, aged 49+, between 2009and 2015, for original data (n = 4379 anxiety symptoms, n = 4417 depression symptoms) and multiple imputation pooled data (n_{MI}=6585 for both depression, and anxiety symptoms)

	No anxiety vs mild, moderate or severe anxiety symptoms		No depression vs mild, moderate or severe depressive symptoms	
	n = 4379[a] OR (95% CI)	n = 6585[b] OR (95% CI)	n = 4417[a] OR_{MI} (95% CI)	n = 6585[b] OR_{MI} (95% CI)
	$X^2(16)$ = 43.80***		$X^2(16)$ = 57.64***	
History of prostate cancer diagnosis	$X^2(2)$ = 4.63*		$X^2(2)$ = 6.89*	
Yes	2.45 (1.07,5.62)*	1.81 (0.81,4.05)	2.05 (1.04,4.02)*	2.44 (1.35,4.41)**
Other cancer	1.03 (0.47,2.28)	90 (0.54,1.49)	0.67 (0.35,1.28)	1.00 (0.65,1.52)
No	1.0 Reference	1.0 Reference	1.0 Reference	1.0 Reference
Age	$X^2(1)$ = 19.04***		$X^2(1)$ = 16.36***	
49-59-years old	2.48 (1.65,3.72)***	1.67 (1.35,2.75)***	1.88 (1.38,2.54)***	1.54 (1.29,1.84)***
60-69-years old	1.0 Reference	1.0 Reference	1.0 Reference	1.0 Reference
Household income	$X^2(4)$ = 12.62*		$X^2(4)$ = 21.78*	
<$50 000	3.42 (1.66,7.05)**	1.79 (1.16,2.75)**	2.55 (1.48,4.40)**	1.78 (1.26,2.52)**
$50 000-74 999	1.95 (0.95,4.01)	1.30 (0.84,1.99)	2.14 (1.28,3.60)**	1.51 (1.07,2.12)*
$75 000-99 999	1.83 (0.93,3.63)	1.45 (0.98,2.14)	1.46 (0.88,2.43)	1.23 (0.88,1.72)
$100 000-149 99	1.67 (0.87,3.21)	1.24 (0.85,1.81)	1.02 (0.61,1.68)	1.12 (0.81,1.56)
$150 000 or more	1.0 Reference	1.0 Reference	1.0 Reference	1.0 Reference
Education	$X^2(3)$=1.62		$X^2(3)$=3.16	
High-school or less	1.12 (0.60,2.10)	1.38 (.95,2.02)	0.95 (0.58,1.55)	1.35 (1.00,1.82)
Community college	0.85 (0.48,1.50)	1.42 (1.00,2.02)	0.86 (0.56,1.33)	1.32 (1.00,1.82)
Undergraduate degree	0.91 (0.49,1.66)	1.24 (0.86,1.80)	0.68 (0.42,1.11)	1.06 (0.79,1.43)
Graduate degree	1.0 Reference	1.0 Reference	1.0 Reference	1.0 Reference
Province	$X^2(3)$=0.98		$X^2(3)$=0.23	
Nova Scotia	0.95 (0.59,1.52)	1.02 (0.74,1.42)	1.05 (0.72,1.53)	1.05 (0.79,1.38)
New Brunswick	0.94 (0.60,1.47)	0.89 (0.60,1.32)	0.98 (0.68,1.40)	0.91 (0.65,1.27)
Prince Edward Island	0.84 (0.31,2.27)	0.77 (0.34,1.76)	0.96 (0.44,2.07)	0.94 (0.45,1.95)
Newfoundland and Labrador	1.0 Reference	1.0 Reference	1.0 Reference	1.0 Reference
Ethnicity	$X^2(1)$=.63		$X^2(1)$=.08	
Other	0.73 (0.34,1.57)	1.09 (0.69,1.74)	1.08 (0.64,1.83)	1.38 (0.97,1.96)
Caucasian	1.0 Reference	1.0 Reference	1.0 Reference	1.0 Reference
Current marital status	$X^2(1)$=3.65		$X^2(1)$=4.26*	
Divorced, or single	1.64 (0.99,2.74)	1.39 (1.03,1.87)	1.55 (1.02,2.35)*	1.42 (1.12,1.81)*
Married or with partner	1.0 Reference	1.0 Reference	1.0 Reference	1.0 Reference
Survivorship	$X^2(1)$=.34		$X^2(1)$=1.33	
Number of months since diagnosis; 0 to 69 months.	0.99 (0.95,1.03)	1.00 (0.99,1.01)	1.01 (0.99,1.04)	1.00 (0.99,1.01)

***P < .001; **P < .01; *P < .05, two-tailed test

[a]Original data

[b]Multiple imputations pooled data based on 73 imputations

$50 000-74 999, 3 for $75 000-99 999, 4 for $100,000-149 999, and 5 for $150 000 or more. Ethnicity was coded as 1 for Caucasian/White and 2 for non-white in order to account for a lack of ethnic diversity in the cohort, which is reflective of the larger Atlantic Canadian population (eg, 87% of participants in Atlantic PATH identified as Caucasian/White, while 95% of the Atlantic Canadian population is Caucasian/White.[15] To ensure that our findings were not influenced by any changes in sample attributes across months of survivorship, we also created a variable for and held fixed survivorship time (months elapsed between first cancer diagnosis and survey completion).

2.2 | Statistical analyses

All analyses were performed SPSS V25. Logistic regression analyses were used to examine the relationship between the presence or absence of PCa or other types of cancer and anxiety or depression symptoms, in controlled (age, relationship status, education, province of residence, household income, ethnicity and survivorship time) and uncontrolled analyses. Cross-tab analyses were used to first assess the association between current anxiety or depression status (binary) and the presence or absence of lifetime history of PCa or other forms of cancer or no cancer.

The range of missing data rates across the variables of interest were 33.5% (n = 2206 missing) for anxiety, 32.9% (n = 2168 missing) for depression, 37.7% (n = 2483 missing) for the presence or absence of history of cancer (prostate or other), 6.5% (n = 425) for household income, 4.5% (n = 296) for ethnicity, 0.4% (n = 29) for education, 0.4% (n = 25) for province, and 0.4% (n = 27) for marital status. Little's MCAR X^2 (234) =2479.91, $P < .001$ indicated that data for variables missing more than 5%, was not missing at random. Although a visual examination of the missing data did not reveal any systematic patterns multiple imputation (MI) was used to supplement the analyses and add confidence to the results obtained. MI was performed using SPSS V.25, using aniterative Markov Chain Monte Carlo (MCMC) algorithm known as fully conditional specification (FCS) or chained equations imputation. The number of imputations, 73, was randomly generated to represent a value within the range of 33 to 100, as recommended by the literature.[22,23]

2.3 | Sensitivity analyses

SPSS V.25 allows for sensitivity analyses (in this case, cross tabs and logistic regression) to be conducted using the original data set and the generated pooled dataset (based on the 73 imputed data sets) in one output. These sensitivity analyses were conducted in order to determine if our results depend on how the missing data was handled.[22] Results were pooled in a summary measure following MI with an analytic sample of 6585 for each of our two outcomes (depression and anxiety) and were compared with the listwise exclusion original dataset which had analytic samples of 4417 and 4379 responses for each of our two outcomes (depression and anxiety), respectively. It should also be noted that due to MI adjustments, decimal sample sizes and degrees of freedom are normal and may occur (due to imputation aggregates) for some statistical tests.[22,23]

3 | RESULTS

An estimated 3.9% of men in the original sample (n = 158) or 3.5% in the MI pooled sample (n_{MI} = 231.2) reported having had a history of PCa diagnosis, 11.3% (n = 462) or 11.68% (n_{MI} = 769.4) reported having had a history of other forms of cancer and 84.9% (n = 3482) or 84.81% (n_{MI} = 5584.4) reported never having had a diagnosis of cancer in their lifetime, respectively. An estimated 9.2% (n = 403) and 14.7% (n = 651) men in our Atlantic Canada sample screened positive for the presence of mild, moderate or severe anxiety or depression, or 10% (n = 660.9) and 15.2% (n = 1000.2) based on the original and pooled multiple imputations data, respectively.

Logistic regression analyses (based on original and MI pooled data sets) evaluating the relationship between main predictor (history of lifetime PCa, or other forms of cancer diagnosis), candidate covariates with mental health outcomes are presented in the online Supplementary materials section. Table 1 shows the results of logistic regression analyses for each of the outcomes, regressing the presence of a lifetime history of PCa or other types of cancer while adjusting for covariates. Analyses revealed that men with a lifetime history of PCa had 2.45 (OR_{MI} = 1.81) or 2.05 (OR_{MI} = 2.44) statistically significant higher odds for screening positive for current mild, moderate or severe anxiety or depression status, respectively, compared with those with no lifetime history of cancer. Men with a lifetime history of other types of cancer had comparable depression and anxiety levels compared with those with no lifetime history of cancer. Younger men (49-59 years old) had 2.48 (OR_{MI} = 1.67) or 1.88 (OR_{MI} = 1.54) statistically significant higher odds of screening positive for current anxiety or depression, respectively, compared with older men (60-69 years old). Men with a household income lower than $50,000 a year had 3.42 ($OR_{MI}$ = 1.79) or 2.55 (OR_{MI} = 1.78) statistically significant higher odds for screening positive for anxiety or depression, respectively. Men who identified with a current household income between $50,000 and $74,999 a year had double the odds, OR = 2.14 (OR_{MI} = 1.51) of depression compared with the highest income group. Lastly, men who identified being divorced, widowed, separated, or single/never married had statistically higher odds, OR = 1.55 (OR_{MI} = 1.42) for screening positive for depressive symptoms. Education, province, ethnicity and survivorship time since diagnosis did not statistically significantly contribute to differentiating between the levels of the outcomes.

4 | DISCUSSION

Depression or anxiety symptoms were present among 9.2% or 14.7% of men in this voluntary sample of Atlantic Canadian men, respectively. These numbers are comparable with national population prevalence estimates for lifetime symptoms compatible with generalized anxiety disorder (GAD) and depression (8.7% and 11.3%, respectively) reported for Canadians ages 15 or older.[24-27]

Almost 4% of the men in this sample had a lifetime history of PCa, compared with 11% of the men who identified having had a lifetime history of other types of cancer (other than PCa). To our knowledge, these estimates are the most recent reports on the prevalence of lifetime history of these conditions in a Canadian population-based sample. These percentages are 2.7% and 7.72% higher than prevalence estimates of lifetime history of these conditions from a 2005 Canadian Community Health Survey report.[28] The increase from 2005 to the time period between 2009 and2015 we report here, is expected and could represent the result of an increase in the population of older adults during these time periods, alone or in conjunction with increased lifetime survivorship among cancer patients due to better

detection and improvements in curative treatments. When controlling for possible confounds (including number of months elapsed since diagnosis), for men who had a lifetime history of PCa (but not those with any other form of cancer other than prostate) odds were double or more than double for screening positive for current mild, moderate or severe depression or anxiety symptoms, respectively, compared with those with no lifetime history of cancer. To our knowledge, this is the first study comparing mental health outcomes among PCa survivors, male survivors of other forms of cancer, and those who never had a cancer diagnosis.

There are a number of factors that may influence mental health outcomes among men with PCa, including physical symptoms (eg, urinary incontinence), uncertainties associated with the cancer diagnosis, side-effects related to treatment (eg, hormone therapy), changes in quality of life as a result of treatment (eg, erectile dysfunction); changes in self-esteem and perceptions of masculinity, and anxiety during the post-treatment follow-up period, particularly for those individuals with repeated testing for recurrence.[5,11] Here we note that cancer survivorship, measured by number of months that elapsed since diagnosis, did not statistically significantly differentiate between poor anxiety or depression outcomes, while having or not a history of PCa was an important delineator between the levels of these variables. Although a comprehensive recent published review of the literature documented an increased risk of depression in PCa survivors, our novel findings begin to shed light on the particular vulnerability of this population, compared with other forms of cancer, for these conditions.[5] In light of the growing emphasis placed on cancer survivorship, evidence presented here, further supports the critical need for intervention early on and during PCa survivorship.[5,11,29-31]

Previous reports have also noted that PCa survivors are at an increased risk of suicide ideation and attempt, and this increased risk is present even more than a decade after the diagnosis.[5,32,33] Future studies should attempt to examine the relationship between suicidal symptoms and long-term mental health in this group, to ensure that mental health issues in patients with prostate cancer are not underdiagnosed and undertreated.

4.1 | Study limitations

While important, the results of the current study are not without limitations. First, the sample in the current study was voluntary and the findings may not be generalizable to PCa survivors from different demographic backgrounds. Outcome assessment was restricted to participants' self-report and therefore may be subject to bias. The primary outcomes differentiated between the presence or absence of mild, moderate, or severe depression and anxiety. Using a higher cut-off point than mild anxiety or depression may have greater clinical utility, therefore,this analysis may not have distinguished between symptoms that are severe enough to warrant treatment. Subsequent studies should investigate further the clinical relevance of these various cutoff points. In addition, although the study used well-validated self-report measures, clinical interviews may provide more detailed measures of depression and anxiety. Furthermore, analyses were not controlled for other factors such as multimorbidity, suicide ideation and attempt, and substance use, known in the literature to be important predictors of mental health issues in the general population, especially among older adults.[5,34] Future studies should attempt to control for these covariates in addition to examining any role that treatment modality may play in the relationship between lifetime history of PCa and mental health issues.[5,35,36]

The reliance on self-reported data represent a potential limitation. Given the longitudinal nature of the Atlantic PATH study (participants in the cross-sectional cohort will be followed for over a 30-year period) and future links with administrative health data, however, it will become possible in the following years to confirm participants' self-reported cancer diagnoses via administrative health data. The participants may not be entirely representative of the general population of Atlantic Canada as the majority of participants in the larger cohort are female which is common in cohort studies.[15] This may have led to an underestimation ofthe effect of mental health on PCa survivors in Atlantic Canada. Finally, our outcomes include missing data (a little over 30%). To address the issue of missing data known to be a problem that may cause bias or lead to inefficient analyses, we employed the recommended practice of MI to supplement original data analyses and increase confidence in the results we obtained.[37,38]

4.2 | Clinical implications

Despite these limitations, the findings of the current study add significantly to the current understanding of the relationship between PCa and mental health. Unlike other segments of the population, survivors of PCa are faced with several possible side effects of treatment that go to the heart of their identity as men, including erectile dysfunction, urinary incontinence, bowel issues, or feeling disconnected in their relationship due to lack of sexual function.[11,38-40] Therefore, for mental health interventions to be successful, future interventions may need to focus on identifying those survivorship needs that lead to mental health issues and address them through patient education and/or empowerment programs offered early in the survivorship journey in order to successfully control and prevent the development of mental health issues.[41] Clinicians know assessing survivors' direct oncological outcomes (eg, urinary, bowel and sexual function) is critical to addressing physical health, but may not be aware that mental health issues and survivorship needs are also critical for identifying men at risk of poor oncological and quality of life outcomes.[5]

Based on results we present here and recent reviews on depression and anxiety among PCa survivors, we consider that screening and treating anxiety and depression during PCa survivorship is a key priority for PCa clinical oncology teams in order to insure oncological outcomes are not negatively affected by the onset of mental health issues among survivors of PCa and their persistence during the cancer journey.[5,29] This research points out the vulnerability of PCa survivors compared with that of survivors of other forms of cancer. The findings of this research, coupled with a growing emphasis on cancer survivorship, highlight the importance of a multidisciplinary effort to prioritize and deliver comprehensive mental health support to both patients and survivors of PCa.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

DATA AVAILABILITY STATEMENT

The data and biological samples collected as part of the Atlantic PATH study are available to the academic research community through a formal application process.

ORCID

Gabriela Ilie https://orcid.org/0000-0002-1602-6374

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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